CRISPR-Cas9 integrates exogeneous sorting new recombinant DNA in the model tree *Populus trichocarpa*

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Running title: XRCC4 deficient enhances HDR efficiency

Abstract

One of the major challenges facing researchers is using an efficient homology-directed DNA repair (HDR) to replace the targeted fragment on the genome of tree species with the desired DNA fragment. In the past, researches have been conducted on genetic modifications in mammals, animals, and plants using HDR effector proteins, CtIP and MRE11, to guide double-stranded breaks (DSBs) more precisely. Whereas previously the genome editing using HDR in poplar trees appeared impossible or very complex, here we exhibited that the deficiency of XRCC4, a cofactor for DNA ligase IV that is a key role in nonhomologous end-joining (NHEJ), caused to enhance the HDR efficiency up to 10%, and dramatically decremented polymorphisms. We also could introduce exogenous bleomycin to the poplar genome and generate stable lines resistant to the zeocin antibiotic.

Keywords: CRISPR, XRCC4, CtIP, MRE11, HDR, *Populus trichocarpa*

Introduction

Precise, targeted genetic modification in trees has been challenging because of the efficient NHEJ factors and also the difficulty of delivery of template DNA for HDR into the cell nucleus. HDR has always been used to precisely repair DSBs, while NHEJs do the random and irregular repair in the DSB area. NHEJ has shown a predominant pathway and occurs among the cell cycle widely (Panier and Boulton, 2014), and HDR rarely occurs (Puchta, 2005) because of the low efficiency of transferring DNA or RNA fragments into the cell nucleus resulting in difficulties to accurately target and modify plant genomes. Up to date, many studies have been carried out to improve the genetic modification of crops by HDR. For instance, one study has been carried out to increase *ARGOS8* expression by replacing the GOS2 promoter via HDR to drive *ARGOS8* expression (Shi et al., 2017). Another report showed ten-fold enhancement in the efficiency of the insertion of the 35S promoter in the upstream of the *ANT1* gene in tomato (Cermak et al., 2015). Some researchers also exhibited the promotion in gene-targeting efficiency in potato (Butler et al., 2016), tomato (Dahan-Meir et al., 2018), rice (Sun et al., 2016; Wang et al., 2017), wheat (Gil-Humanes et al., 2017), cassava (Hummel et al., 2018), soybean (Li et al., 2015), and maize (Svitashev et al., 2015).

Although it has been previously reported the use of protoplasts for this purpose (Svitashev et al., 2016), the methods have been very inefficient. Due to the difficulty of moving the donor DNA template (DDT) to the required location within the cell nucleus, researches of the use of particle bombardment and virus-based replicons have been reported to increase this translocation, but the target relocation or replacement is still ongoing (Gil-Humanes et al., 2017; Wang et al., 2017). Therefore, this is one of the major problems in the genetic modification of trees. Previous data indicate that to increase HDR efficiency, it is necessary to increase the number of cells containing DDTs at S/G2 cell division phases (Yang et al., 2016). *Agrobacterium* has been widely used to transduce genes into plant cell nuclei (Movahedi et al., 2015). This method was improved to increase transformation efficiency (Movahedi et al., 2014), but there was no report of improving the Agrobacteria method delivery to increase the efficiency of transferring DDT and consequently the recovery of DSBs as HDR. Furthermore, the positive effects of recombinant homologous factors and their effects on enhancing HDR efficiency in mammalians have been already reported (Tran et al., 2019), with at least a 2-fold increase of HDR and a 6-fold increase of HDR / NHEJ ratio. Cas9 integrates with MRE11, CtIP, and Rad51, Rad52, and promotes significant HDR

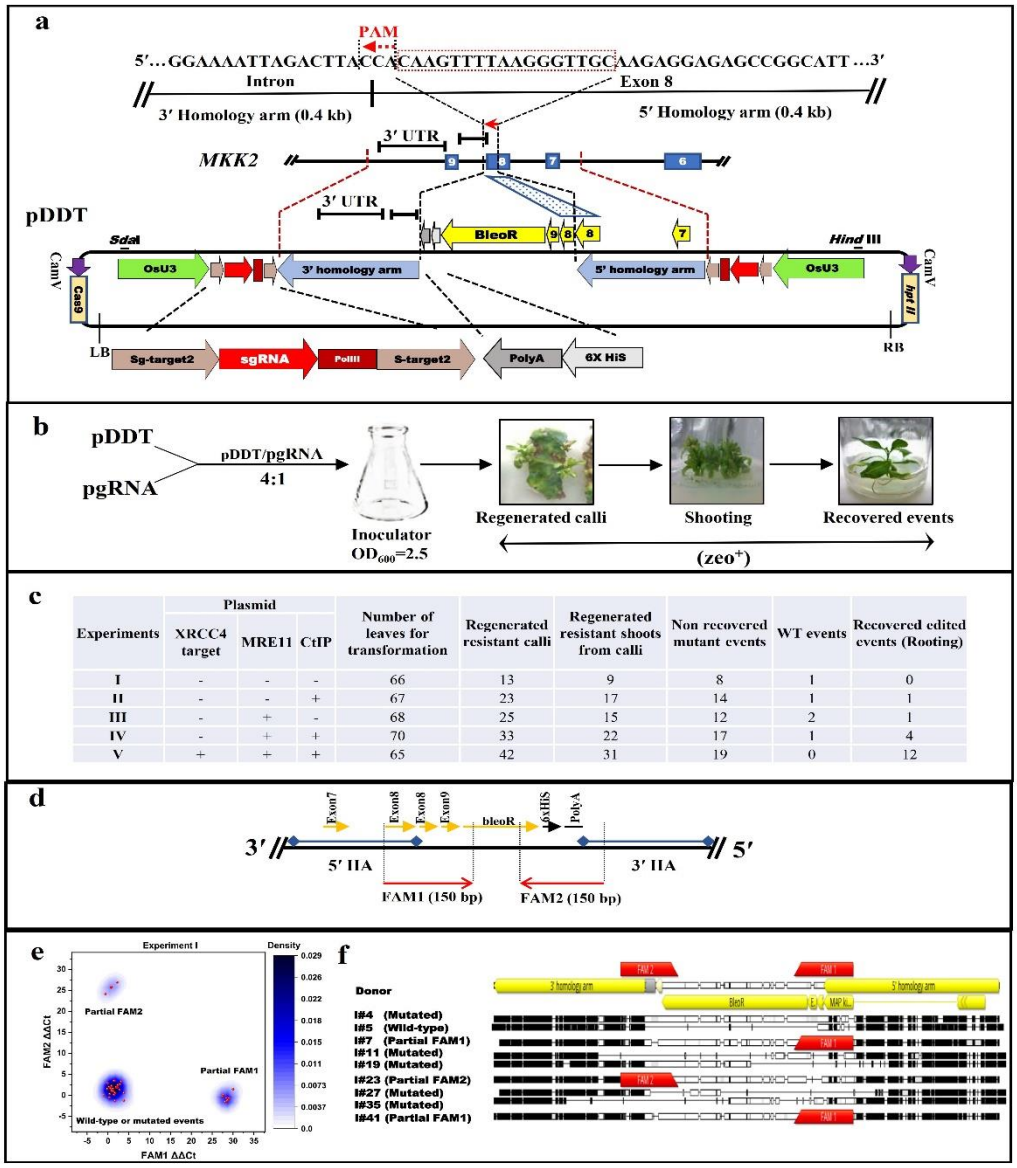
efficiency in human cells and decreases significantly NHEJ (Tran et al., 2019). On the other hand, inhibition of DNA ligase IV (LIG4), Ku 70, Ku 80, and XRCC4, which are known as the most important NHEJ factors (Friesner and Britt, 2003; Maruyama et al., 2015; Pierce et al., 2001; Tran et al., 2019), increase the HDR efficiency up to 19-fold (Tran et al., 2019). XRCC4 is one cofactor of LIG4 to interact with KU 70 and KU 80 and ligate the DSB (Grawunder et al., 1998b). Ku70 and Ku80 protect DSB from discrediting with forming one heterodimeric complex to bind tightly and load additional repair proteins such as DNA ligase IV, which is outwardly involved only in NHEJ (Grawunder et al., 1998a). On the other hand, the effect of off-targets on efficient precise genome editing and ways to reduce their effects has been already studied (Hajiahmadi et al., 2019; Li et al., 2019; Wu and Yin, 2019).

In this study, we hypothesized that inhibition of nonhomologous recombination cofactors XRCC4 promotes the HDR efficiency in poplar trees. We could overcome to make one recombinant chromosomal DNA in *P. trichocarpa* with a haploid chromosome of 19 by inhibiting activities of the NHEJ pathway (Maruyama et al., 2015) and enhancing the activities of the HDR pathway (Tran et al., 2019). Using this approach, we used the optimized length of homologous arms 400 bp (Song and Stieger, 2017).

Results and discussion

Poplars genome exhibited no exogenous integration without impacting HDR effector proteins

We started to recognize CRISPR sites located on the *MKK2* gene near the 3' UTR and scored all detected targets (Doench et al., 2014; Hsu et al., 2013) concerning higher scores denoting higher activity, specificity, and less off-target activity. We discovered one target that is located on exon 8 (Non off-target on CDS throughout the whole *Populus trichocarpa* genome) (Figure 1A and Supplementary Table 1). To investigate whether XRCC4 deficiency improves the integration efficiency of DDT at the desired locus, we first tested the insertion of DDT without targeting *XRCC4* and also fusing CtIP and MRE11. For this, we designed one plasmid for harboring the gRNA scaffold (pgRNA) and one plasmid harboring DDT (pDDT) (Figure 1A; Supplementary 1). We designed a special unique target (with no on- and -off-targets through whole poplar genome) besides DDT to cleave and release DDT and increase HDR efficiency (Zhang et al., 2017) (Figure 1A, pDDT). We used the optimized of *Agrobacterium tumefaciens* strain EHA105 stimulant and



Experiments	Plasmid			Number of leaves for transformation	Regenerated resistant calli	Regenerated resistant shoots from calli	Non recovered mutant events	WT events	Recovered edited events (Rooting)
	XRCC4 target	MRE11	CtIP						
I	-	-	-	66	13	9	8	1	0
II	-	-	+	67	23	17	14	1	1
III	-	+	-	68	25	15	12	2	1
IV	-	+	+	70	33	22	17	1	4
V	+	+	+	65	42	31	19	0	12

Figure 1. Exogenous *BleoR* integration into the poplar genome generated by Cas9. **(A)** Protospacer Adjacent Motif (PAM) was detected at the end of exon8 to lead Cas9. 400 bp sequences from both sides of the CRISPR target were selected for HDR in this study. The 5' homology arm included part sequences of the intron between exon6 and -7, exon7, intron sequences between exon7 and -8, and a part of exon8. The 3' homology arm included intron sequences between exon8 and -9 and 3' UTR of the *MKK2* locus up to 400 bp. We designed DDT included remained sequences of exon8, exon9, BleoR CDS, 6xHis, and PolyA sequences flanked by the 3'- and 5' homology arms. We added two special targets besides of DDT. The DDT then was ligated into the pRGEB31 vector to form pDDT. **(B)** pDDT and pgRNA were mixed 4:1 and introduced to the *Agrobacterium tumefaciens* to form inoculator suspension. we condensed inoculator up to OD600=2.5 and then dipped all cut off leaves. The putatively transformed calli were regenerated on zeocin. We allowed transformed calli to elongate and shoot. The properly transformed shoots were then

transferred on rooting media and allowed to be recovered events. **(C)** Designed experiments for this study involved a normal transformation of pDDT and pgRNA (I), Overloaded CtIP (II), MRE11 (III), CtIP+MRE11 (IV), and CtIP+MRE11 and XRCC4 target (V). **(D)** The design of the TaqMan real-time PCR assay for the detection of HDR sequences and evaluation included FAM1 and -2 DNA binding probes. **(E)** the 2D kernel density plot of TaqMan real-time PCR for FAM1 and FAM 2 fluorescent intensities related to the experiment I. There is no density for the edited event. Samples were analyzed in quadruplicate. **(F)** Schematic alignment of events involved in experiment I. Regarding the alignment, five events revealed no FAM signals and one event revealed sequences similar to the wild-type.

pathogenic suspension OD_{600} = 2.5 (~2×10^9 cell ml^{-1}) with the optimized ratio of 4:1 pDDT/pgRNA to increase DDT fragments during S/G2 cell division (Tran et al., 2019) and to avoid off-target editing caused by the extra accumulation of pgRNA (Hajiahmadi et al., 2019) (Figure 1B). We carried out five different sets of HDR experiments (Figure 1C) in *Populus* calli to test whether HDR happened with various HDR factors to integrate exogenous *BleoR* CDS precisely and its expression to recover poplars on zeocin, contained DDT transferring alone, DDT and CtIP fusion with Cas9, DDT and MRE11 fusion with Cas9, DDT and complex of CtIP and MRE11 fusion with Cas9, and finally DDT and complex of CtIP and MRE11 accompanied with XRCC4 deficiency. We then used TaqMan real-time PCR to detect HDR possibilities and investigate XRCC4 deficiency (Figure 1D). To detect HDR efficiency, it was necessary to have two probes FAM1 including exon8 and exon9 from *MKK2* (114bp) attached by 36 bp from 5' *BleoR* CDS and FAM2 including 57 bp from 3' homology arm, 48 bp from attached poly-A and 6xHis, and 45 bp from attached 3' *BleoR* CDS (Figure 1D). Because we didn't achieve recovered poplar on zeocin in Experiment I (ExI) (Figure 1C), it was clear that DDT couldn't integrate *BleoR* into the poplar genome. We carried out real-time PCR of nine regenerated shoots from calli (with quadruplicate), and the 2D kernel density plot exhibited more signal accumulation ~0.022 in wild-type (WT) or mutated events, and lesser ~0.0073 in partial FAM2 (Figure 1E; Supplementary 2). Then, we carried out Sanger sequencing to align events and reveal fluorescent FAM signals (Figure 1F; Supplementary 3).

BleoR exogenous integrated scantily to the poplar genome by enhancing both expressions of CtIP and MRE11

We decided to design plasmid included a fused CtIP and Cas9 (pgCtIP) instead of pgRNA with the ratio of 4:1 pDDT/pgCtIP, to test whether it is possible to promote HDR efficiency in poplars via Experiment II (ExII) (Figure 2A). We obtained more fluorescent signal accumulation

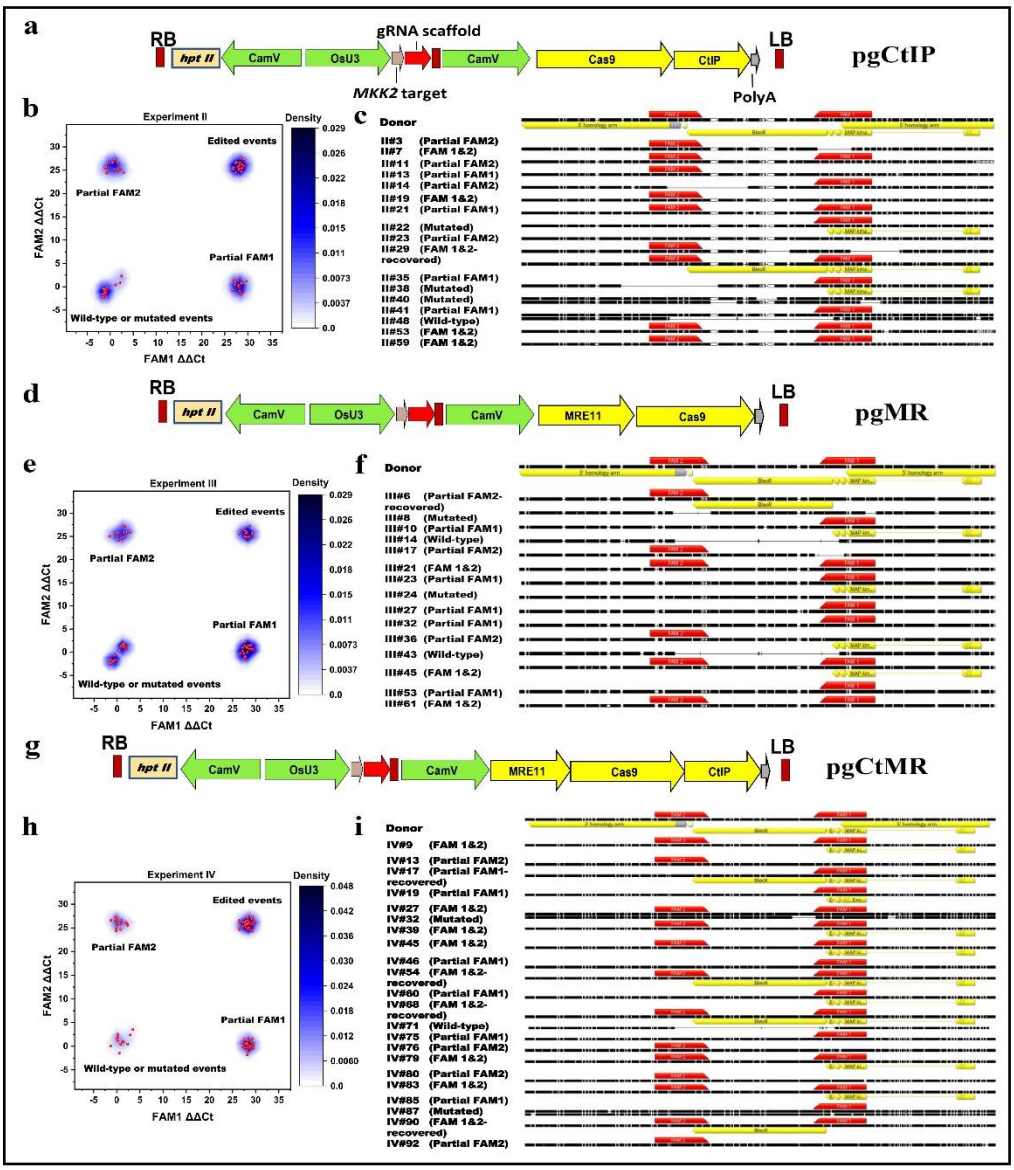


Figure 2. Comparison of improvement of the edited events with the other transformants partial and mutated through experiments II, III, and IV. (**A**) The fusion of CtIP to the C-terminal of Cas9 caused to form pgCtIP vector. (**B**) Density plot of FAM1 and -2 intensities revealed an expansion in edited events against partial, mutant, and wild-types. (**C**) Event alignments involved in experiment II. Three events expressed *MKK2* (Partial FAM1 #21, FAM1 and -2 #29, and partial FAM1 #35). (**D**) The fusion of MRE11 to the N-terminal of Cas9 caused to form pgMR vector. (**E**) The density plot of FAM1 and -2 ΔΔCt revealed an increased intensity of partial FAM1 events. (**F**) Event alignments involved in experiment III. Four events expressed *MKK2* (#10, #23, #36, and #45) and one partial FAM2 event (#6) expressed *BleoR* and caused to be recovered. Only one edited event (#45 FAM1 and -2) expressed *MKK2*. (**G**) The fusion of both MRE11 and CtIP to Cas9 began to form pgCtMR vector. (**H**) Density plot revealed a remarkable increase of edited events

signals in confronting with three earlier experiments. (**I**) event alignments involved in experiment IV. Nine events expressed *MKK2* (#9, #17, #39, #45, #54, #60, #68, #79, and #83) and four events expressed *BleoR* (Recovered) (#17, #54, #68, and #90). Three recovered events (#54, #68, and #90) exhibited both FAM1 and -2, and one recovered event exposed partial FAM1 (#17).

in FAM1&2 (Edited events) at ~0.022 and lesser in partial FAM1, and -FAM2, mutated, and WT events at ~0.018 (Figure 2B; Supplementary 2). DNA sequencing alignment of 17 regenerated shoots from calli on zeocin exhibited HDR efficiency with one recovered poplar (Appendant *BleoR* into poplar genome) (Figure 2C; Supplementary 4). Furthermore, to investigate whether MRE11 is as effective as CtIP in increase HDR efficiency in poplar, we designed plasmid harboring a combined MRE11 and Cas9 (pgMR) instead of pgRNA with the same ratio 4:1 via Experiment III (ExIII) (Figure 2D). MRE11 enhanced signal accumulation in partial FAM1 ~0.022 more than partial FAM1 and edited events ~0.015 (Figure 2E; Supplementary 2). In this experiment, we discovered three events included signals in both FAM1&2 and one recovered poplar (Figure 2C, Supplementary 5). DNA sequencing alignment of 15 regenerated shoots revealed that recovered event included *BleoR* attached by only 3' homology arm (partial FAM2) (Figure 2C, Supplementary 5). Because we couldn't achieve the desired result in overcoming NHEJ to integrate *BleoR* CDS, we decided to design Experiment IV (ExIV), and one plasmid harboring fused both MRE11 and CtIP with Cas9 (pgCtMR) (Figure 2G). This complex enhanced HDR efficiency and exhibited more edited events. The 2D kernel density plot revealed FAM1&2 signal accumulation ~0.036, partial FAM1 ~0.024, partial FAM2 ~0.018, and mutated and WT events ≤0.012 (Figure 2H; Supplementary 2). The complex of CtIP and MRE11 with Cas9 also promoted the integration of *BleoR* sequences and increased recovered events (Figure 2I; Supplementary 6).

XRCC4 deficient dramatically enhanced HDR efficiency and decreased polymorphisms

We concluded that for improving the integration of *BleoR* into the poplar genome, it might be better to target *XRCC4*. We used pgCtMR plasmid and re-designed that by adding one CRISPR site (Located on 5' region of target CDS) to mutate *XRCC4* (Non-off-target site on whole poplar genome; Activity score: 0.415; Specificity score: 100%) (Doench et al., 2014; Hsu et al., 2013) (pggCtMR) (Figure 3A) and carried out the Experiment V (ExV) (Figure 1C) with the ratio of 4:1 pDDT/pggCtMR. XRCC4 deficiency meaningfully enhanced HDR efficiency and increased edited events. The 2D kernel density plot exhibited FAM1&2 signal accumulation ~0.052, partial FAM1 ≤0.026, partial FAM2 ≤0.017, and mutated and WT events ≤0.0087 (Figure 3B;

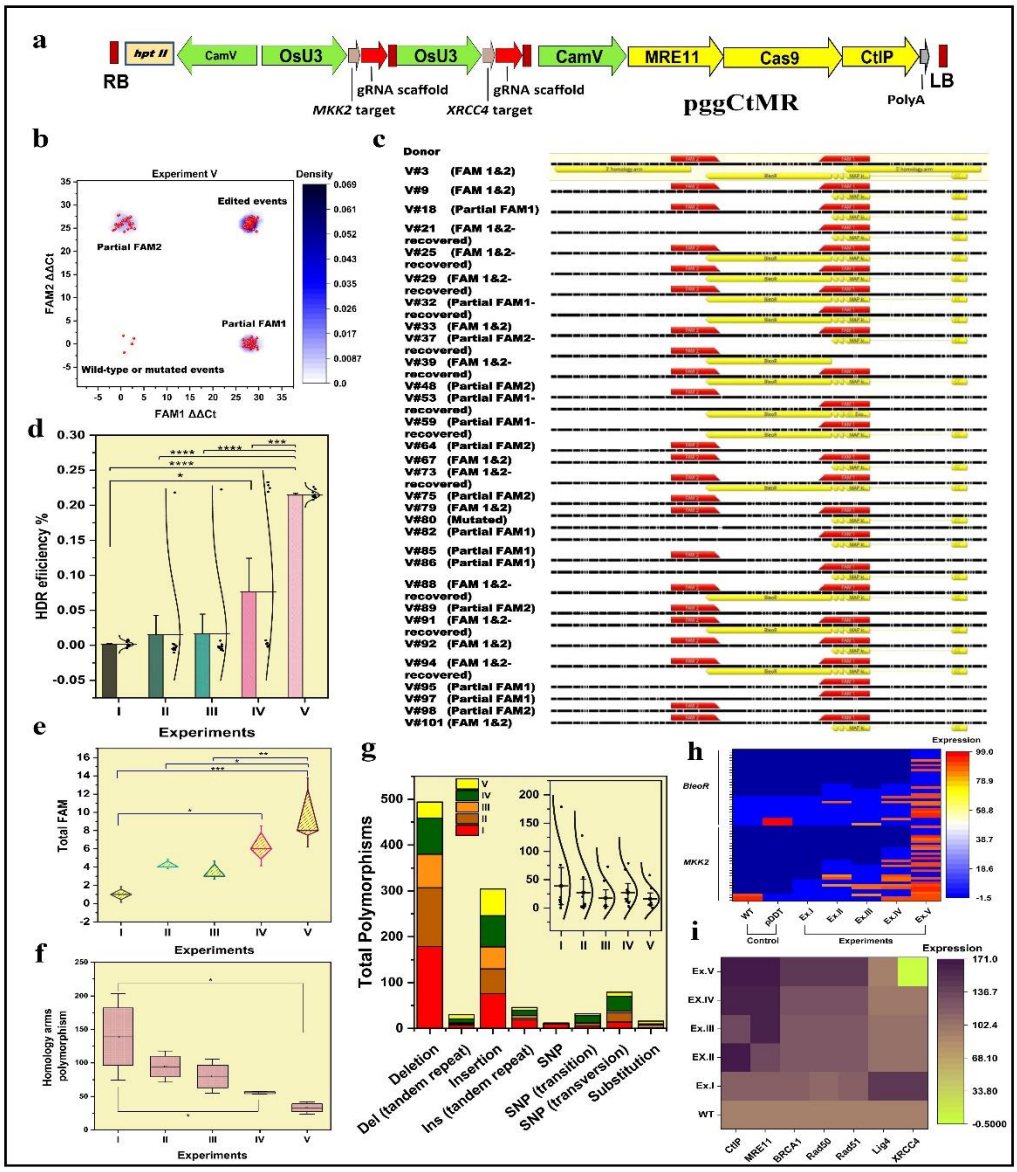


Figure 3. *XRCC4* targeting, HDR efficiency, and polymorphism evaluation. (A) XRCC4 target sequences were added to the pgCtMR to form the pggCtMR vector. **(B)** The density plot revealed a significant increase of FAM1 and -2 intensities in edited events in comparison with the earlier experiments and significant decrease intensities in WT and mutated events. **(C)** Event alignments involved in experiment V. Surprisingly, twenty events expressed *MKK2* and twelve events exhibited *BleoR* and rooted (recovered). Three of recovered events (#37, #53, and #59) showed partial HDR (partial FAM). Fifteen events revealed FAM1 and -2 signals (edited) and only one event was visualized as mutated. **(D)** Bar plot of promotion of HDR efficiency in experiments. HDR efficiency plot revealed that XRCC4 deficient (ExV) let to form HDR significantly more than the fusion of CtIP (ExII), MRE11 (ExIII), and CtIP+MRE11 (Ex.V) with the Cas9. Also, ExIV meaningfully revealed more HDR than ExII and -III. Twelve biological replicates of regenerated resistant calli were selected for this assay with three technical repeats. Bars represent the mean

of date. Curves describe the normal distribution of data. Error bars interpret standard error (SE). **(E)** The identification of total FAM signals (FAM1 and -2) visualized in the experiments showed more signs remarkably measured in ExV than ExI, II, and-III. **(F)** Identification of the polymorphisms that happened in homology arms through experiments. Box and Whisker plot revealed that most polymorphisms happened in homology arms by ExI and it was significantly more than those in ExV and -IV. Error bars represent SE. **(G)** Stacked column plot of total polymorphisms happened in DDT integration into the poplar genome. Deletion and insertion happened much more than the other types. SNP and substitution happened less than the other types. Whisker and normal distribution curves exposed that the total polymorphisms caused by *XRCC4* deficient were less than the other experiments. **(H)** Evaluation of the expression of *MKK2* and *BleoR* through the experiments. Heat map plot revealed that the highest expression of *MKK2* and *BleoR* occurred in ExV. Nine biological replicates with three technical repeats were used in this assay. WT and pDDT were used as the control for *MKK2* and *BleoR* expression respectively. **(I)** The Heat map of the interaction of proteins included in HDR and NHEJ. Overexpression *CtIP* and/or *MRE11* caused to enhance the expression of *BRCA1*, *Rad50*, and *Rad51* and to demote the expression of *Lig4* and *XRCC4*. The highest expression of the HDR factors visualized in ExV means that XRCC4 deficient caused to decrease the expression of NHEJ factor Lig4 and led to intensifying HDR efficiency. Three biological replicates with three technical repeats were used in this assay.

Supplementary 2). We then carried out sequencing of 31 regenerated seedlings and discovered 12 recovered events, and it means we could overcome NHEJ and integrate *BleoR* in the precise quarry in the poplar genome (Figure 3C; Supplementary 7). We performed real-time PCR to evaluate *BleoR* expression in all experiments (ExI to ExV) (Figure 1C) to calculate HDR efficiency (Figure 3D; Supplementary 8). We discovered that XRCC4 deficiency (ExV) promoted HDR efficiency meaningfully 10 times in comparing with the fusion of Cas9 with HDR factors CtIP (ExII), and MRE11 (ExIII) and also 2.8 times in comparing with the fusion of Cas9 and complex of CtIP and MRE11 (ExIV) (Figure 3D). Based on the promising results, we decided to analyze the total achieved FAM fluorescent signals. The results exhibited that we significantly accomplished the most partial FAM1, -FAM2, and edited events (FAM1&2) from the ExV in comparison with the other experiments (Figure 3E). To test whether the HDR efficiency depends on the happened polymorphisms we analyzed the polymorphisms of homology arms and also different types of variants, protein effects, and genotyping (Supplementary Table 2). The box and whisker plot exhibited that XRCC4 deficiency in the ExV improved HDR in homology arms and statistically decremented polymorphisms in comparison with the ExI and also more than the ExII, -III and -IV (Figure 3F). Our analysis detected eight types of polymorphisms (Supplementary table 2)

including deletions, deletion tandem repeats, insertions, insertion tandem repeats, SNPs, SNP transitions (A to C or G to T and reversely), SNP transversions (Purines to pyrimidines or reversely), and substitutions (Figure 3G). We detected the highest frequency of deletion polymorphisms in the ExI, and the least of that in the ExV (Figure 3G). The HDR factors CtIP decremented deletion tandem repeats (ExII) and MRE11 decremented SNPs, SNP transitions, and SNP transversions, and the complex of HDR factors with Cas9 (ExIV) decremented substitution polymorphisms (Figure 3G). Moreover, the box (Data overlap) and whisker plot (With normal data distribution curve) of total polymorphisms revealed that using of HDR recombination factors and also suppression of NHEJ factors decrement total polymorphisms and lead to the occurrence of HDR in poplar (Figure 3G). Moreover, we evaluated the ratio of *BleoR* and *MKK2* expressions and discovered the direct relative between increase HDR efficiency to the expression of HDR and NHEJ recombination factors (Figure 3H) and their expression. The heat-map exhibited that XRCC4 deficiency enhanced the expression on *BleoR* (HDR efficiency %) and *MKK2* in the ExV more than the overloading of HDR recombination factors (ExII, ExIII, and ExIV) (Figure 3H). We also performed real-time PCR to evaluate the interaction proteins involved in NHEJ and HDR pathways in poplar in our experiments. The heat-map plot analysis exhibited that the overloading of proteins CtIP, MRE11, and the complex of them upregulated BRCA1, Rad50, and Rad51, and downregulated Lig4, and XRCC4 (Figure 3I). In the ExI, NHEJ revealed the dominant pathway with the more average expression 145% of Lig4 and XRCC4 than the HDR pathway with the average expression 115% of CtIP, MRE11, BRCA1, Rad50, and Rad51 (Figure 3I). The role of these pathways was changed a little in ExII, ExIII, and ExV with the average expression ~124% of BRCA1, Rad50, and Rad51, and the decreased average expression 104% of Lig4 and XRCC4, leading to increase HDR and discover recovered events (Figure 3I). XRCC4 deficiency (ExV) caused to significantly change the dominant pathway to HDR and revealed the average expression 146% of BRCA1, Rad50, and Rad51 in comparison with the decreased expression 93% of Lig4 (Figure 3I) leading to enhance HDR efficiency and discover significant recovered events. In summary, we have proved that XRCC4 deficiency can apply for promoting HDR in poplar, therefore greatly expanding our capacity to improve hereditary developments in poplar. This breakthrough technology is likely to promote the biotechnological research, breeding program, and forest conservation of tree species.

Methods

Targets and protein detection

We decided to target the *MKK2* gene from *Populus trichocarpa* (POPTR_0018s05420g; Chromosome 18). We used Uniprot (https://www.uniprot.org/) to download MKK2 protein and then used the BLAST database of the National Center for Biotechnology Information (NCBI) (https://blast.ncbi.nlm.nih.gov/) to download full DNA sequences and CDS, which was then ligated into the pEASY-TA cloning vector and verified by Sanger sequencing (GenScript, Nanjing). We used Geneious Prime® 2020.1.1 to analyze locus and detect targets (Supplementary Table 1)(Doench et al., 2014; Hsu et al., 2013). The target sequences heading the PAM motif was concerned from the exon8 area of the *MKK2* and exon1 area of the *XRCC4* (POPTR_0010s08650g, Chromosome 10) genes. Furthermore, we used Uniprot to detect CtIP (POPTR_001G269700v3), MRE11 (POPTR_0001s41800g), BRCA1 (POPTR_0005s26150g), Rad50 (POPTR_0001s32760g), Rad51 (POPTR_0014s06360g), Lig4 (POPTR_0018s13870g).

Target oligo synthesis

For targeting indicated DNA sequences, we designed a pair of oligos *MKK2* Oligo-F and -R (Supplementary Table 3) flanked by *Bsa*I adaptors. Synthesized oligos were then ligated into digested pRGEB31 vectors by *Bsa*I restriction enzyme(Xie and Yang, 2013) to construct pgRNA (Supplementary 1, pgRNA). Afterward, we transferred all vectors into *E. coli* (DH5α) and propagated under the normal conditions. Vectors were then extracted using the plasmid midi kit (Qiagen, USA) and confirmed by sanger sequencing (GenScript, Nanjing).

Synthesis of DDT and pDDT

To design DDT, we divided DDT into five fragments (Supplementary 9a). To construct fragment one (Supplementary 9a) we used primers OS1-F and -R (Supplementary Table 3) to isolate OsU3 promoter and gRNA scaffold from pRGEB31 and add *Hind*III and *BamH*I endonucleases to the 5' and 3' respectively. Then we used designed special gRNA oligo1-F and -R (Sgo1-F and -R)(Supplementary Table 3) as the described details 30 to form special gRNA target1 duplex (Sgt1) and ligated to the fragment one. Then, we carried out normal PCR and purified products to clone into a pEASY T3 cloning vector (TransGen Biotech Co.), screen, and sequences. To construct fragment two (Supplementary 9), we isolated 5' homology arm (400 bp) sequences from *Populus trichocarpa* genome applying primers 5' Ho-F-1 and -R-1 (Supplementary Table 3), cloned into the pEASY vector and sequenced. Then, we applied

primers *BamH*I-special target1 (St1)-5' Ho-F-2 and 5' Ho-R-2-39 bp from complemented 5' of fragment 3 (Supplementary 9a). Then we carried out normal PCR and ligated that into the pEASY vector, screened and sequenced. We designed primers BleoR-1092F and -2276R (Supplementary 9a; Supplementary Table 3) for running PCR and isolate *BleoR* CDS from PCR®-XL-Topo® vector, purified and sequenced to confirm. Then we utilized primers BleoR-overlap1-3 (BP1-3) forward and reverse (Supplementary 9a; Supplementary Table 3) to add the remained sequences from exon8 and also exon9 to the 5' region of *BleoR* CDS and also 6XHis and PolyA tail to the 3' region (Supplementary 9a). Therefore, we designed overlap PCR primers (Supplementary 9a; Supplementary Table 3) and using isolated *BleoR* CDS as the template to form fragment three. Afterward, we isolated 3' homology arm (400 bp) using primers 3' Ho-F-1 and -R-1 (Supplementary Table 3) and carried out normal PCR to clone into the pEASY vector and sequence. Then, we applied the primers 30 bp Poly-T-3' Ho-F-2 and 3' Ho-R-2-St2-*Nco*I (Supplementary 9a; Supplementary Table 3) and constructed the fragment four. Finally, we used primers Os2-F-*Nco*I and *Sda*I-Os2-R to perform normal PCR and isolate the OsU3 promoter and gRNA scaffold (Supplementary Table 3), to purify and clone into the pEASY vector and sequence. Then we formed sgt2 using oligos sgo2-F and -R and ligated into the purified to construct fragment five, perform PCR and sequence. To construct pDDT, we ligated fragments three and two using PCR (Supplementary 9b). For this, we designed 39 bp overhang on fragment 2 that was complementary to the end of fragment three to form preliminary DDT (Supplementary 9b). In this PCR, we prepared a PCR reaction with 500 ng of each fragment. So basically, we used everything in PCR reaction except primers. We denatured fragments at 95 degrees for 5 minutes. Then we performed two cycles annealing and extension. For this, we allowed PCR products to anneal at 68 degrees to avoid nonspecific hybridization amongst the long PCR products for 30 seconds and then allowed to extend for one minute at 74 degrees to have a double-stranded product. Then we added the primers to the distal ends of the fragments two and three and performed one normal PCR. We purified PCR products and ligated into the pEASY vector to sequence and confirm. Then we ligated preliminary DDT product to fragment four as described before and formed secondary DDT products (Supplementary 9b). After sequencing and confirmation, we used the restriction cloning technique (We used digested fragments each of them 50 ng, 10x T4 DNA ligase buffer 0.5 ul, T4 DNA ligase (NEB) 1 ul and H_2O to 5 ul and then we incubated that reaction at 25 degrees for 4 hours and transferred into *E. Coli* DH5α competent cells to sequence and confirm) to ligate

secondary DDT product to the fragments one and four (Supplementary 9b) to achieve DDT products. Subsequently, we used again the restriction cloning technique to merge the DDT product and pRGEB31 vector (Supplementary 9b) and form the pDDT vector (Supplementary 9b).

Synthesis of pgCtIP, pgMR, pgCtMR, and pggCtMR

To design a fused CtIP and Cas9 cassette, we isolated the CaMV35S promoter, 3xFLAG, and Cas9 CDS from pRGEB31 (Supplementary 10a; Supplementary Table 3), and then we performed PCR and ligated them into the pEASY vector to sequence and confirm. To achieve CtIP CDS, we extracted total RNA (450 ng/ L) from young leaves of *Populus trichocarpa* applying TRIzol and carried out reverse transcription with 2 ug RNA and oligo-dT primers to synthesize the first cDNA strand (PrimeScript One-Step RT-PCR Kit Ver.2, Takara Biotechnology, Dalian, China). Then we used primers *BamH*I-CtIP-F and *StuI*-CtIP-R (Supplementary 10a; Supplementary Table 3) to isolate CtIP CDS. We used primers *Stu*I-PolyA-F and *Pme*I-PolyA-R (Supplementary Table 3) to isolated 3'UTR and PolyA fragments from the pCAG-T3-hCAS-pA plasmid and then ligated into the pEASY vector and sequenced. We ligated CaMV35S and 3xFLAG fragments using restriction cloning and formed backbone 1 (Supplementary 10a). Then we used restriction cloning to ligate Cas9 and CtIP and form the backbone 2 (Supplementary 10a). We ligated backbone 1 and -2 using *Hind*III restriction cloning to form backbone 3 (Supplementary 10a). Finally, we ligated backbone 3 and 3'UTR-PolyA fragment using *Stu*I restriction cloning to construct the CtIP cassette. We digested and then ligated CtIP cassette and pRGEB31 by *Sda*I and *Pme*I endonucleases respectively to form pgCtIP (Figure 2A; Supplementary 10a). To construct a fusion of MRE11 and Cas9, we isolated CaMV35 promoter, 3xFLAG, Cas9, 3'UTR, and PolyA like the previous steps (Supplementary 10b; Supplementary Table 3). To isolate MRE11 CDS we recruited extracted total RNA and RT-PCR again and used the primers *Not*I-MRE-F and *Nde*I-MRE-R (Supplementary 10b; Supplementary Table 3). The isolated CaMV35S and 3xFLAG fragments ligated together according to the *Xho*I endonuclease homology site to form backbone 1 (Supplementary 10b). We built backbone 2 using the isolated Cas9 and 3'UTR-PolyA fragments (Supplementary 10b; Supplementary Table 3). Then, we ligated backbone 1, backbone 2 and also isolated MRE11 CDS from RT-PCR products applying *Not*I and *Nde*I endonucleases restriction cloning to form MR cassette (Supplementary 10b) and afterward ligated the digested MR cassette and pRGEB31 by *Sda*I and *Pme*I endonuclease homology sites to construct pgMR vector (Figure 2D; Supplementary 10b). To construct the CtMR cassette, we

isolated CaMV35S and 3xFLAG fragments and ligated them using *Xho*I restriction cloning to form backbone 1 (Supplementary 11a, Supplementary Table 3). We isolated MRE11 CDS by *Not*I-MRE-F and *Nde*I-MRE-R primers and then ligated to the backbone 1 to release backbone 2 (Supplementary 11a, Supplementary Table 3). Afterward, we isolated Cas9 and RT-PCR product CtIP CDS applying primers (Supplementary Table 3) and then ligated them using *BamH*I restriction cloning to form backbone 3 (Supplementary 11a). We then used backbone 3 and isolated 3'UTR-PolyA fragment to form backbone 4 (Supplementary 11a). Finally, we used backbone 2 and -4 to form CtMR cassette and then used *Sda*I and *Pme*I to digest and then ligate CtMR and pRGEB31 to form pgCtMR vector (Supplementary 11a). We then decided to construct the *XRCC4* cassette to target *MKK2* and *XRCC4* genes. We recruited primers *Hind*III-XR-Cass1-F and *Kas*I-XR-Cass1-R (Supplementary 11b; Supplementary Table 3) to isolate the OsU3 promoter and gRNA scaffold from pRGEB31 vector and then recruited MKK2 Oligo-F and -R (Supplementary 10d; Supplementary Table 3) to form MKK2 target duplex and ligated. We isolated again the OsU3 promoter and gRNA scaffold using primers *Ksa*I-XR-Cass2-F and *Sda*I-XR-Cass2-R (Supplementary 11b; Supplementary Table 3) and also recruited XRCC4-Oligo1 and -2 to form XRCC4 target duplex and ligated. We ligated two completed fragments to form XRCC4-Cassette (Backbone 1) (Supplementary 11b). Afterward, we used backbone 1 and pRGEB31 vector to form backbone 2 (Supplementary 11b). Finally, we digested backbone 2 and constructed the CtMR vector by *Sda*I and *Pme*I and then ligated them to form the pggCtMR vector (Supplementary 11b).

TaqMan real-time PCR

To test whether the designed experiments were able to increase the exact merging of exogenous *BleoR* on both sides to the genome binding regions, we decided to use Applied Biosystem real-time PCR (Applied Biosystems, USA) and run TaqMan assay using dye labels such as FAM and VIC that attaches to the 5' region of the probe and non-fluorescent quencher (NFQ) that attaches to the 3' region of the probe. That's why we designed primers (Supplementary Table 3) to probe two 150 bp fragments FAM1 and -2 (Figure 1D; Supplementary 12) on the *MKK2* gene as the target assay and also designed primers to probe one 106 bp fragment VIC on the *actin* gene as the reference (Stable copy number) (Supplementary 12).

Evaluation of HDR efficiency

Regarding the purpose of this study to integrate the exogeneous *BleoR* CDS into the poplar genome, the ΔΔCt mean of *BleoR* was calculated in our experiments. We picked randomly twelve of the most grown events (Regenerated calli on selection media) from each experiment (Supplementary 8) to extract genomic DNA using the DNeasy Plant Mini Kit (Qiagen, USA) following the manufacturer's instructions. We used genomic DNA as the template and applied Fast Start Universal SYBR Green Master (Rox; No. 04913914001: Roche, USA) and primers BleoR-52F and BleoR-151R (Supplementary Table 3) with three technical repeats for each event.

Transformation

We cultivated *Populus trichocarpa* seedlings in a phytotron at 23±2°C under a 16/8 light/dark time(Movahedi et al., 2015). To generate transgenic lines, we removed leaves from four weeks old grown young poplars and dipped them in the optimized (Movahedi et al., 2014)of *Agrobacterium tumefaciens* stimulant and pathogenic suspension (OD_{600}: 2.5, 120 min, pH ~5, Acetosyringone (As): 200 µM) for 5 min with gentle shaking and then transferred in semi-solid woody plant medium (WPM) enriched with 0.05 mg/L Indole-3-butyric acid (IBA), 0.006 mg/L thidiazuron (TDZ), 200 µM As and 0.5% (w/v) agar. We then incubated stimulated explants in a dark area at 23°C for 2 days. Afterward, assumed transformants were co-cultivated in selection media enriched with 0.1 mg/L IBA, 0.006 mg/L TDZ, 400 mg/L cefotaxime, 8 mg/L hygromycin, 100 mg/L zeocin and 0.8% (w/v) agar. After 4 weeks, regenerated shoots were sub-cultured independently in media with 0.1 mg/L IBA, 0.001 mg/L TDZ, 400 mg/L cefotaxime, 8 mg/L hygromycin, 100 mg/L zeocin and 0.8% (w/v) agar to lengthen. After 6-8 weeks, elongated shoots were introduced in MS media with 0.1 mg/L IBA, 100 mg/L cefotaxime, 100 mg/L zeocin, and 0.8% (w/v) agar to root. Three lines were used for each experiment independently and each line included 18 individuals.

DNA sequencing and Statistical analysis

Poplar seedlings were cultivated to generate T_0 poplars. Young leaves then were cut off and introduced to the Agrobacterium for transferring DDT and regenerating T_1 calli events. Genomic DNAs were extracted from three weeks regenerated resistant shoots using the DNeasy Plant Mini Kit (Qiagen, USA). We performed PCR using Easy Taq polymerase (TransGene Biotech), 100 ng genomic DNA as a template, and primers MKK2-S-7F and MKK2-S-1139R (Supplementary Table 3) to sequence and analysis (Figure 1F, 2C, 2F, 2I, and 3C; Supplementary

3,4,5,6, and 7). All data were analyzed using ANOVA One-Way with Turkey means comparison calculated by OriginPro 2018 and Excel 2019 software (Microsoft, Redmond, WA, USA). Differences were analyzed statistically meaningful when the confidence intervals presented no overlap of the mean values with an error value of 0.05.

Supplementary information

Supplemental Information is available for this paper.

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Author contribution

A.M. conceived the project. A.M and H.W. performed the experiments. Z.H.C., W.S., J.Z., D.L., H.R., and Q.Z. reviewed the manuscript and confirmed it. A.M. and H.W. wrote the manuscript. Q.Z. supervised this project.

Conflict of interest

The authors declare that they have no conflict of interest.

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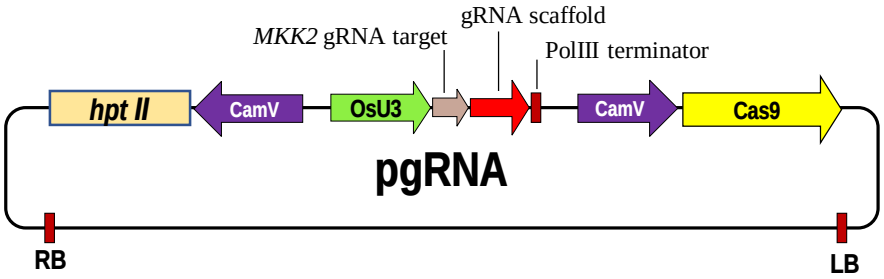
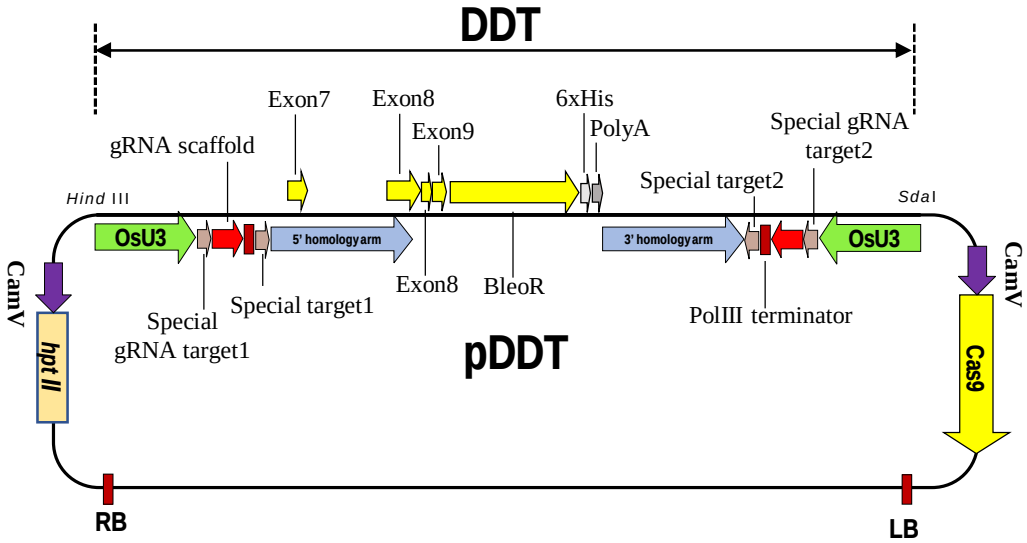
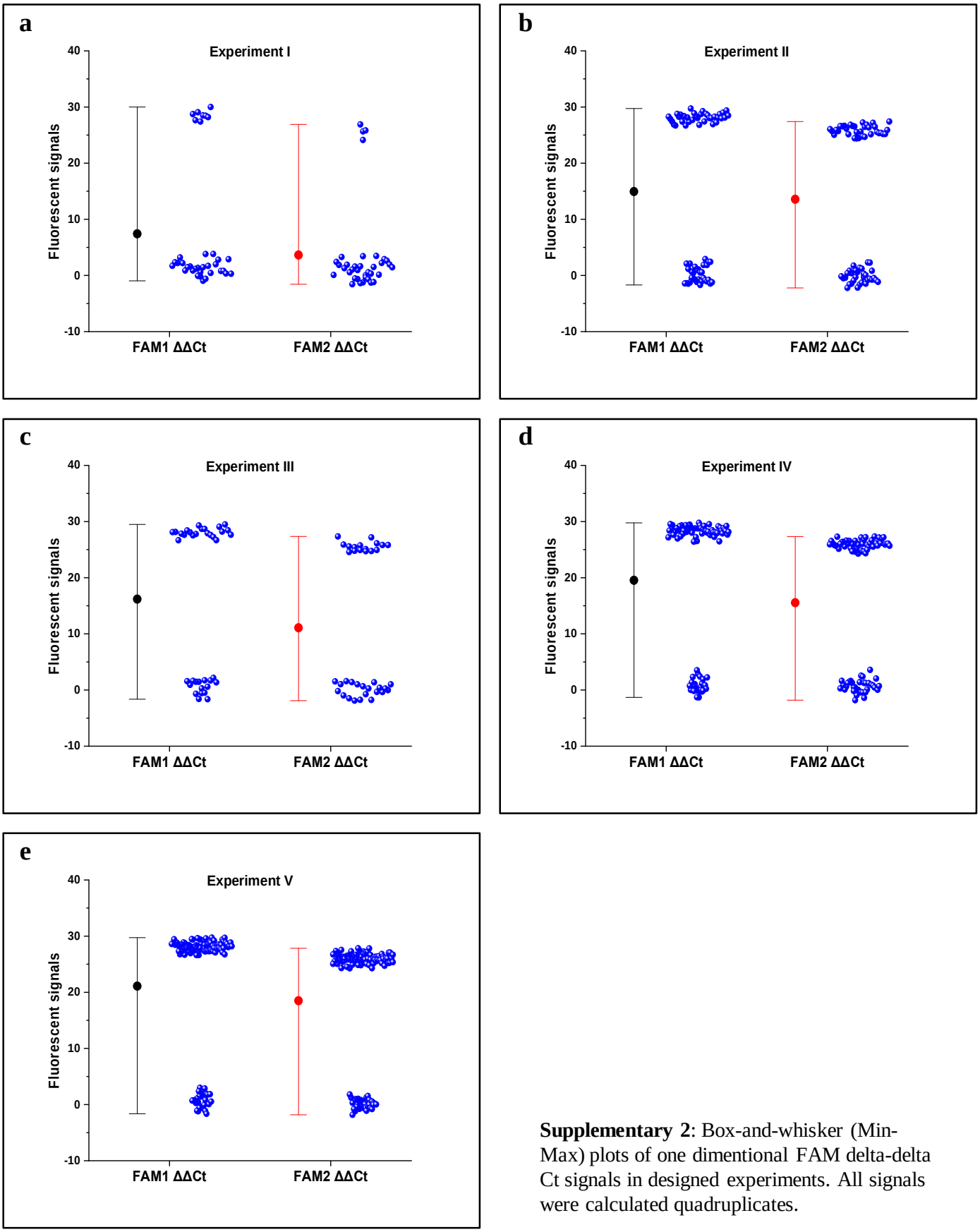
a



b



Supplementary 1: Schematic of pgRNA, DDT and pDDT **a**, pgRNA included the *MKK2* target seed and Cas9. **b**, pDDT included DDT ligated into pRGEB31 by restriction enzyme cloning method.



Supplementary 2: Box-and-whisker (Min-Max) plots of one dimentional FAM delta-delta Ct signals in designed experiments. All signals were calculated quadruplicates.

Supplementary 3: Allignment of events involved in experiment I.

```
Donor (Control)          TTTTGTGAATTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAAT-TTCAGCAAGTTGATTTATTTCAAGCCACAAT-GACAGTT
                                                   3' homology arm

I#5 (Wild-type)          TCACTTTTTGTGAATTGCTAATGGTTTGAAAACCTCAG---TGGTCACTGTAAT-TTCAGCAAGTTGATTTATTTCAAGCCACAAT-GACAGTT
I#4 (Mutated)                TTTTGTGAATTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAAT-TTCAGCAAGTTGATTTATTTCAAGCCACAAT-GACAGTT
I#7 (Partial FAM1)                                GGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTTCAGCAAGTTGATTTATTTCAAGCCACAAT-GACAGTT
I#11 (Mutated)               TTTTGTGAATTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAAT-TTCAGCAAGTTGATTTATTTCAAGCCACAAT-GACAGTT
I#19 (Mutated)               TTTTGTGAATTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAAT-TTCAGCAAGTTGATTTATTTCAAGCCACAAT-GACAGTT
I#23 (Partial FAM2)          TTTTGTGAATTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAAT-TTCAGCAAGTTGATTTATTTCAAGCCACAATAGACAGTT
I#27 (Mutated)                                    GGTTTGAAAACCTCAGCCCTGGTCACTGTAAT-TTCAGCAAGTTGATTTATTTCAAGCCACAAT-GACAGTT
I#35 (Mutated)               TTTTGTGAATTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAAT-TTCAGCAAGTTGATTTATTTCAAGCCACAAT-GACAGTT
I#41 (Partial FAM1)          TTTTGTGA-TTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAAT-TTCAGCAAGTTGATTTATTTCAAGCCACAAT-GACAGTT

Donor (Control)          AAGAATCTTTCTTCAGGCCTTCAAAATTTCAATAGATAACTTCCCATAACTCTCAAGAGTCTGATATAGTATCTG-----------CACTTGTC
                         3' homology arm

I#5 (Wild-type)          AAGAATCTTTCTTCAGGCCTTCAAAATTTCAATAGATAACTTCCCATAACTCTCAAGAGTCTGATATAGTATCTGC----------ACTTGTC
I#4 (Mutated)            AAGAATCTTTCTTCAGGCCTTCAAAATTTCAATAGATAACTTCCCATAACTCTCAAGAGTCTGATATAGTATCTGC----------ACTTGTC
I#7 (Partial FAM1)       AAGAATCTTTCTTCAGGCCTTCAAAATTTCAATAGATAACTTCCCATAACTCTCAAGAGTCTGATATAGTATCTGC----------ACTTGTC
I#11 (Mutated)           AAGAATCTTTCTTCAGGCCTTCAAAATTTCAATAGATAACTTCCCATAACTCTCAAGAGTCTGATATAGTATCTGC---------A--CTTGTC
I#19 (Mutated)           AAGAATCTTTCTTCAGGCCTTCAAAATTTCAATAGATAACTTCCCATAACTCTCAAGAGTCTGATATAGTATCTGC----------ACTTGTC
I#23 (Partial FAM2)      AAGAATCTTTCTTCAGGCCTTCAAAATTTCAATAGATAACTTCCCATAACTCTCAAGAGTCTGATATAGTATCTGC----------ACTTGTC
I#27 (Mutated)           AAGAATCTTTCTTCAGGCCTTCAAAATTTCAATAGATAACTTCCCATAACTCTCAAGAGTCTGATATAGTATCTGC----------ACTTGTC
I#35 (Mutated)           AAGAATCTTTCTTCAGGCCTTCAAAATTTCAATAGATAACTTCCCATAACTCTCAAGAGTCTGATATAGTATCTGC----------ACTTGTC
I#41 (Partial FAM1)      AAGAATCTTTCTTCAGGCCTTCAAAATTTCAATAGATAACTTCCCATAACTCTCAAGAGTCTGATATAGTATCTGCAAGAACACAACACTTGTC

Donor (Control)          -AAACACAATGGCT-TAAATTCAACTCTAAAGTACATGAATTCTCATAAGAGTTATGGTCGACATGGTAAATGCATTA-ATTGCATAGACACAG
                         3' homology arm

I#5 (Wild-type)          -AAACACAATGGCT-TAAATTCAACTCTAAAGTACAGTAATTCTCATAAGAGTGATGGTCGACATGGTAAATGCATTA-ATTGGATAGACACAG
I#4 (Mutated)            -AAACACAATGGCT-TAAATTCAACTCTAAAGTACATGAATTCTCATAAGAGTTATGGTCGACATGGTAAATGCATTA-ATTGCATAGACACAG
I#7 (Partial FAM1)       -AAACACAATGGCT-TAAATTCAACTCTAAAGTACATGAATTCTCATAAGAGTTATGGTCGACATGGTAAATGCATTA-ATTGCATAGACACAG
I#11 (Mutated)           -AAACACAATGGCTGTAAATTCAACTCTAAAGTACATGAATTCTCATAAGAGTTATGGTCGACATGGTAAATGCATTA-ATTGCATAGACACAG
I#19 (Mutated)           AAAACACAATGGCT-----------------TACATGAATTCTCATAAGAGTTATGGTCGACATGGTAAATGCATTA-ATTGCATAGACACAG
I#23 (Partial FAM2)      -AAACACAATGGCT-TAAATTCAACTCTAAAGTACATGAATTCTCATAAGAGTTATGGTCGACATGGTAAATGCATTAAATTGCATAGACACAG
I#27 (Mutated)           -AAACACAATGGCT-TAAATTCAACTCTAAAGTACATGAATTCTCATAAGAGTTATGGTCGACATGGTAAATGCATTA-ATTGCATAGACACAG
I#35 (Mutated)           -AAACACAATGGCT-TAAATTC-------------------------------------------------------- -------------CAG
I#41 (Partial FAM1)      -AAACACAATGGCT-TAAATTCAACTCTAAAGTACATGAATTCTCATAAGAGTTATGGTCGACATGGTAAATGCATTA-ATTGCATAGACACAG

                                                                                                   FAM 2
Donor (Control)          GCGAACTATTAAATGATT-AATAAGACTTGGATTATGCAACTACATCTTCACAAGAACTCCATACAAAAAAAGAAATAATAAGAAAAAACATTT
                         3' homology arm

I#5 (Wild-type)          GCGAACTATCAAATGATT-AATAAGACTTGGATTATGCAACTACATCTTCACAAGAACTCCATACAAAAAAAGAAATAATAAGAAAAAACATTT
I#4 (Mutated)            GCGAACTATTAAATGATT-AATAAGACTTGGATTATGCAACTACATCTTCACAAGAACTCCATACAAAAAAAGAAATAATAAGAAAAAACA-TT
I#7 (Partial FAM1)       GCGAACTATTAAATGATT-AATAAGACTTGGATTATGCAACTACATCTTCACAAGAACTCCATACAAAAAAAGAAATAATAAGAAAAAACATTT
I#11 (Mutated)           GCGAACTATTAAATGATT-----------------------------------------------------------------G-----------
I#19 (Mutated)           GCGAACTATTAAATGATT-AATAAGACTTGGATTATGCAACTACATCTTCACAAGAACTCCATACAAAAAAAGAAATAATAAGA-AAAACATTT
I#23 (Partial FAM2)      -CGAACTATTAAATGATT----------------AAGCAACTACATCTTCACAAGAACTCCATACAAAAAAAGAAATAATAAGAAAAAACATTT
I#27 (Mutated)           GCGAACTATTAAATGATTAAATAAGACTTGGATTATGCAACTACATCTTCACAAGAACTCCATACAAAAAAAGAAATAATAAGAAAAAACATTT
I#35 (Mutated)           GC---------------- -------------------------------------------------------------------C----
I#41 (Partial FAM1)      GCGAACTATTAAATGATT-AATAAGACTTGGATTATGCAACTACATCTTCACAAGAACTCCATACAAAAAAAGAAATAATAAGAAAAAACATTT

                                                FAM 2
Donor (Control)          GAC---------CAA--ATGATTTCAAGAAATGATGTGAATGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGA
                                   3' homology arm                          poly(A)                    6..

I#5 (Wild-type)          GA-----------AACTATGATTTCAAGAAATGATGTGAATGGGAAAATTAGACTTA-----------------------------------
I#4 (Mutated)            GAC  C------AA  ATGATTTCAAGAAATGATGTGAATGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGA
I#7 (Partial FAM1)       GACCCCCCTTATCAA  ATGATTTCAAGAAATGATGTGAATGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTT-------------------
I#11 (Mutated)           ---------------  ----------------------------------------------------------------------------
I#19 (Mutated)           GAC----------CAA  ATGATTTCAAGAAATGATGTGAATGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGA
I#23 (Partial FAM2)      GAC   C------AA  ATGATTTCAAGAAATGATGTGAATGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGA
I#27 (Mutated)           GACCAAAACGCGAAA  ATGATTTCAAGAAATGATGTGAATGGGAAAATTAGACTTATTTTTTTTTTTTTTT-----------------------
I#35 (Mutated)           ---------------  ----------------------------------------------------------------------------
I#41 (Partial FAM1)      GACC---------AA  ATGATTTCAAGAAATGATGTGAATGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTT---T------------

                                                FAM 2
Donor (Control)          TGATGATGATGTCAGTCCTGCTCCTCGGCCACGAAGTGCACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGC
                         6xHis ...
                                                   BleoR

I#5 (Wild-type)          ----------------------------------------------------------------------------------C----------
I#4 (Mutated)            TGATGATGATGTCAGTCCTGCTCCTCGGCCACGAAGTGCACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGC
I#7 (Partial FAM1)       -GATGATGATGTCAGTCCTGCTCCTCGGCCACGAAGTGCACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGC
I#11 (Mutated)           ----------------------------------------------------------------------------TCC---------------
I#19 (Mutated)           TGATGATGATGTCAGTCCTGCTCCTCGGCCACGAAGTGCACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGC
I#23 (Partial FAM2)      TGATGATGATGTCAGTCCTGCTCCTCGGCCACGAAGTGCACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGC
I#27 (Mutated)           ------------------------------------------------------------------CTC-----------------GC
I#35 (Mutated)           ------------------------------------------------------------------------GC----------------
I#41 (Partial FAM1)      -GATGATGATGTCAGTCCTGCTCCTCGGCCACGAAGTGCACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGC
```

Donor (Control)
BleoR
I#5 (Wild-type)
I#4 (Mutated)
I#7 (Partial FAM1)
I#11 (Mutated)
I#19 (Mutated)
I#23 (Partial FAM2)
I#27 (Mutated)
I#35 (Mutated)
I#41 (Partial FAM1)
FAM 1
Exon9; MAP kinase kinase fa...
Exon8
5' homology arm
MAP kinase kinase family protein CDS

```
Donor (Control)      GCAAAAGAAGGGTGGGATATTAGC-AGTCTGCTGA--------------GTATTAATGAC---ATTCCAT----A--------------TTGAT
                     <<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<
                     5' homology arm

I#5 (Wild-type)      GCAAAAGAAGGGTGGGATATTAGC-AGTCTGCTG-A-------------GTATTAATGA-C--ATTCCAT----A--------------TTGAT
I#4 (Mutated)        GCAAAAGAAGGGTGGGATATTAGC-AGTCTGCTG-A-------------GTATTAATGA-C--ATTCCAT----A--------------TTGAT
I#7 (Partial FAM1)   GCAAAAGAAGGGTGGGATATTAGCGAGTCTGCTG--------------AGTATTAATGA-C-ATTCCAT----A--A-----------TTGAT
I#11 (Mutated)       GCAAAAGAAGGGTGGGATATTAGC-AGTCTGCTG-A-------------GTATTAATGATCAAATACCATCAGCCATTCC-----ATATTGAT
I#19 (Mutated)       GCAAAAGAAGGGTGGGATATTAGC-AGTCTGCTG-A-------------GTATTAATGA--CATTCCAT----A--------------TTGAT
I#23 (Partial FAM2)  GCAAAAGAAGGGTGGGATATTAGC-AGTCTGCTG-A-------------GTATTAATGA--CATTCCATGATGATGTCAGTCCTGCTATTGAT
I#27 (Mutated)       GCAAAAGAAGGGTGGGATATTAGC-AGTCTGCTGCAGGGCGAACTCCGAGTATTAATGA--CATTCCAT----A--A-----------TTGAT
I#35 (Mutated)       GCAAAAGAAGGGTGGGATATTAGC-AGTCTGCTG---------A-----GTATTAATGA--CATTCCAT----A--A-----------TTGAT
I#41 (Partial FAM1)  GCAAAAGAAGGGTGGGATATTAGC-AGTCTGCTG---------A-----GTATTAATGA--CATTCCAT----A--A-----------TTGAT

Donor (Control)      AGAGAGGAGAAAAGAGTAAAGGACG-TGGA-GTGCCAGTAACAGGCAGACAGCTAATTGCCCCACCCAGTTTAACAATCATAGGACTTCAAATA
                     <<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<
                     5' homology arm

I#5 (Wild-type)      AGAGAGGAGAAAAGAGTAAAGGACG-TGGA-GTGCCAGTAACAGGCAGCCAGCTAATTGCCCCACCCTGTTTAACAATCATAGGATTTCAAATA
I#4 (Mutated)        AGAGAGGAGAAAAGAGTAAAGGACG-TGGAGGTGCCAGT----------------ATTGCCCCACCCAGTTTAACAATCATAGGACTTCAAATA
I#7 (Partial FAM1)   AGAGAGGAGAAAAGAGTAAAGGACG-TGGA-GTGCCAGTAACAGGCAGACAGCTAATTGCCCCACCCAGTTTAACAATCATA-GACTTCAAATA
I#11 (Mutated)       AGAGAGGAGAAAAGAGTAAAGGACG-TGGA-GTGCCAGTAACAGGCAGACAGCTAATTGCCCCACCCAGTTTAACAATCATAGGACTTCAAATA
I#19 (Mutated)       AGAGAGGAGAAAAGAGTAAAGGACGGTGGA-GTGCCAGTAACAGGCAGACAGCTAATTGCCCCACCCAGTTTAACAATCATAGGACTTCAAATA
I#23 (Partial FAM2)  AGAGAGGAGAAAAGAGTAAAGGACG-TGGA-GTGCCAGTAACAGGCAGACAGCTAATTGCCCCACCCAGTTTAACAATCATAGGACTTCAAATA
I#27 (Mutated)       AGAGAGGAGAAAAGAGTAA-GGACG-TGGA-GTGCCAGTAACAGGCAGACAGCTAATTGCCCCACCCAGTTTAACAATCATAGGACTTCAAATA
I#35 (Mutated)       AGAGAGGAGAAAAGAGTAAAGGACG-TGGA-GTGCCAGTAACAGGCAGACAGCTAATTGCCCCACCCAGTTTAACAATCATAGGACTTCAAATA
I#41 (Partial FAM1)  AGAGAGGAGAAAAGAGTAAAGGACG-TGGA-GTGCCAGTAACAGGCAGACAGCTAATTGCCCCACCCAGTTTAACAATCATAGGACTTCAAATA

Donor (Control)      CCA-TCAGTTCATGTGCTGCCTGTCTA---------------T-CCTTTGG-------------A--TCTTTCTGCAC-ACTGGAAGAAGACAG
                     <<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<
                     5' homology arm
                     <<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<
                     MAP kinase kinase family protein CDS

I#5 (Wild-type)      CCA-TCAGTTCATGTGCTGCCTGTCTA---------------T-CCTTTGG-------------A--TCTTTCTGC--------AAGAAGACAG
I#4 (Mutated)        CCA-TCAGTTCATGTGCTGCCTGTCTA---------------TCCTTTGG-------------A-TCTTTCTGCAC-ACTGGAAGAAGACAG
I#7 (Partial FAM1)   CCA-TCAGTTCATGTGCTGCCTGTCTAAAACCTCAGCCCTGGTTCCTTTGGAGTTCGAGTATGCAGATCTTTCTGCAC-ACTGGAAGAAGACAG
I#11 (Mutated)       CCA-TCAGTTCATGTGCTGCCTGTCTA---------T-------CCTTTGG-------A-------TCTTTCTGCAC-ACTGGAAGAAGACAG
I#19 (Mutated)       CCA-TCAGTTCATGTGCTGCCTGTCTA---------T-------CCTTTGG-------A-------TCTTTCTGCAC-ACTGGAAGAAGACAG
I#23 (Partial FAM2)  CCA-TCAGTTCATGTGCTGCCTGTCTA----------T------CCTTTGG--------A------TCTTTCTGCAC-ACTGGAAGAAGACAG
I#27 (Mutated)       CCACTCAGTTCATGTGCTGCCTGTCTA----------T------CCTTTGGA-------T------CTTTCTGCAC-ACTGGAAGAAGACAG
I#35 (Mutated)       CCA-TCAGTTCATGTGCTGCCTGTCTA---------T-------CCTTTGGA-------T------CTTTCTGCACTACTGGAAGAAGACAG
I#41 (Partial FAM1)  CCA-TCAGTTCATG---TGCCTGTCTA---------T-------CCTTTGGA-------T------CTTTCTGCAC-ACTGGAAGAAGACAG

Donor (Control)      AACCACAGAATGAAAATCA-GTAAC
                     <<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<<
                     5' homology arm

I#5 (Wild-type)      AACCACAGAATGAAAATCA-GTAACTTCACAAAATCA
I#4 (Mutated)        AACCACAGAATGAAAATCA-GTAAC
I#7 (Partial FAM1)   AACCACAGAATGAAAATCA-GTAAC
I#11 (Mutated)       AACCACAGAATGAAAATCA-GTAACTTCACAAAATCATCTGGCC
I#19 (Mutated)       AACCACAGAATGAAAATCA-GTAACTTCACAAAATCATCTGGCC
I#23 (Partial FAM2)  AACCACAGAATGAAAATCA-GTAAC
I#27 (Mutated)       AACCACAGAATGAAAATCA-GTAACTTCACAAAATCATCTGGCC
I#35 (Mutated)       AACCACAGAATGAAAATCA-GTAACTTCACAAAATCATCTGGCC
I#41 (Partial FAM1)  AACCACAGAATGAAAATCAAGTAAC
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Supplementary 4: Allignment of events involved in experiment II.

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Donor (Control)                 TTTTGTGAATTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAGCCACAATGACA
                                                                  3' homology arm

II#3 (Partial FAM2)             TTTTGTGAATTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAGCCACAATGACA
II#7 (FAM1&2)                   TTTTGTGAATTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAGCCACAATGACA
II#11 (Partial FAM2)            TTTTGTGAATTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAGCCACAATGACA
II#13 (Partial FAM1)            TTTTGTGAATTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAGCCACAATGACA
II#14 (Partial FAM2)            TTTTGTGAATTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAGCCACAATGACA
II#19 (FAM1&2)                  TTTTGTGAATTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAGCCACAATGACA
II#21 (Partial FAM1)            TTTTGTGAATTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAGCCACAATGACA
II#22 (Mutated)                 TTTTGTGAATTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAGCCACAATGACA
II#23 (Partial FAM2)            TTTTGTGAATTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAGCCACAATGACA
II#29 (FAM1&2-Recovered)        TTTTGTGAATTGCT-ATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAGCCACAATGACA
II#35 (Partial FAM1)            TTTTGTGAATTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAGCCACAATGACA
II#38 (Mutated)                 TTTTGTGAATTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTT-----AGTTGATTTATTTCAAGCCACAATGACA
II#40 (Mutated)                 TTTTGTGAATTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAGCCACAATGACA
II#41 (Partial FAM1)            TTTTGTGAATTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAGCCACAATGACA
II#48 (Wild-type)               TTTTGTGAATTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAGCCACAATGACA
II#53 (FAM1&2)                  TTTTGTGAATTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAGCCACAATGACA
II#59 (FAM1&2)                  TTTTGTGAATTGCTAATGGTTTGAAAACCCCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAGCCACAATGACA

Donor (Control)                 GTTAAGAATCTTTCTTCAGGCCTT---CAAAATTTC-AATAGAT-AACTTCCCATAACTCTCAAGAGTCTGATATAGTAT---C
                                                                  3' homology arm

II#3 (Partial FAM2)             GTT-AGAATCTTTCTTCAGGCCTT---CAAAATTTC-AATAGAT-AACTTCCCATAACTCTCAAGAGTCTGATATAGTAT---C
II#7 (FAM1&2)                   GTTAAGAATCTTTCTTCAGGCCTT---CAAAATTTC-AATAGATCAACTTCCCATAACTCTCAAGAGTCTGATATAGTAT---C
II#11 (Partial FAM2)            GTTAAGAATCTTTCTTCAGGCCTT---CAAAATTTC-AATAGAT-AACTTCCCATAACTCTCAAGAGTCTGATATAGTAT---C
II#13 (Partial FAM1)            GTTAAGAATCTTTCTTCAGGCCTT---CAAAATTTC-AATAGAT-AACTTCCCATAACTCTCAAGAGTCTGATATAGTAT---C
II#14 (Partial FAM2)            GTTAAGAATCTTTCTTCAGGCCTTTTACAAAATTTC-AATAGAT-AACTTCCCATAACTCTCAAGAGTCTGATATAGTAT---C
II#19 (FAM1&2)                  GTTAAGAATCTTTCTTCAGGCCTT---CAAAATTTC-AATAGAT-AACTTCCCATAACTCTCAAGAGTCTGATATAGTAT---C
II#21 (Partial FAM1)            GTTAAGAATCTTTCTTCAGGCCTT---CAAAATTTC-AATAGAT-AACTTCCCATAACTCTCAAGAGTCTGATATAGTAT---C
II#22 (Mutated)                 GTTAAGAATCTTTCTTCAGGCCTT---CAAAATTTC-AATAGAT-AACTTCCCATAACTCTCAAGAGTCTGATATAGTAT---C
II#23 (Partial FAM2)            GTTAAGAATCTTTCTTCAGGCCTT---CAAAATTTC-AATAGAT-AACTTCCCATAACTCTCAAGAGTCTGATATAGTAT---C
II#29 (FAM1&2-Recovered)        GTTAAGAATCTTTCTTCAGGCCTT---CAAAATTTC-AATAGAT-AACTTCCCATAACTCTCAAGAGTCTGATATAGTAT---C
II#35 (Partial FAM1)            GTTAAGAATCTTTCTTCAGGCCTT---CAAAATTTC-AATAGAT-AACTTCCCATAACTCTCAAGAGTCTGATATAGTAT---C
II#38 (Mutated)                 GTTAAGAATCTTTCTTCAGGCCTT---CAAAATTTC-AATAGAT-AACTTCCCATAACTCTCAAGAGTCTGATATAGTATTAAC
II#40 (Mutated)                 GTTAAGAATCTTTCTTCAGGCCTT---CAAAATTTC-AATAGAT-AACTTCCCATAACTCTCAAGAGTCTGATATAGTAT---C
II#41 (Partial FAM1)            GTTAAGAATCTTTCTTCAGGCCTT---CAAAATTTC-AATAGAT-AACTTCCCATAACTCTCAAGAGTCTGATATAGTAT---C
II#48 (Wild-type)               GTTAAGAATCTTTCTTCAGGCCTT---CAAAATTTC-AATAGAT-AACTTCCCATAACTCTCAAGAGTCTGATATAGTAT---C
II#53 (FAM1&2)                  GTTAAGAATCTTTCTTCAGGCCTT---CAAAATTTCTAATAGAT-AACTTCCCATAACTCTCAAGAGTCTGATATAGTAT---C
II#59 (FAM1&2)                  GTTAAGAATCTTTCTTCAGGCCTT---CAAAATTTC-AATAGAT-AACTTCCCATAACTCTCAAGAGTCTGATATAGTAT---C

Donor (Control)                 TGCACTTGTCAAACA-CAAT-GGCTT-AAATTCAACTCTAAAGTA--------C-ATGAATTCTCATAAGAGTTATGGTCGACA
                                                                  3' homology arm

II#3 (Partial FAM2)             TG---TTGTCAAACA-CAAT-GGCTT-AAATTCAACTCTAAAGTA--------C-ATGAATTCTCAAAAAGAGTTATGGTCGACA
II#7 (FAM1&2)                   TGCACTTGTCAAACA-CAAT-GGCTT-AAATTCAACTCTAAAGTA--------C-ATGAATTCTCATAAGA-TTATGGTCGACA
II#11 (Partial FAM2)            TGCACTTGTCAAACA-CAAT-GGCTT-AAATTCAACTCTAAAGTA--------C-ATGAATTCTCATAAGAGTTATGGTCGACA
II#13 (Partial FAM1)            TGCACTTGTCAAACA-CAAT-GGCTT-AAATTCAACTCTAAAGTA--------C-ATGAATTCTCATAAGAGTTATGGTCGACA
II#14 (Partial FAM2)            TGCACTTGTCAAACA-CAAT-GGCTT--AATTCAACTCTAAAGTA--------C-ATGAATTCTCATAAGAGTTATGGTCGACA
II#19 (FAM1&2)                  TGCACTTGTCAAACA-CAAT-GGCTT-AAATTCAACTCTAAAGTA--------C-ATGAATTCTCATAAGAGTTATGGTCGACA
II#21 (Partial FAM1)            TGCACTTGTCAAACA-CAAT-GGCTT-AAATTCAACTCTAAAGTA--------C-ATGAATTCTCATAAGAGTTATGGTCGACA
II#22 (Mutated)                 TGCACTTGTCAAACA-CAAT-GGCTT-AAATTCAACTCTAAAGTA--------C-ATGAATTCTCATAAGAGTTATGGTCGACA
II#23 (Partial FAM2)            TGCACTTGTCAAACA-CAAT-GGCTT-AAATTCAACTCTAAAGTA--------C-ATGAATTCTCATAAGAGTTATGGTCGACA
II#29 (FAM1&2-Recovered)        TGCACTTGTCAAACA-CAATCGGCTT-AAATTCAACTCTAAAGTAATTAATCCC-ATGAATTCTCATAAGAGTTATGGTCGACA
II#35 (Partial FAM1)            TGCACTTGTCAAACA-CAAT-GGCTTAAAATTCAACTCTAAAGTA--------C-ATGAATTCTCATAAGAGTTATGGTCGACA
II#38 (Mutated)                 TGCACTTGTCAAACA-CAAT-GGCTT-AAATTCAACTCTAAAGTA--------C-ATGAATTCTCATAAGAGTTATGGTCGACA
II#40 (Mutated)                 TGCACTTGTCAAACA-CAAT-GGCTT-AAATTCAACTCTAAAGTA--------C-ATGAATTCTCATAAGAGTTATGGTCGACA
II#41 (Partial FAM1)            TGCACTTGTCAAACA-CAAT-GGCTT-AAATTCAACTCTAAAGTA--------C-ATGAATTCTCATAAGAGTTATGGTCGACA
II#48 (Wild-type)               TGCACTTGTCAAACACCAAT-GGCTT-AAATTCAACTCTAAAGTA--------C-ATGAATTCTCATAAGAGTTATCGTCGACA
II#53 (FAM1&2)                  TGCACTTGTCAAACA-CAAT-GGCTT-AAATTCAACTCTAAAGTA--------C-ATGAATTCTCATAAGAGTTATGGTCGACA
II#59 (FAM1&2)                  TGCACTTGTCAAACA-CAAT-GGCTT-AAATTCAACTCTAAAGTACCCCATAGCGATGAATTCTCATAAGAGTTATGGTCGACA

Donor (Control)                 TGGTAAATGCATTAATTGCATAGACACAGGCGAACTAT----TAAATGATTAATAAGACTTGGATTA-TGCAACTACATCTTCA
                                                                  3' homology arm

II#3 (Partial FAM2)             TGGTAAATGCATTAATTGCATAGACACAGGCGAACTAT----TAAATGATTAATAAGACTTGGATTA-TGCAACTACATCTTCA
II#7 (FAM1&2)                   TGGTAAATGCATTAATTGCATAGACACAGGCGAACTAT----TAAATGATTAATAAGACTTGGATTA-TGCAACTACATCTTCA
II#11 (Partial FAM2)            TGGTAAATGCATTAATTGCATAGACACAGGCGAACTAT----TAAATGATTAATAAGACTTGGATTA-TGCAACTACATCTTCA
II#13 (Partial FAM1)            TGGTAAATGCATTAATTGCATAGACACAGGCGAACTAT----TAAATGATTAATAAGACTTGGATT--------TACATCTTCA
II#14 (Partial FAM2)            TGGTAAATGCATTAATTGCATAGACACAGGCGAACTAT----TAAATGATTAATAAGACTTGGATTA-TGCAACTACATCTTCA
II#19 (FAM1&2)                  TGGTAAATG-ATTAATTGCATAGACACAGGCGAACTAT----TAAATGATTAATAAGACTTGGATTA-TGCAACTACATCTTCA
II#21 (Partial FAM1)            TGGTAAATGCATTAATTGCATAGACACAGGCGAACTAT----TAAATGATTAATAAGACTTGGATTA-TGCAACTACATCTTCA
II#22 (Mutated)                 TGGTAAATGCATTAATTGCATAGACACAGGCGAACTAT----TAAATGATTAATAAGACTTGGATTA-TGCAACTACATCTTCA
II#23 (Partial FAM2)            TGGTAAATGCATTAATTGCATAGACACAGGCGAACTAT----TAAATGATTAATAAGACTTGGATTA-TGCAACTACATCTTCA
II#29 (FAM1&2-Recovered)        TGGTAAATGCATTAATTGCATAGACACAGGCGAACTAT----TAAATGATTAATAAGACTTGGATTATTGCAACTACATCTTCA
II#35 (Partial FAM1)            TGGTAAATGCATTAATTGCATAGACACAGGCGAACTAT----TAAATGATTAATAAGACTTGGATTA-TGCAACTACATCTTCA
II#38 (Mutated)                 TGGTAAATGCATTAATTGCATAGACACAGGCGAACTAT----TAAATGATTAATAAGACTTGGATTA-TGCAACTACATCTTCA
II#40 (Mutated)                 TGGTAAATGCATTAATTGCATAGAC-CAGGCGAACTAT----TAAATGATTAATAAGACTTGGATTA-TGCAACTACATCTTCA
II#41 (Partial FAM1)            TGGTAAATGCATTAATTGCATAGACACAGGCGAACTAT----TAAATGATTAATAAGACTTGGATTA-TGCAACTACATCTTCA
II#48 (Wild-type)               TGGTAAATGCATTAATTGCATAGACACAGGCGAACTATCCGCTAAATGATTAATAAGACTTGGATTA-TGCAACTACATCTTCA
II#53 (FAM1&2)                  TGGTAAATGCATTAATTGCATAGACACAGGCGAACTAT----TAAATGATTAATAAGACTTGGATTA-TGCAACTACATCTTCA
II#59 (FAM1&2)                  TGGTAAATGCATTAATTGCATAGACACAGGCGAACTAT----TAAATGATTAATAAGACTTGGATTA-TGCAACTACATCTTCA
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                                                                                                FAM 2
Donor (Control)                CAAG-AACTCCATACAAAAAAAGAAATAATAAGAAAAA-ACATTTGACCAAATGATTTCAAGAAATGATGTGAATGGGAAAATT
                               3' homology arm

II#3 (Partial FAM2)            CAAG-AACTCCATACAAAAAAAGAAATAATAAGAAAAA-ACATTTGACCAAATGATTTCAAGAAATGATGTGAATGGGAAAATT
II#7 (FAM1&2)                  CAAG-AACTCCATACAAAAAAAGAAATAATAAGAAAAA-ACATTTGACCAAATGATTTCAAGAAATGATGTGAATGGGAAAATT
II#11 (Partial FAM2)           CAAG-AACTCCATACAAAAAAAGAAATAATAAGAAAAA-ACATTTGACCAAATGATTTCAAGAAATGATGTGAATGGGAAAATT
II#13 (Partial FAM1)           CAAG-AACTCCATACAAAAAAAGAAATAATAAGAAAAA-ACATTTGACCAAATGATTTCAAGAAATGATGTGAATGGGAAAATT
II#14 (Partial FAM2)           CAAG-AACTCCATACAAAAAAAGAAATAATAAGAAAAA-ACATTTGACCAAATGATTTCAAGAAATGATGTGAATGGGAAAATT
II#19 (FAM1&2)                 CAAGAAACTCCATACAAAAAAAGAAATAATAAGAAAAA-ACATTTGACCAAATGATTTCAAGAAATGATGTGAATGGGAAAATT
II#21 (Partial FAM1)           CAAG-AACTCCATACAAAAAAAGAAATAATAAGAAAAA-ACATTTTACCAAATGATTTCAAGAAATGATGTGAATGGGAAAATT
II#22 (Mutated)                CAAG-AACTCCATACAAAAAAAGAAATAATAAGAACAA-AACTTTGACCAAATGATTTCAAGAAATGATGTGAATGGGAAAATT
II#23 (Partial FAM2)           CAAG-AACTCCATACAAAAAAAGAAATAATAAGAAAAA-ACATTTGACCAAATGATTTCAAGAAATGATGTGAATGGGAAAATT
II#29 (FAM1&2-Recovered)       CAAG-AACTCCATACAAAAAAAGAAATAATAAGAAAAA-ACATTTGACCAAATGATTTCAAGAAATGATGTGAATGGGAAAATT
II#35 (Partial FAM1)           CAA-AACTCCATACAAAAAAAGAAATAATAAGAAAAA--------ACAAATGATTTCAAGAAATGATGTGAATGGGAAAATT
II#38 (Mutated)                CAAG-AACTCCATACAAAAAAAGAAATAATAAGAAAAACACATTTGACCAAATGATTTCAAGAAATGATGTGAATGGGAAAATT
II#40 (Mutated)                CAAG-AACTCCATACAAAAAAAGAAATAATAAGAAAAA-ACATTTGACCAAATGATTTCAAGAAATGATGTGAATGGGAAAATT
II#41 (Partial FAM1)           CAAG-AACTCCATACAAAAAAAGAAATAATAAGAAAAA--CATTTGACCAAATGATTTCAAGAAATGATGTGAATGGGAAAATT
II#48 (Wild-type)              CAAG-AACTCCATACAAAAAAAGAAATAATAAGAAAAA-ACATTTGACCAAATGATTTCAAGAAATGATGTGAATGGGAAAATT
II#53 (FAM1&2)                 CAAG-AACTCCATACAAAAAAAGAAATAATAAGAAAAA-ACATTTGACCAAATGATTTCAAGAAATGATGTGAATGGGAAAATT
II#59 (FAM1&2)                 CAAG-AACTCCATACAAAAAAAGAAATAATAAGAAAAA-ACATTTGACCAAATGATTTCAAGAAATGATGTGAATGGGAAAATT

                               FAM 2
Donor (Control)                A-GACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCT-GCTCCTCGGCCACGAAGTG
                               3' ...  poly(A)  6xHis tag
                                                                                   BleoR

II#3 (Partial FAM2)            A-GACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCT-GCTCCTCGGCCACGAAGTG
II#7 (FAM1&2)                  A-GACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCT-GCTCCTCGGCCACGAAGTG
II#11 (Partial FAM2)           A-GACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCT-GCTCCTCGGCCACGAAGTG
II#13 (Partial FAM1)           A-G-------------------------------------------------------------------------------
II#14 (Partial FAM2)           A-GACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCT-GCTCCTCGGCCACGAAGTG
II#19 (FAM1&2)                 A-GACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCT-GCTCCTCGGCCACGAAGTG
II#21 (Partial FAM1)           A-GACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCT-GCTCCTCGGCCACGAAGTG
II#22 (Mutated)                A-GACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCTGGCTCCTCGGCCACGAAGTG
II#23 (Partial FAM2)           A-GACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCT-GCTCCTCGGCCACGAAGTG
II#29 (FAM1&2-Recovered)       A-GACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCT-GCTCCTCGGCCACGAAGTG
II#35 (Partial FAM1)           A-GACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCT-GCTCCTCGGCCACGAAGTG
II#38 (Mutated)                A-GACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCT-GCTCCTCGGCCACGAAGTG
II#40 (Mutated)                A-GAGTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCT-GCTCCTCGGCCACGAAGTG
II#41 (Partial FAM1)           ACGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGA----GATGATGTCAGTCCT-GCTCCTCGGCCACGAAGTG
II#48 (Wild-type)              A-GACTTA--------------------------------------------------------------------------
II#53 (FAM1&2)                 A-GACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCT-GCTCCTCGGCCACGAAGTG
II#59 (FAM1&2)                 A-GACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCT-GCTCCTCGGCCACGAAGTG

                               FAM 2
Donor (Control)                CACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCT-CGGTCATGGCCGGCCCGGAGG

                               BleoR

II#3 (Partial FAM2)            CACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCT-CGGTCATGGCCGGCCCGGAGG
II#7 (FAM1&2)                  CACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCT-CGGTCATGGCCGGCCCGGAGG
II#11 (Partial FAM2)           CACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCT-CGGTCATGGCCGGCCCGGAGG
II#13 (Partial FAM1)           ------------------------------------------------------------------------------------
II#14 (Partial FAM2)           CACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCT-CGGTCATGGCCGGCCCGGAGG
II#19 (FAM1&2)                 CACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCT-CGGTCATGGCCGGCCCGGAGG
II#21 (Partial FAM1)           CACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCT-CGGTCATGGCCGGCCCGGAGG
II#22 (Mutated)                CACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCG----CGGTCATGGCCGGCCCGGAGG
II#23 (Partial FAM2)           CACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCTCCGGTCATGGCCGGCCCGGAGG
II#29 (FAM1&2-Recovered)       CACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCT-CGGTCATGGCCGGCCCGGAGG
II#35 (Partial FAM1)           CACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCT-CGGTCATGGCCGGCCCGGAGG
II#38 (Mutated)                CACGCAGTTGCCGGCCAGGTCGCGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCT-CGGTCATGGCCGGCCCGGAGG
II#40 (Mutated)                CACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCC----------------------------------------
II#41 (Partial FAM1)           CACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCT-CGGTCATGGCCGGCCCGGAGG
II#48 (Wild-type)              ------------------------------------------------------------------------------------
II#53 (FAM1&2)                 CACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCT-CGGTCATGGCCGGCCCGGAGG
II#59 (FAM1&2)                 CACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCT-CGGTCATGGCCGGCCCGGAGG

Donor (Control)                CGTCCCGGAAGTTCGTGGACACGACCTCCGA---CCACTCGGCGTACAGCTCGTCC-AGGCCGCGCACCCACACCCAGGCCAGG

                               BleoR

II#3 (Partial FAM2)            CGTCCCGGAAGTTCGTGGACACGACCTCCGA---CCACTCGGCGTACAGCTCGTCC-AGGCCGCGCACCCACACCCAGGCCAGG
II#7 (FAM1&2)                  CGTCCCGGAAGTTCGTGGACACGACCTCCGA---CCACTCGGCGTACAGCTCGTCC-AGGCCGCGCACCCACACCCAGGCCAGG
II#11 (Partial FAM2)           CGTCCCGGAAGTTCGTGGACACGACCTCCGA---CCACTCGGCGTACAGCTCGTCC-AGGCCGCGCACCCACACCCAGGCCAGG
II#13 (Partial FAM1)           ------------------------------------------------------------AGGCCGCGCACCCACACCCAGGCCAGG
II#14 (Partial FAM2)           CGTCCCGGAAGTTCGTGGACACGACCTCCGA---CCACTCGGCGTACAGCTCGTCCAAGGCCGCGCACCCACACCCAGGCCAGG
II#19 (FAM1&2)                 CGTCCCGGAAGTTCGTGGACACGACCTCCGA---CCACTCGGCGTACAGCTCGTCC-AGGCCGCGCACCCACACC------AGG
II#21 (Partial FAM1)           CGTCCCGGAAGTTCGTGGACACGACCTCCGA---CCACTCGGCGTACAGCTCGTCC-AGGCCGCGCACCCACACCCAGGCCAGG
II#22 (Mutated)                CGTCCCGGAAGTTCGTGGACACGACCTCCGA---CCACTCGGCGTACAGCTCGTCC-AGGCCGCGCACCCACACCCAGGCCAGG
II#23 (Partial FAM2)           CGTCCCGGAAGTTCGTGGACACGACCTCCGA---CCACTCGGCGTACAGCTTGTCC-AGGCCGCGCACCCACACCCAGGCCAGG
II#29 (FAM1&2-Recovered)       CGTCCCGGAAGTTCGTGGACACGACCTCCGA---CCACTCGGCGTACAGCTCGTCC-AGGCCGCGCACCCACACCCAGGCCAGG
II#35 (Partial FAM1)           CGTCCCGGAAGTTCGTGGACACGACCTCCGATCCCCCACTCGGCGTACAGCTCGTCT-AGGCCGCGCACCCACACCCAGGCCAGG
II#38 (Mutated)                CGTCCCGGAAGTTCGTGGACACGACCTCCGA---CCACTCGGCGTACAGCTCGTCC-AGGCCGCGCACCCACACCCAGGCC---
II#40 (Mutated)                ------------------------------------CCACTCGGCGTACAGCTCGTCC-AGGCCGCGCACCCACACCCAGGCCAGG
II#41 (Partial FAM1)           CGTCCCGGAAGTTCGTGGACACGACCTCCGA---CCACTCGGCGTACAGCTCGTCC-AGGCCTCGCACCCACACCCAGGCCAGG
II#48 (Wild-type)              ------------------------------------CCA-------------------------------------------
II#53 (FAM1&2)                 CGTCCCGGAAGTTCGTGGACACGAGGCTCCGA---CCACTCGGCGTACAGCTCGTCC-AGGCCGCGCACCCACACCCAGGCCAGG
II#59 (FAM1&2)                 CGTCCCGGAAGTTCGTGGACACGACCTCCGA---CCACTCGGCGTACAGCTCGTCC-AGGCCGCGCACCCACACCCAGGCCAGG
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Donor (Control)                GTGTTGTCCGGCAC-CACCTGGTCCTGGACCGCGCTGATGAACAGGGTCACGTCGTCCCGGACCACACCGGCGAAGTCGTC---
                               BleoR
II#3 (Partial FAM2)            GTGTTGTCCGGCAC-CACCTGGTCCTGGACCGCGCTGATGAACAGGGTCACGTCGTCCCGGACCACACCGGCGAAGTCGTC---
II#7 (FAM1&2)                  GTGTTGT---GCAC-CACCTGGTCCTGGACCGCGCTGATGAACAGGGTCACGTCGTCCCGGACCACACCGGCGAAGTCGTC---
II#11 (Partial FAM2)           GTGTTGTCCGGCCC--ACCTGGTCCTGGACCGCGCTGATGAACAGGGTCACGTCGTCCCGGACCACACCGGCGAAGTCGTC---
II#13 (Partial FAM1)           GTGTTGTCCGGCAC-CACCTGGTCCTGGACCGCGCTGATGAACAGGGTCACGTCGTCCCGGACCACACCGGCGAAGTCGTC---
II#14 (Partial FAM2)           GTGTTGTCCGGCAC-CACCTGGTCCTGGA-------GATGAACAGGGTCACGTCGTCCCGGACCACACCGGCGAAGTCGTC---
II#19 (FAM1&2)                 GTGTTGTCCGGCAC-CACCTGGTCCTGGACCGCGCTGATGAACAGGGTCACGTCGTCCCGGACCACACCGGCGAAGTCGTC---
II#21 (Partial FAM1)           GTGTTGTCCGGCAC-CACCTGGTC---GACCGCGCTGATGAACAGGGTCACGTCGTCCCGGACCACACCGGCGAAGTCGTCCGG
II#22 (Mutated)                GTGTTGTCCGGCAC-CACCTGGTCCTGGACCGCGCTGATGAACAGGGTCACGTCGTCCCGGACCACACCGGCGAAGTCGTC---
II#23 (Partial FAM2)           GTGTTGTCCGGCAC-----------------------------------------------------------CGTC---
II#29 (FAM1&2-Recovered)       GTGTTGTCCGGCAC-CACCTGGTCCTGGACCGCGCTGATGAACAGGGTCACGTCGTCCCGGACCACACCGGCGAAGTCGTC---
II#35 (Partial FAM1)           GTGTTGTCCGGCACGCACCTGGTCCTGGACCGCGCTGATGAACAGGGTCACGTCGTCCCGGACCACACCGGCGAAGTCGTC---
II#38 (Mutated)                --------------------------------------------GTCGTCCCGGACCACACCGGCGAAGTCGTC---
II#40 (Mutated)                GTGTTGTCCGGCAC-CACCTGGTCCTGGACCGCGCTGATGAACAGGGTCACGTCGTCCCGGACCACACCGGCGAAGTCGTC---
II#41 (Partial FAM1)           GTGTTGTCCGGCAC-CACCTGGTCCTGGACCGCGCTGATGAACAGGGTCACGTCGTCCCGGACCACACCGGCGAAGTCGTC---
II#48 (Wild-type)              ---------------------------------------------------------------------------------
II#53 (FAM1&2)                 GTG-----------------------------------------GGTCACGTCGTCCCGGACCACACCGGCGAAGTCGTC---
II#59 (FAM1&2)                 GTGTTGTCCGGCAC-CACCTGGTCCTGGACCGCGCTGA-----AGGGTCACGTCGTCCCGGACCACACCGGCGAAGTCGTC---

Donor (Control)                ---CTCCACGAAGTCCCG-GGAGAACCCGAGCCGGTCGGTCCAGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCG
                               BleoR
II#3 (Partial FAM2)            ---CTCCACGAAGTCCCG-GGAGAACCCGAGCCGGTCGGTCCAGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCG
II#7 (FAM1&2)                  ---CTCCACGAAGTCCCG-GGAGAACCCGAGCCGGTCGGTCACGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCG
II#11 (Partial FAM2)           ---CTCCACGAAGTCCCG-GGAGAACCCGAGCCGGTCGGTCCAGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCG
II#13 (Partial FAM1)           ---CTCCACGAAGTCCCG-GGAGAACCCGAGCCGGTCGGTCCAGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCG
II#14 (Partial FAM2)           ---CTCCACGAAGTCCCG-GGAGAACCCGAGCCGGTCGGTCCAGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCG
II#19 (FAM1&2)                 ---CTCCACGAAGTCCCG-GGAGAACCCGAGCCGGTCGGTCCAGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCG
II#21 (Partial FAM1)           GGACTCCACGAAGTCCCG-GGAGAACCCGAGCCGGTCGGTCCAGAAC-CGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCG
II#22 (Mutated)                ---CTCCACGAAGTCCCG-GGAGAACCCGAGCCGGTCGGTCCAGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCG
II#23 (Partial FAM2)           ---CTCCACGAAGTCCCGAGGAGAACCCGAGCCGGTCGGTCCAGAACTCGACCGCT-CGGCGACGTCGCGCGCGGTGAGCACCG
II#29 (FAM1&2-Recovered)       ---CTCCACGAAGTCCCG-GGAGAACCCGAGCCGGTCGGTCCAGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCG
II#35 (Partial FAM1)           ---CTCCACGAAGTCCCG-GGAGAACCCGAGCCGGTCGGTCCAGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCG
II#38 (Mutated)                ---CTCCACGAAGTCCCG-GGAGAACCCGAGCCGGTCGGTCCAGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCG
II#40 (Mutated)                ---CTCCACGAAGTCCCG-GGAGAACCCGAGCCGGTCGGTCCAGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCG
II#41 (Partial FAM1)           ---CTCCATGAAGTCCCG-GGAGAACCCGAGCCGGTCGGTCCAGAACTCGACCGCTACGGCGACGTCGCGCGCGGTGAGCACCG
II#48 (Wild-type)              -------------------GGAGAACCCGAGCCGGTCGGTCCAGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCG
II#53 (FAM1&2)                 ---CTCCACGAAGTCCCG-GGAGAACCCGAGCCGGTCGGTCCAGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCG
II#59 (FAM1&2)                 ---CTCCACGAAGTCCCG-GGAGAACCCGAGCCGGTCGGTCCAGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCG

Donor (Control)                GAACGGCACTGGTCAACTTGGCCATCTACATC-TTCACAAGAACA-CAAGTTTTAAGGGTTGCAAGAGGAGAGCCG---GCATT
                                                                                                 5' homology arm
                               BleoR                Exon9; MAP kinase k...   Exon8                MAP kinase kin...
II#3 (Partial FAM2)            -------------------------------------------- ------------ ------------------------------ -----
II#7 (FAM1&2)                  GAACGGCACTGGTCAACTTGGCCATCTACATC-TTCACAAGAACA-CAAGTTTTAAGGGTTGCAAGAGGAGAGCCG---GCATT
II#11 (Partial FAM2)           GAACGGCACTGGTCAACTTGGCCATCTACATC-TTCACAAGAACA-CAAGTTTTAAGGGTTGCAAGAGGAGAGCCG---GCATT
II#13 (Partial FAM1)           GAACGGCACTGGTCAACTTGGCCATCTACATC-TTCACAAGAACA-CAAGTTTTAAGGGTTGCAAGAGGAGAGCCG---GCATT
II#14 (Partial FAM2)           GAACGGCACTGGTCAACTTGGCCATCTACATCTTTCACAAGAACA-CAAGTTTTAAGGGTTGCAAGAGGAGAGCCG---GCATT
II#19 (FAM1&2)                 GAACGGCACTGGTCAACTTGGCCATCTACATC-TTCACAAGAACA-CAAGTTTTAAGGGTTGCAAGAGGAGAGCCG---GCATT
II#21 (Partial FAM1)           GAACGGCACTGGTCAACTTGGCCATCTACATC-TTCACAAGAACA-CAAGTTTTAAGGGTTGCAAGAGGAGAGCCG---GCATT
II#22 (Mutated)                GAACGGCACTGGTCAACTTGGCCATCTACATC-TTCACAAGAACA-CAAGTTTTAAGGGTTGCAAGAGGAGAGCCG---GCATT
II#23 (Partial FAM2)           GAACGGCACTGGTCAACTTGGCCATCTACATC-TTCACAAGAACA-CAAGTTTTAAGGGTTGCAAGAGGAGAGCCGAATGCATT
II#29 (FAM1&2-Recovered)       GAACGGCACTGGTCAACTTGGCCATCTACATC-TTCACAAGAACA-CAAGTTTTAAGGGTTGCAAGAGGAGAGCCG---GCATT
II#35 (Partial FAM1)           GAACGGCACTGGTCAACTTGGCCATCTACATC-TTCACAAGAACA-CAAGTTTTAAGGGTTGCAAGAGGAGAGCCG---GCATT
II#38 (Mutated)                GAACGGCACTGGTCAACTTGGCCATCTACATC-TTCACAAGAACA-CAAGTTTTAAGGGTTGCAAGAGGAGAGCCG---GCATT
II#40 (Mutated)                GAACGGCACTGGTCAACTTGGCCATCTACATC-TTCACAAGAACATCAAGTTTTAAGGGTTGCAAGAGGAGAGCCG---GCATT
II#41 (Partial FAM1)           GAACGGCACTGGTCAACTTGGCCATCTACATC-TTCACAAGAACA-CAAGTTTTAAGGGTTGCAAGAGGAGAGCCG---GCATT
II#48 (Wild-type)              -------------------------------------------- ------------ CAAGTTTTAAGGGTTGC---------GCCG---GCATT
II#53 (FAM1&2)                 GAACGGCACTGGTCAACTTGGCCATCTACATC-TTCACAAGAACA-CAAGTTTTAAGGGTTGCAAGAGGAGAGCCG---GCATT
II#59 (FAM1&2)                 GAACGGCACTGGTCAACTTGGCCATCTACATC-TTCACAAGAACA-CAAGTTTTAAGGGTTGCAAGAGGAGAGCCG---GCATT

Donor (Control)                TGTAAAGTAT---GTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTG-TGCCTGGTATTGAAA---TTAGA
                                            5' homology arm
                                            MAP kinase kinase family protein CDS
II#3 (Partial FAM2)            ---------------TCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTG-TGCCTGGTATTGAAA---TTAGA
II#7 (FAM1&2)                  TGTAAAGTAT---GTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTG-TGCCTGGTATTGAAA---TTAGA
II#11 (Partial FAM2)           TGTAAAGGAT---GTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTG-TGCCTGGTATTGAAA---TTAGA
II#13 (Partial FAM1)           TGTAAAGTAT---GTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTG-TGCCTGGTATTGAAA---TTAGA
II#14 (Partial FAM2)           TGTAAAGTAT---GTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTG-TGCCTGGTATTGAAA---TTAGA
II#19 (FAM1&2)                 TGTAAAGTAT---GTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTG-TGCCTGGTATTGAAA---TTAGA
II#21 (Partial FAM1)           TGTAAAGTAT---GTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTG-TGCCTGGTATTGAAA---TTAGA
II#22 (Mutated)                TGTAAAGTATACCGTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTG-TGCCTGGTATTGAAA---TTAGA
II#23 (Partial FAM2)           TGTAAAGTAT---------------------------------------------------- ---------------- -----
II#29 (FAM1&2-Recovered)       TGTAAAGTAT---GTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTG-TGCCTGGTATTGAAA---TTAGA
II#35 (Partial FAM1)           TGTAAAGTAT---GTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTG-TGCCTGGTATTGAAA---TTAGA
II#38 (Mutated)                TGTAAAGTAT---GTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTGATGCCTGGTATTGAAA---TTAGA
II#40 (Mutated)                TGTAAAGTAT---GTCGCGAGATCCACATGCAGGTCC------------------------ ---------------- -----
II#41 (Partial FAM1)           TGTAAAGTAT---GTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTG-TGCCTGGTATTGAAACGGTTAGA
II#48 (Wild-type)              TGTAAAGTAT---GTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTG-TGCCTGGTATTGAAA---TTAGA
II#53 (FAM1&2)                 TGTAAAGTAT---GTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTG-TGCCTGGTATTGAAA---TTAGA
II#59 (FAM1&2)                 TGTAAAGTAT---GTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTG-TGCCTGGTATTGAAA---TTAGA
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Donor (Control)                 AAGAGAAAAA-GAAGAGTCAGA-----TCCATGAGCG-TCCACTAATAGCATACACATGT-TTTGAA-CATATTGAAAAGAGGC
                                                          5' homology arm

II#3 (Partial FAM2)             AAGAGAAAAA GAAGAGTCAGA-----TCCATGAGCG TCCACTAATAGCATACACATGT TTTGAA CATATTGAAAAGAGGC
II#7 (FAM1&2)                   AAGAGAAAAA GAAGAGTCAGA-----TCCATGAGCG TCCACTAATAGCATACACATGTCTTTGAA CATATTGAAAAG----
II#11 (Partial FAM2)            AAGAGAAAAACGAAGAGTCAGA-----TCCATGAGCG TCCACTAATAGC-------TGT TTTGAA CATATTGAAAAGAGGC
II#13 (Partial FAM1)            AAGAGAAAAA GAAGAGTCAGA-----TCCATGAGCG TCCACTAATAGCATACACATGT TTTGAA CATATTGAAAAGAGGC
II#14 (Partial FAM2)            AAGAGAAAAA GAAGAGTCAGA-----TCCATGAGCG TCCACTAATAGCATACACATGT TTTGAA CATATTGAAAAGAGGC
II#19 (FAM1&2)                  AAGAGAAAAA GAAGAGTCAGAAAGACTCCATGAGCG TCCACTAATAGCATACACATGT TTTGAA CATATTGAAAAGAGGC
II#21 (Partial FAM1)            AAGAGAAAAA GAAGAGTCAGA-----TCCATGAGCGTTCCACTAATAGCATACACATGT TTTGAA CATATTGAAAAGAGGC
II#22 (Mutated)                 AAGAGAAAAA GAAGAGTCAGA-----TCCATGAGCG TCCACTAATAGCATACACATGT TTTGAA CATATTGAAAAGAGGC
II#23 (Partial FAM2)            ---------- ----------     ---------- T--------------------- TTTGAA CATATTGAAAAGAGGC
II#29 (FAM1&2-Recovered)        AAGAGAAAAA GAAGAGTCAGA-----TCCATGAGCG TCCACTAATAGCATACACATGT TTTGAA CATATTGAAAAGAGGC
II#35 (Partial FAM1)            AAGAGAAAAA GAAGAGTCAGA-----TCCATGAGCG TCCACTAATAGCATACACATGT TTTGAA CATATTGAAAAGAGGC
II#38 (Mutated)                 AAGAGAAAAA GAAGAGTCAGA-----TCCATGAGCG TCCACTAATAGCATACACATGT TTTGAA CATATTGAAAAGAGGC
II#40 (Mutated)                 ------AAAA GAAGAGTCAGA-----TCCATGAGCG TCCACTAATAGCATACACATGT TTTGAA CATATTGAAAAGAGGC
II#41 (Partial FAM1)            AAGAGAAAAA GAAGAGTCAGA-----TCCATGAGCG TCCACTAATAGCATACACATGT TTTGAA CATATTGAAAAGAGGC
II#48 (Wild-type)               AAGAGAAAAA GAAGAGTCAGA-----TCCATGAGCG TCC----ATAGCATACACATGT TTTGAA CATATTGAAAAGAGGC
II#53 (FAM1&2)                  AAGAGAAAAA GAAGA------     --CATGAGCG TCCACTAATAGCATACACATGT TTTGAACCATATTGAAAAGAGGC
II#59 (FAM1&2)                  AAGAGAAAAA GAAGAGTCAGA-----TCCATGAGCG TCCACTAATAGCATACACATGT TTTGAA CATATTGAAAAGAGGC

Donor (Control)                 AAAAGAAGGGTGGGA-TATTAGCAGTCTGCTGAG-TATTAATGACATTCCATA-TTGATAGAGAGGAGAAAAGAGTAAAGGACG
                                                          5' homology arm

II#3 (Partial FAM2)             AAAAGAAGGGTGGGA TATTAGCAGTCTGCTGAGTTATTAATGACATTCCATA TTGATAGAGAGGAGAAAAGAGTAAAGGACG
II#7 (FAM1&2)                   --CACAAGGGTGGGA TATTAGCAGTCTGCTGAG TATTAATGACATTCCATA TTGATAGAGAGGAGAAAAGAGTAAAGGACG
II#11 (Partial FAM2)            AAAAGAAGGGTGGGA TATTAGCAGTCTGCTGAG TATTAATGACATTCCATA TTGATAGAGAGGAGAAAAGAGTAAAGGACG
II#13 (Partial FAM1)            AAAAGAAGGGTGGGA TATTAGCAGTCTGCTGAG TATTAATGACATTCCATA TTGATAGAGAGGAGAAAAGAGTAAAGGACG
II#14 (Partial FAM2)            AAAAGAAGGGTGGGA TATTAGCAGTCTGCTGAG TATTAATGACATTCCATA TTGATAGAGAGGAGAAAAGAGTAAAGGACG
II#19 (FAM1&2)                  AAAAGAAGGGTGGGA TATTAGCAGTCTGCTGAG TATTAATGACATTCCATA TTGATAGAGAGGAGAAAAGAGTAAAGGACG
II#21 (Partial FAM1)            AAAAGAAGGGTGGGAGTATTAGCAGTCTGCTGAG TATTAATGACATTCCATA TTGATAGAGAGGAGAAAAGAGTAAAGGACG
II#22 (Mutated)                 AAAAGAAGGGTGGGA TATTAGCAGTCTGCTGAG TATTAATGACATTCCATA TTGATAGAGAGGAGAAAAGGGTAAAGGACG
II#23 (Partial FAM2)            AAAAGAAGGGTGGGA TATTAGCAGTCTGCTGAG TATTAATGACATTCCATA TTGATAGAGAGGAGAAAAGAGTAAAGGACG
II#29 (FAM1&2-Recovered)        AAAAGAAGGGTGGGA TATTAGCA----GCTGAG TATTAATGACATTCCATA TTGATAGAGAGGAGAAAAGAGTAAAGGACG
II#35 (Partial FAM1)            AAAAGAAGGGTGGGA TATTAGCAGTCTGCTGAG TATTAATGACATTCCATA TTGATAGAGAGGAGAAAAGAGTAAAGGACG
II#38 (Mutated)                 AAAAGAAGGGTGGGA TATTAGCAGTCTGCTGAG TATT-ATGACATTCCATA TTGATAGAGAGGAGAAAAGAGTAAAGGACG
II#40 (Mutated)                 AAAAGAAGGGTGGGA TATTAGCAGTCTGCTGAG TATTAATGACATTCCATA TTGATAGAGAGGAGAAAAGAGTAAAGGACG
II#41 (Partial FAM1)            AAAAGAAGGGTGGGA TATTAGCAGTCTGCTGAG TATTAATGACATTCCATA TTGATAGAGAGGAGAAAAGAGTAAAGGACG
II#48 (Wild-type)               AAAAGAAGGGTGGGA TATT-GCAGTCTGCTGAG TATTAATGACATTCCATA TTGATAGAGAGGAGAAAAGAGTAAAGGACG
II#53 (FAM1&2)                  AAAAGAAGGGTGGGA TATTAGCAGTCTGCTGAG TATTAATG-CATTCCATA TTGATAGAGAGGAGAAAAGAGTAAAGGACG
II#59 (FAM1&2)                  AAAAGAAGGGTGGGA TATTAGCAGTCTGCTGAG TATTAATGACATTCCATATTTGATAGAGAGGAGAAAAGAGTAAAGGACG

Donor (Control)                 TG-GAGTGCCAG----TAACAGGCAGACAGCTAATTGCCCCACCCAG--TTTAACAATCATAGGACTTCAAATACCATCAGTTC
                                                          5' homology arm

II#3 (Partial FAM2)             TG GAGTGCCAGTGAATAACAGGCAGACAGCTAATTGCCCCACCCAG  TTTAACAATCATAGGACTTCAAATACCATCAGTTC
II#7 (FAM1&2)                   TG GAGTGCCAG   TAACAGGCAGACAGCTAATTGCCCCACCCAG  TTTAACAATCATAGGACTTCAAATACCATCAGTTC
II#11 (Partial FAM2)            TG GAGTGCCAG   TAACAGGCAGACAGCTAATTGCCCCACCCAGACTTTAACAATCATAGGACTTCAAATACCATCAGTTC
II#13 (Partial FAM1)            TG GAGTGCCAG   TAACAGGCAGACAGCTAATTGCCCCACCCAG  TTTAACAATCATAGGACTTCAAATACCATCAGTTC
II#14 (Partial FAM2)            TG GAGTGCCAG   TAACAGGCAGACAGCTAATTGCCCCACCCAG  TTTAACAATCATAGGACTTCAAATACCATCAGTTC
II#19 (FAM1&2)                  TGTGAGTGCCAG   TAACAGGCAGACAGCTAATTGCCCCACCCAG  TTTAACAATCATAGGACTTCAAATACCATCAGTTC
II#21 (Partial FAM1)            TG GAGTGCCAG   TAACAGGCAGACAGCTAATTGCCCCACCCAG  TTTAACAATCATAGGACTTCAAATACCATCAGTTC
II#22 (Mutated)                 TG GAGTGCCAG   TAACAGGCAGACAGCTAATTGCCCCACCCAG  TTTAACAATCATAGGACTTCAAATACCATCAGTTC
II#23 (Partial FAM2)            TG GAGTGCCAG   TAACAGGCAGACAGCTAATTGCCCCACCCAG  TTTAACAATCATAGGACTTCAAATACCATCAGTTC
II#29 (FAM1&2-Recovered)        TG GAGTGCCAG   TAACAGGCAGACAGCTAATTGCCCCACCCAG  TTTAACAATCATAGGACTTCAAATACCATCAGTTC
II#35 (Partial FAM1)            TG GAGTGCCAG   TAACAGGCAGACAGCTAATTGCCCCACCCAG  TTTAACAATCATAGGACTTCAAATACCATCAGTTC
II#38 (Mutated)                 TG GAGTGCCAG   TAACAGGCAGACAGCTAATTGCCCCACCCAG  TTTAACAATCATAGGACTTCAAATACCATCAGTTC
II#40 (Mutated)                 TG GAGTGCCAG   TAACAGGCAGACAGCTAATTGCCCCACCCAG  TTTAACAATCATAGGACTTCAAATACCATCAGTTC
II#41 (Partial FAM1)            TG GAGTGCCAG   TAACAGGCAGACAGCTAATTGCCCCACCCAG  TTTAACAATCATAGGACTTCAAATACCATCAGTTC
II#48 (Wild-type)               TG GAGTGCCAG   TAACAGGCAGACAGCTAATTGCCCCACCCAG  TTTAACAATCATAGGACTTCAAATACCATCAGTTC
II#53 (FAM1&2)                  TG GAGTGCCAG   TAACAGGCAGACAGCTAATTGCCCCACCCAG  TTTAACAATCATAGGACTTCAAATACCATCAGTTC
II#59 (FAM1&2)                  TG GAGTGCCAG   TAACAGGCAGACAGCT-ATTGCCCCACCCAG  TTTAACAATCATAGGACTTCAAATACCATCAGTTC

Donor (Control)                 ATG-TGCTGCCTGTCTATCCT-TTGGATCTTT------CTGCAC-ACTGGAAGAAGACAGAACCACAGAATGA--AAATCAGTA
                                                          5' homology arm
                                                MAP kinase kinase family protein CDS

II#3 (Partial FAM2)             ATG TGCTGCCTGTCTATCCT TTGGATCTTT------CTGCAC ACTGGAAGAAGACAGAACCACAGAATGA  AAATCAGTA
II#7 (FAM1&2)                   CTG TGCTGCCTGTCTATCCT TTGGATCTTT------CTGCAC ACTGGAAGAAGACAGAACCACAGAATGA  AAATCAGTA
II#11 (Partial FAM2)            ATG TGCTGCCTGTCTATCCTATTGGATCTTT------CTGCAC ACTGGAAGAAGACAGAACCACAGAATGA  AAATCAGTA
II#13 (Partial FAM1)            ATG TGCTGCCTGTCTATCCT TTGGATCTT-------CTGCACTACTGGAAGAAGACAGAACCACAGAATGA  AAATCAGTA
II#14 (Partial FAM2)            ATG TGCTGCCTGTCTATCCT TTGGATCTTT------CTGCAC ACTGGAAGAAGACAGAACCACAGAATGA  AAATCAGTA
II#19 (FAM1&2)                  ATG TGCTGCATGTCTATCCT TTGGATCTCT------CTGCAC ACTGGAAGAAGACAGAACCACAGAATGA  AAATCAGTA
II#21 (Partial FAM1)            ATG TGCTGCCTGTCTATCCT TTGGATCTTT------CTGCAC ACTGGAAGAAGACAGAACCACAGAATGA  AAATCAGTA
II#22 (Mutated)                 ATG TGCTGCCTGTCTATCCT TTGGATCTTT------CTGCAC ACTGGAAGAAGACAGAACCACAGAATGA  AAATCAGTA
II#23 (Partial FAM2)            ATG TGCTGCCTGTCTATCCT TTGGATCTTT------CTGCAC ACTGGAAGAAGACAGAACCACAGAATGA  AAATCAGTA
II#29 (FAM1&2-Recovered)        ATG TGCTGCCTGTCTATCCT TTGGATCTTT------CTGCAC ACTGGAAGAAGACAGAACCACAGAATGA  AAATCAGTA
II#35 (Partial FAM1)            ATG TGCTGCCTGTCTATCCT TTGGATCTTT------CTGCAC ACTGGAAGAAGACAGAACCACAGAATGA  AAATCAGTA
II#38 (Mutated)                 ATG TGCTGCCTGTCTATCCT TTGGATCTTT------CTGCAC ACTGGAAGAAGACAGAACCACAGAATGA  AAATCAGTA
II#40 (Mutated)                 ATG TGCTGCCTGTCTATCCT TTGGATCTTT------CTGCAC ACTGGAAGAAGACAGAACCACAGAATGA  AAATCAGTA
II#41 (Partial FAM1)            ATG TGCTGCCTGTCTATCCT TTGGATCTTT------CTGCAC ACTGGAAGAAGACAGAACCACAGAATGA  AAATCAGTA
II#48 (Wild-type)               ATGTTGCTGCCTGTCTATCCT TTGGATCT--------------AAGAAGACAGAACCACAGAATGAATAAATCAGTA
II#53 (FAM1&2)                  ATG TGCTGCCTGTCTATCCT TTGGATCTTTCCCACGCTGCAC ACTGGAAGAAGACAGAACCACAGAATGA  AAATCAGTA
II#59 (FAM1&2)                  ATG TGCTGCCTGAATATCCT TTGCATCTTT------CTGCAC ACT----GAAGACAGAACCACAGAATGA  AAATCAGTA
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Donor (Control)	AC
II#3 (Partial FAM2)	AC
II#7 (FAM1&2)	AC
II#11 (Partial FAM2)	AC
II#13 (Partial FAM1)	AC
II#14 (Partial FAM2)	AC
II#19 (FAM1&2)	AC
II#21 (Partial FAM1)	AC
II#22 (Mutated)	AC
II#23 (Partial FAM2)	AC
II#29 (FAM1&2-Recovered)	AC
II#35 (Partial FAM1)	AC
II#38 (Mutated)	AC
II#40 (Mutated)	AC
II#41 (Partial FAM1)	AC
II#48 (Wild-type)	AC
II#53 (FAM1&2)	AC
II#59 (FAM1&2)	AC

Supplementary 5: Allignment of events involved in experiment III.

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Donor (Control)                    TTTTGTGAATTGCTA-----ATGGTT-TGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAG
                                                                   3' homology arm

III#6 (Partial FAM2-recovered)     TTTTGTGAATTGCTAAGCTCATGGTT-TGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAG
III#8 (Mutated)                    TTTTGTGAATTGCTA-----ATGGTT-TGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAG
III#10 (Partial FAM1)              TTTTGTGAATTGCTA-----ATGGTT-TGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAG
III#14 (Wild-type)                 TTTTGTGAATTGCTA-----ATGGTT-TGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAG
III#17 (Partial FAM2)              TTTTGTGAATTGCTA-----ATGGTTCTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAG
III#21 (FAM 1&2)                   TTTTGTGAATTGCTA-----ATGGTT-TGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAG
III#23 (Partial FAM1)                    GAATTGCTA-----ATGGTT-TGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAG
III#24 (Mutated)                   TTTTGTGAATTGCTA-----ATGGTT-TGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAG
III#27 (Partial FAM1)              TTTTGTGAATTGCTA-----ATGGTT-TGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAG
III#32 (Partial FAM1)              TTTTGTGAATTGCTA-----ATGGTT-TGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAG
III#36 (Partial FAM2)              TTTTGTGAATTGCTA-----ATGGTT-TGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAG
III#43 (Wild-type)                 TTTTGTGAATTGCTA-----ATGGTT-TGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAG
III#45 (FAM 1&2)                   TTTTGTGAATTGCTA-----ATGGTT-TGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAG
III#53 (Partial FAM1)              TTTTGTGAATTGCTA-----ATGGTT-TGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAG
III#61 (FAM 1&2)                   TTTTGTGAATTGCTA-----ATGGTT-TGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAG

Donor (Control)                    CCACAATGACAGTTAAGAATCTTTCTTCAGGCCTTCAAAATTTC---------AATAGATAACTTCCCATAACTCTCAAGAGTCTGATA
                                                                   3' homology arm

III#6 (Partial FAM2-recovered)     CCACAATGACAGTTAAGAATCTTTCTTCAGGCCTTCAAAATTTC---------AATAGATAACTTCCCATAACTCTCAAGAGTCTGATA
III#8 (Mutated)                    CCACAATGACAGTTAAGAATCTTTCTTCTGGCCTTCAAAATTTC---------AATAGATAACTTCCCATAACTCTCAAGAGTCTAGTA
III#10 (Partial FAM1)              CCACAATGACAGTTAAGAATCTTTCTTCAGGCCTTCAAAATTTC---------AATAGATAACTTCCCATAACTCTCAAGAGTCTGATA
III#14 (Wild-type)                 CCACAATGACAGTTAAGAATCTTTCTTCAGGCCTTCAAAATTTC---------AATAGATAACTTCCCATAACTCTCAAGAGTCTGATA
III#17 (Partial FAM2)              CCACAATGACAGTTAAGAATCTTTCTTCAGGCCTTCAAAATTTC---------AATAGATAACTTCCCATAACTCTCAAGAGTCTGATA
III#21 (FAM 1&2)                   CCACAATGACAGTTAAGAATCTTTCTTCAGGCCTTCAAAATTTC---------AATAGATAACTTCCCATAACTCTCAAGAGTCTGATA
III#23 (Partial FAM1)              CCACAATGACAGTTAAGAATCTTTCTTCAGGCCTTCAAAATTTC---------AATAGATAACTTCCCATAACTCTCAAGAGTCTGATA
III#24 (Mutated)                   CCACAATGACAGTTAAGAATCTTTCTTCAGGCCTTCAAAATTTC---------AATAGATAACTTCCCATAACTCTCAAGAGTCTGATA
III#27 (Partial FAM1)              CCACAATGACAGTTAAGAATCTTTCTTCAGGCCTTCAAAATTTC---------AATAGATAACTTCCCATAACTCTCAAGAGTCTGATA
III#32 (Partial FAM1)              CCACAATGACAGTTAAGAATCTTTCTTCAGGCCTTCAAAATTTC---------AATAGATAACTTCCCATAACTCTCAAGAGTCTGATA
III#36 (Partial FAM2)              CCACAATGACAGTTAAGAATCTTTCTTCAGGCCTTCAAAATTTC---------AATAGATAACTTCCCATAACTCTCAAGAGTCTGATA
III#43 (Wild-type)                 CCACAATGACAGTTAAGAATCTTTCTTCAGGCCTTCAAAATTTCCGTAAGGTCAATAGATAACTTCCCATAACTCTCAAGAGTCTGATA
III#45 (FAM 1&2)                   CCACAATGACAGTTAAGAATCTTTCTTCAGGCCTTCAAAATTTC---------AATAGATAACTTCCCATAACTCTCAAGAGTCTGATA
III#53 (Partial FAM1)              CCACAATGACAGTTAAGAATCTTTCTTCAGGCCTTCAAAATTTC---------AATAGATAACTTCCCATAACTCTCAAGAGTCTGATA
III#61 (FAM 1&2)                   CCACAATGACAGTTAAGAATCTTTCTTCAGGCCTTCAAAATTTC---------AATAGATAACTTCCCATAACTCTCAAGAGTCTGATA

Donor (Control)                    TAGTATCTGCACTTGTCAAAC-ACAATGGCTTAAATTCAACTCTAAAGTACATGAATTCTCA-TAAGAGTTATGGTCGACATGG-----
                                                                   3' homology arm

III#6 (Partial FAM2-recovered)     TAGTATCTGCACTTGTCAAAC-ACAATGGCTTAAATTCAACTCTAAAGTACATGAATTCTCA-TAAGAGTTATGGTCGACATGG-----
III#8 (Mutated)                    TAGTATCTGCACTTGTCAAAC-ACAATGGCTTAAATTCAACTCTAAAGTACATGAATTCTCA-TAAGAGTTATGGTCGACATGG-----
III#10 (Partial FAM1)              TAGTATCTGCACTTGTCAAAC-ACAATGGCTTAAATTCAACTCTAAAGTACATGAATTCTCA-TAAGAGTTATGGTCGACATGG-----
III#14 (Wild-type)                 TAGTATCTGCACTTGTCAAAC-ACAATGGCTTAAATTCAACTCTAAAGTACATGAATTCTCA-TAAGAGTTATGGTCGACATGG-----
III#17 (Partial FAM2)              TAGTATCTGCACTTGTCAAAC-ACAATGGCTTAAATTCAACTCTAAAGTACATGAATTCTCA-TAAGAGTTATGGTCGACATGG-----
III#21 (FAM 1&2)                   TAGTATCTGCACTTGTCAAAC-ACAATGGCTTAAATTCAACTCTAAAGTACATGAATTCTCACTAAGAGTTATGGTCGACATGGT----
III#23 (Partial FAM1)              TAGTATCTGCACTTGTCAAAC-ACAATGGCTTAAATTCAACTCTAAAGTACATGAATTCTCA-TAAGAGTTATGGTCGACATGG-----
III#24 (Mutated)                   TAGTATCTGCACTTGTCAAAC-ACAATGGCTTAAATTCAACTCTAAAGTACATGAATTCTCA-TAAGAGTTATGGTCGACATGG-----
III#27 (Partial FAM1)              TAGTATCTGCACTTGTCAAAC-ACAATGGCTTAAATTCAACTCTAAAGTACATGAATTCTCA-TAAGAGTTATGGTCGACATGG-----
III#32 (Partial FAM1)              TAGTATCTGCACTTGTCAAAC-ACAATGGCTTAAATTCAACTCTAAAGTACATGAATTCTCA-TAAGAGTTATGGTCGACATGG-----
III#36 (Partial FAM2)              TAGTATCTGCACTTGTCAAACAACAATGGCTTAAATTCAACTCTAAAGTACATGAATTCTCA-TAAGAGTTATGGTCGACATGG-----
III#43 (Wild-type)                 TAGTATCTGCACTTGTCAAAC-ACAATGGCTTAAATTCAACTCTAAAGTACATGAATTCTCA-TAAGAGTTATGGTCGACATGG-----
III#45 (FAM 1&2)                   TAG-ATCTGCACTTGTCAAAC-ACAATGGCTTAAATTCAATCATAAAGTACATGAATTCTCA-TAAGAGTTATGGTCGACATGG-----
III#53 (Partial FAM1)              TAGTATCTGCACTTGTCAAAC-ACAATGGCT------CAACTCTAAAGTACATGAATTCTCA-TAAGAGTTATGGTCGACATGG-----
III#61 (FAM 1&2)                   TAGTATCTGCACTTGTCAAAC-ACAATGGCTTAAATTCAACTCTAAAGTACATGAATTCTCA-TAAGAGTTATGGTCGACATGGGCGCT

Donor (Control)                    ----TAAATGCATTAATTGCATAGACACAGGCG-------AACTATTAAATGATTAATAAGACTTGGATTATGCAACTACATCTTCACA
                                                                   3' homology arm

III#6 (Partial FAM2-recovered)     ----TAAATGCATTAATTGCATAGACACAGGCG-------AACTATTAAATGATTAATAAGACTTGGATTATGCAACTACATCTTCACA
III#8 (Mutated)                    ----TAAATGCATTAATTGCATAGACACAGGCG-------AACTATTAAATGATTAATAAGACTTGGATTATGCAACTACATCTTCACA
III#10 (Partial FAM1)              ----TAAATGCATTAATTGCATAGACACAGGCG-------AACTATTAAATGATTAATAAGACTTGGATTATGCAACTACATCTTCACA
III#14 (Wild-type)                 ----TAAATGCATTAATTGCATAGACACAGGCG-------A------AAATGATTAAT-AGACTTGGATTATGCAACTACATCTTCACA
III#17 (Partial FAM2)              ----TAAATGCATTAATTGCATAGACACAGGCG-------AACTATTAAATG---AATAAGACTTGGATTATGCAACTACATCTTCACA
III#21 (FAM 1&2)                   ----AAATGCATTAATTGCATAGACACAGGCG-------AACTATTAAATGATTAATAAGACTTGGATTATGCAACTACATCTTCACA
III#23 (Partial FAM1)              ----TAAATGCATTAATTGCATAGACACAGGCG-------AACTATTAAATGATTAATAAGACTTGGATTATGCAACTACATCTTCACA
III#24 (Mutated)                   ----TAAATGCATTAATTGCATAGACACAGGCG-------AACTATTAAATGATTAATAAGACTTGGATTATGCAACTACATCTTCACA
III#27 (Partial FAM1)              ----TAAATGCATTAATTGCATAGACACAGGCG-------AACTATTAAATGATTAATAAGACTTGGATTATGCAACTACATCTTCACA
III#32 (Partial FAM1)              ----TAAATGCATTAATTGCATAGACACAGGCG-------AACTATTAAATGATTAATAAGACTTGGATTATGC-ACTACATCTTCACA
III#36 (Partial FAM2)              ----TAAATGCATTAATTGCATAGACACAGGCGTGGGTTCAACTATTAAATGATTAATAAGACTTGGATTATGCAACTACATCTTCACA
III#43 (Wild-type)                 ----TAAATGCATTAATTGCATAGACACAGGCG-------AACTATTAAATGATTAATAAGACTTGGATTATGCAACTACATCTTCACA
III#45 (FAM 1&2)                   ----TAAATGCATTAATTGCATAGACACAGGCG-------AACTATTAAATGATTAATAAGACTTGGATTATGCAACTACATCTTCACA
III#53 (Partial FAM1)              ----TAAATGCATTAATTGCATAGACACAGGCG-------AACTATTAAATGATTAATAAGACTTGGATTATGCAACTACATCTTCACA
III#61 (FAM 1&2)                   TTAGTAAATGCATTAATTGCATAGACACAGGCGA------ACTATTAAATGATTAATAAGACTTGGATTATGCAACTACATCTTCACA
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Supplementary 4: Allignment of events involved in experiment II.

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                                                                  FAM 2
Donor (Control)                AGAACTCCATACAAAAAAAGAAATAATAAGAAAAAACATTTGAC---------CAAATGATTTCAAG-------AAATGATGTGAATGG
                               3' homology arm

III#6 (Partial FAM2-recovered) AGAACTCCATACAAAAAAAGAAATAATAAGAAAAAACATTTGAC--------CAAATGATTTCAAG-------AAATGATGTGAATGG
III#8 (Mutated)                AGAACTCCATACAAAAAAAGAAATAATAAGAAAAAACATTTGAC--------CAAATGATTTCAAG-------AAATGATGTGAATGG
III#10 (Partial FAM1)          AGAACTCCATACAAAAAAAGAAATAATAAGAAAAAACA--TGAC--------CAAATGATTTCAAG-------AAATGATGTGAATGG
III#14 (Wild-type)             AGAACTCCATACAAAAAAAGAAATAATAAGAAAAAACATTTGAC------C -AAATGATTTCAAG-------AAATGATGTGAATGG
III#17 (Partial FAM2)          AGAACTCCATACAAAAAAAGAAATAATAAGAAAAAACATTTGAC------C -AAATGATTTCAAG-------AAATGATGTGAATGG
III#21 (FAM 1&2)               AGAA-------CAAAAAAAGAAATAATAAGAAAAAACATTTGAC-------C-AAATGATTTCAAG-------AAATGATGTGAATGG
III#23 (Partial FAM1)          AGAACTCCATACAAAAAAAGAAATAATAAGAAAAAACATTTGAC-------C-AAATGATTTCAAG-------AAATGATGTGAATGG
III#24 (Mutated)               AGAACTCCATACAAAAAAAGAAATAATAAGAAAAAACATTTGAC------C -AAATGATTTCAAG-------AAATGATGTGAATGG
III#27 (Partial FAM1)          AGAACTCCATACAAAAAAAGAAATAATAAGAAAAAACATTTGAC------C -AAATGATTTCAAGCCAATTCAAATGATGTGAATGG
III#32 (Partial FAM1)          AGAACTCCATACAAAAAAAGAAATAATAAGAAAAAACATTTGAC------C -AAATGATTTCAAG-------AAATGATGTGAATGG
III#36 (Partial FAM2)          AGAACTCCATACAAAAAAAGAAATAATAAGAAAAAACATTTGAC--------CAAATGATTTCAAG-------AAATGATGTGAATGG
III#43 (Wild-type)             AGA--------CAAAAAAAGAAATAATAAGAAAAAACATTTGAC--------CAAATGATTTCAAG-------AAATGATGTGAATGG
III#45 (FAM 1&2)               AGAACTCCATACAAAAAAAGAAATAATAAGAAAAAACATTTGAC------C -AAATGATTTCAAGA------ -AATGATGTGAATGG
III#53 (Partial FAM1)          AGAACTCCATACAAAAAAAGAAATAATAAGAAAAAACATTTGACTGGGGTTTACAAATGATTTCAAG-------AAATGATGTGAATGG
III#61 (FAM 1&2)               AGAACTCCATACAAAAAAAGAAATAATAAGAAAAAACATTTGAC--------CAAATGATTTCAAG-------AAATGATGTGAATGG

                                                                  FAM 2
Donor (Control)                GAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATG--TCAGTCCTGCTCCTCGGCCACGAAG
                               3' homolog...  poly(A)  6xHis tag
                                                                                  BleoR
III#6 (Partial FAM2-recovered) GAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATG--TCAGTCCTGCTCCTCGGCCACGAAG
III#8 (Mutated)                GAAAATT-------------------------------------------------------------------------------C----------
III#10 (Partial FAM1)          GAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATG--TCAGTCCTGCTCCTCGGCCACGAAG
III#14 (Wild-type)             GAAAATTAGACTT-------------------------------------------------------------------------------
III#17 (Partial FAM2)          GAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATG--TCAGTCCTGCTCCTCGGCCACGAAG
III#21 (FAM 1&2)               GAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATG--TCAGTCCTGCTCCTCGGCCACGAAG
III#23 (Partial FAM1)          GAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGAATCAGTCCTGCTCCTCGGCCACGAAG
III#24 (Mutated)               GAAAATTAG--TTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATG--TCAGTCCTGCTCCTCGGCCACGAAG
III#27 (Partial FAM1)          GAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATG--TCAGTCCTGCTCCTCGGCCACGAAG
III#32 (Partial FAM1)          GAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATG--TCAGTCCTGCTCCTCGGCCACGAAG
III#36 (Partial FAM2)          GAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATG--TCAGTCCTGCTCCTCGGCCACGAAG
III#43 (Wild-type)             GAAAATTAGACTT-------------------------------------------------------------------------------A--
III#45 (FAM 1&2)               GAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATG--TCAGTCCTGCTCCTCGGCCACGAAG
III#53 (Partial FAM1)          GAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATG--TCAGTCCTGCTCCTCGGCCACGAAG
III#61 (FAM 1&2)               GAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATG--TCAGTCCTGCTCCTCGGCCACGAAG

                                FAM 2
Donor (Control)                T-GCACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACG-GCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCG

                               BleoR
III#6 (Partial FAM2-recovered) T GCACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACG GCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCG
III#8 (Mutated)                - ---------------------------AGGGCGAACTCCCGCCCCCACG GCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCG
III#10 (Partial FAM1)          T GCACGCAGTT----GCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACG GCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCG
III#14 (Wild-type)             - ------------------------------------------------ ------------------------------------
III#17 (Partial FAM2)          T GCACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACG GCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCG
III#21 (FAM 1&2)               T GCACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACG GCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCG
III#23 (Partial FAM1)          T GCACGCAGTTGCCGGCCGGGTCGCGC-GGGCGAACTCCCGCCCCCACG GCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCG
III#24 (Mutated)               T GCACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACG GCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCG
III#27 (Partial FAM1)          T GCACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACG GCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCG
III#32 (Partial FAM1)          TAGTAAAC-GTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACG GCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCG
III#36 (Partial FAM2)          T GCACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACG GCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCG
III#43 (Wild-type)             - ------------------------------------------------ ------------------------------------
III#45 (FAM 1&2)               T GCACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACGTGCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCG
III#53 (Partial FAM1)          T GCACGCAGTTGCCGGCCGGGTC-CGCAGGGCGAACTCCCGCCCCCACG GCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCG
III#61 (FAM 1&2)               T GCACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACG GCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCG

Donor (Control)                T-CCCGGAAGTTCGTGGACACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGCGCACCCA-------CACCCAGGCCAGGGT

                               BleoR
III#6 (Partial FAM2-recovered) T CCCGGAAGTTCGTGGACACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGCGCACCCA-----C -ACCCAGGCCAGGGT
III#8 (Mutated)                T CCCGGAAGTTCGTGGACACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGCGCACCCA-------CACCCAGGCCAGGGT
III#10 (Partial FAM1)          T CCCGGAAGTTCGTGGACACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGCGCACCCA-------CACCCAGGCCAGGGT
III#14 (Wild-type)             - -------------------------------------------------------------------------ACC-----------
III#17 (Partial FAM2)          T CCCGGAAGTTCGTGGACACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGCGCACCCA-------CACCCAGGCCAGGGT
III#21 (FAM 1&2)               T CCCGGAAGTTCGTGGACACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGCGCACCCA-------CACCCAGGCCAGGGT
III#23 (Partial FAM1)          T CCCGGAAGTTCGTGGACACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGCGCACCCA-----C -ACCCAGGCCAGGGT
III#24 (Mutated)               TTCCCGGAAGTTCGTGGACACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGCGCACCCATGGTACTACACCCAGGCCAGGGT
III#27 (Partial FAM1)          T CCCGGAAGTTCGTGGACACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGCGCACCCA-C-----  -ACCCAGGCCAGGGT
III#32 (Partial FAM1)          T CCCGGAAGTTCGTGGACACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGCGCACCCA-------CACCCAGGCCAGGGT
III#36 (Partial FAM2)          T CCCGGAAGTTCGTGGACACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGCGCACCCA-------CACCCAGGCCAGGGT
III#43 (Wild-type)             - --------------------------------------------------------------------------CC------A----
III#45 (FAM 1&2)               T CCCGGAAGTTCGTGGACACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGCGCACCCA-------CACCCAGGCCAGGGT
III#53 (Partial FAM1)          T CCCGGAAGTTCGTGGACACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGCGCACCCA-C-----  -ACCCAGGCCAGGGT
III#61 (FAM 1&2)               T CCCGGAAGTTCGTGGACACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGCGCACCCA-------CACCCAGGCCAGGGT
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Donor (Control)                 GTTGTCCGGCACCACCTGGTCCTGGACCGCGCT-GATGAACAGGGTCACGTCGTCCCGGACCACACCGG-CGAAGTCGTCCTCCACGAA

                                BleoR
III#6 (Partial FAM2-recovered)  GTTGTCCGGCACCACCTGGTCCTGGACCGCGCT-GATGAACAGGGTCACGTCGTCCCGGACCACACCGG-CGAAGTCGTCCTCCACGAA
III#8 (Mutated)                 GTTGTCCGGCACCACCTGGTCCTGGACCGCGCT-GATGAACAGGGTCACGTCGTCCCGGACCACACCGGCCGAAGTCGTCCTCCACGAA
III#10 (Partial FAM1)           G---------ACCACCTGGTCCTGGACCGCGCT-GATGAACAGGGTCACGTCGTCCCGGACCACACCGG-CGAAGTCGTCCTCCACGAA
III#14 (Wild-type)              ---------- ---------- ---------- ---------- ---------- ---------- ----------
III#17 (Partial FAM2)           GTTGTCCGGCACCACCTGGTCCTGGACCGCGCT-GATGAACAGGGTCACGTCGTCCCGGACCACACCGG-CGAAGTCGTCCTCCACGAA
III#21 (FAM 1&2)                GTTGTCCGGCACCACCTGGTCCTGGACCGCGCT-GATGAACAGGGTCACGTCGTCCCGGACCACACCGG-CGAAGTCGTCCTCCACGAA
III#23 (Partial FAM1)           GTTGTCCGGCACCACCTGGTCCTGGACCGCGCT-GATGAACAGGGTCACGTCGTCCCGGACCACACCGG-CGAAGTCGTCCTCCACGAA
III#24 (Mutated)                GTTGTCCGGCACCACCTGGTCCTGGACCGCGCT-GATGAACAGGGTCACGTCGTCCCGGACCACACCGG-CGAAGTCGTCCTCCACGAA
III#27 (Partial FAM1)           GTTGTCCGGCACCACCTGGTCCTGGACCGCGCT-GATGAACAGGGTCACGTCGTCCCGGACCACACCGG-CGAAGTCGTCCTCCACGAA
III#32 (Partial FAM1)           GTTGTCCG------CCTGGTCCTGGACCGCGCT-GATGAACAGGGTCACGTCGTCCCGGACCACACCGG-CGAAGTCGTCCTCCACGAA
III#36 (Partial FAM2)           GTTGTCCGGCACCACCTGGTCCTGGACCGCGCT-GATGAACAGGGTCACGTCGTCCCGGACCACACCGG-CGAAGTCGTCCTCCACGAA
III#43 (Wild-type)              ---------- ---------- ---------- ---------- ---------- ---------- ----------
III#45 (FAM 1&2)                GTTGTCCGGCACCACCTGGTCCTGGACCGCGCT-GATGAACAGGGTCACGTCGTCCCGGACCACACCGG-CGAAGTCGTCCTCCACGAA
III#53 (Partial FAM1)           GTTGTCCGGCACCACCTGGTCCTGGACCGCGCT-GATGAACAGGGTCACGTCGTCCCGGACCACACCGG-CGAAGTCGTCCTCCACGAA
III#61 (FAM 1&2)                GTTGTCCGGCACCACCTGGTCCTGGACCGCGCTTGATGAACAGGGTCACGTCGTCCCGGACCACACCGG-CGAAGTCGTCCTCCACGAA

                                                                                                   FAM 1
Donor (Control)                 GTCCCGGGA---------GAACCCGAGCCGGTCGGTCC-----AGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCGGAAC

                                BleoR
III#6 (Partial FAM2-recovered)  GTCCCGGGAG--------AACCCGAGCCGGTCGGTCC-----AGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCGGAAC
III#8 (Mutated)                 GTCCCGGGA---------GAACCCGAGCCGGTCGGTCC-----AGAACTCGAC-GCTCCGGCGACGTCGCGCGCGGTGAGCACCGGAAC
III#10 (Partial FAM1)           GTCCCGGGA---------GAACCCGAGCCGGTCGGTCCA----AGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCGGAAC
III#14 (Wild-type)              --------- ---------- ---------- ---------- ---------- ---------- ----------A----------
III#17 (Partial FAM2)           GTCCCGGGA---------GAACCCGAGCCGGTCGGTCC-----AGAACTCGACCGCTCC-----------G------------------
III#21 (FAM 1&2)                GTCCCGGGA---------GAACCCGAGCCGGTCGGTCCACAATAGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCGGAAC
III#23 (Partial FAM1)           GTCCCGGGA---------GAACCCGAGCCGGTCGGTCC-----AGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCGGAAC
III#24 (Mutated)                GTCCCGGGAG--------AACCCGAGCCGGTCGGTCC-----AGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCGGA-C
III#27 (Partial FAM1)           GTCCCGGGAG--------AAC----GCCGGTCGGTCC-----AGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCGGAAC
III#32 (Partial FAM1)           GTCCCGGGA---------GAACCCGAGCCGGTCGGTCCA----AGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCGGAAC
III#36 (Partial FAM2)           GTCCCGGGA--------G-AACCCGAGCCGGTCGGTCC-----AGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAG-ACCGGAAC
III#43 (Wild-type)              --------- ---------- ---------- ---------- ---------- ---------- ----------C---------
III#45 (FAM 1&2)                GTCCCGGGATTGGAGCTTGAACCCGAGCCGGTCGGTCC-----AGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCGGAAC
III#53 (Partial FAM1)           GTCCCGGGAG--------AACCCGAGCCGGTCGGTCC-----AGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCGGAAC
III#61 (FAM 1&2)                GTCCCGGGA G-------AACCCGAGCCGGTCGGTCC-----AGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCGGAAC

                                FAM 1
Donor (Control)                 GGCACTGGTCAACTTGGCCATCTACATCTTCACAAGAACACAAGTTTTAAGGGTTGCAAGAGG-AGAGC-------CGGCATTTGTAAA
                                                                                  5' homology arm
                                BleoR          Exon9          Exon8          MAP kinase kinase family protein ...
III#6 (Partial FAM2-recovered)  GGCACTGGTCAACTTGGCCATCTACATCTTCACAAGAACACAAGTTTTAAGGGTTGCAAGAGG-AGAGC-------CGGCATTTGTAAA
III#8 (Mutated)                 GGCACTGGTCAACTTGGCCATCTACATCTTCACAAGAACACAAGTTTTAAGGGTTGCAAGAGG-AGAGC-------CGGCATTTGTAAA
III#10 (Partial FAM1)           GGCACTGGTCAACTTGGCCATCTACATCTTCACAAGAACACAAGTTTTAAGGGTTGCAAGAGG-AGAGCC------GGCATTTGTAAA
III#14 (Wild-type)              ----------CAAGTTTTAAGGGTTGCAAGAGGCAGAGCTTAGGTACGGCATTTGTAAA
III#17 (Partial FAM2)           ----------CAAGAGG-AG-GC-------CGGCATTTGTAAA
III#21 (FAM 1&2)                GGCACTGGTCAACTTGGCCATCTACATCTTCACAAGAACACAAGTTTTAAGGGTTGCAAGAGG-AGAGC-------CGGCATTTGTAAA
III#23 (Partial FAM1)           GGCACTGGTCAACTTGGCCATCTACATCTTCACAAGAACACAAGTTTTAAGGGTTGCAAGAGG-AGAGC-------CGGCATTTGTAAA
III#24 (Mutated)                GGCACTGGTCAACTTGGCCATCTACATCTTCACAAGAACACAAGTTTTAAGGGTTGCAAGAGG-AGAGC-------CGGCATTTGTAAA
III#27 (Partial FAM1)           GGCACTGGTCAACTTGGCCATCTACATCTTCACAAGAACACAAGTTTTAAGGGTTGCAAGAGG-AGAGC-------CGGCATTTGTAAA
III#32 (Partial FAM1)           GGCACTGGTCAACTTGGCCATCTACATCTTCACAAGAACACAAGTTTTAAGGGTTGCAAGAGG-AGAGCC------GGCATTTGTAAA
III#36 (Partial FAM2)           GGCACTGGTCAACTTGGCCATCTACATCTTCACAAGAACACAAGTTTTAAGGGTTGCAAGAGG-AGAGC-------CGGCATTTGTAAA
III#43 (Wild-type)              ----------AAGTTTTAAGGGTTGCAAGAGG-AGAGC-------CGGCATTTGTAAA
III#45 (FAM 1&2)                GGCACTGGTCAACTTGGCCATCTACATCTTCACAAGAACACAAGTTTTAAGGGTTGCAAGAGG-AGAGC-------CGGCATTTGTAAA
III#53 (Partial FAM1)           GGCACTGGTCAACTTGGCCATCTACATCTTCACAAGAACACAAGTTTTAAGGGTTGCAAGAGG-AGAGC-------CGGCATTTGTAAA
III#61 (FAM 1&2)                GGCACTGGTCAACTTGGCCATCTACATCTTCACAAGAACACAAGTTTTAAGGGTTGCAAGAGG-AGAGC-------CGGCATTTGTAAA

                                FAM 1
Donor (Control)                 GTATGTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAA-GAAGAGT
                                5' homology arm
                                MAP kinase kinase family protein CDS
III#6 (Partial FAM2-recovered)  GTATGTCGCGAGATCCACATGCAGGTC---ATACAAGTTCCTGAATGGGTGTGCCTGGTATTG---TTAGAAAGAGAAAA-GAAGAGT
III#8 (Mutated)                 GTATGTCGCGAGATCCACATGCAGGTCC----------TATTGAAATTAGAAAGAGAAAAA-GAAGAGT
III#10 (Partial FAM1)           GTATGTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAA-GAAGAGT
III#14 (Wild-type)              GTATGTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAA-GAAGAGT
III#17 (Partial FAM2)           GTATGTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAA-GAAGAGT
III#21 (FAM 1&2)                GTATGTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAA-GAAGAGT
III#23 (Partial FAM1)           GTATGTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAA-GAAGAGT
III#24 (Mutated)                GTATGTCGCGAGATCCACATGCAGGGCCTCATACAAGACCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAA-GAAGAGT
III#27 (Partial FAM1)           GTATGTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAA-GAAGAGT
III#32 (Partial FAM1)           GTATGTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAA-GAAGAGT
III#36 (Partial FAM2)           GTATGTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAA-GAAGAGT
III#43 (Wild-type)              GTATGTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAGGAAGAGT
III#45 (FAM 1&2)                GTATGTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAA-GAAGAGT
III#53 (Partial FAM1)           GTATGTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAA-GAAGAGT
III#61 (FAM 1&2)                GTATGTCGCGAGATCCACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAA-GAAGAGT
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Donor (Control)                 CAGATCCATGAGCGTCCA-CTAATAGCATACACATGTTTTGAACATATT-GAAAAGAGGCAAAAGAAGGGTGGGATATTAGCAGTCTGC
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Supplementary 6: Allignment of events involved in experiment IV.

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Donor                                TTTTGTGAATTGCTAAT-GGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGTTGATTTATTTCAAGCCACAATGACA--GTTA-AGAATCTTTC--TT
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Donor                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    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IV#9 (FAM1&2)                  GAACTCCATACAAAAAAAGAAATACAATAAGAAAAAA-CATTTGACCAAATGATTTCAAGAAATGATGTG--AAT-GGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTT
IV#13 (Partial FAM2)           GAACTCCATACAAAAAAAGAAAT--AATAAGAAAAAA-CATTTGACCAAATGATTTCAAGAAATGATGTG--AAT-GGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTT
IV#17 (Partial FAM1-recovered) GAACTCCATACAAAAAAAGAAATA-ATTAAGAAAAAA-CATTTGACCAAATGATTTCAAGAAATG-TGTG--AAT-GGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTT
IV#19 (Partial FAM1)           GAACTCCATACAAAAAAAGAAAT--AATAAGAAAAAAGCATTTGACCAAATGATTTCAAGAAATGATGTG--AAT-GGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTT
IV#27 (FAM1&2)                 GAACTCCATACAAAAAAAGAAAT--AATAAGAAAAAA-CATTTGACCAAATGATTTCAAGAAATGATGTG--AAT-GGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTT
IV#32 (Mutated)                GAACTCCATACAAAAAAAGAAAT--AATAAGAAAAAA-CATTTGACCAAATGATTTCAAGAAATGATGTG--AAT-GGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTT
IV#39 (FAM1&2)                 GAACTCCATACAAAAAAAGAAAGGTAATAAGAAAAAA-CATTTGACCAAATGATTTCAAGAAATGATGTG--AAT-GGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTT
IV#45 (FAM1&2)                 GAACTCCATACAAAAAAAGAAAT--AATAAGAAAAAA-CATTTGACCAAATGATTTCAAGAAATGATGTG--AAT-GGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTT
IV#46 (Partial FAM1)           GAACTCCATACAAAAAAAGAAAT--AATAAGAAAAAA-CATTTGACCAAATGATTTCAAGAAATGATGTG--AAT-GGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTT
IV#54 (FAM1&2-recovered)       GAACTCCATACAAAAAAAGAAAT--AATAAGAAAAAA-CATTTGACCAAATGATTTCAAGAAATGATGTG--AAT-GGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTT
IV#60 (Partial FAM1)           GAACTCCATACAAAAAAAGAAAT--AATAAGAAAAAA-CATTTGACCAAATGATTTCAAGAAATGATGTG--AAT-GGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTT
IV#68 (FAM1&2-recovered)       GAACTCCATACAAAAAAAGAAAT--AATAAGAAAAAA-CATTTGACCAAATGATTTCAAGAAATGATGTG--AAT-GGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTT
IV#71 (Wild-type)              GAACTCCATACAAAAAAAGAAAT--AATAAGAAAAAA-CATTTGACCAAATGATTTCAAGAAATGATGTG--AAT-GGGAAAATTAGAC--------------------------
IV#75 (Partila FAM1)           GAACTCCATACAAAAAAAGAAAT--AATAAGAAAAAA-CATTTGACCAAATGATTTCAAGAAATGATGTGGAAAT-GGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTT
IV#76 (Partial FAM2)           GAACTCCATACAAAAAAAGAAAT--AATAAGAAAAAA-CATTTGACCAAATGATTTCAAGAAATGATGTG--AAT-GGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTT
IV#79 (FAM1&2)                 GAACTCCATACAAAAAAAGAAAT--AATAAGAAAAAA-CATTTGACCAAATGATTTCAAGAAATGATGTG--AAT-GGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTT
IV#80 (Partial FAM2)           GAACTCCATACAAAAAAAGAAAT--AATAAGAAAAAA-CATTTGACCAAATGATTTCAAGAAATGATGTG--AAT-GGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTT
IV#83 (FAM1&2)                 GAACTCCATACAAAAAAAGAAAT--AATAAGAAAAAA-CATTTGACCAAATGATTTCAAGAAATGATGTG--AAT-GGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTT
IV#85 (Partial FAM1)           GAACTCCATAC-AAAAAAGAAAT--AATAAGAAAAAA-CATTTGACCAAATGATTTCAAGAAATGATGTG--AATGGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTT
IV#87 (Mutated)                GAACTCCATACAAAAAAAGAAAT--AATAAGAAAAAA-CATTTGACCAAATGATTTCAAGAAATGATGTG--AAT-GGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTT
IV#90 (FAM1&2-recovered)       GAACTCCATACAAAAAAAGAAAT--AATAAGAAAAAA-CATTTGACCAAATGATTTCAAGAAATGATGTG--AAT-GGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTT
IV#92 (Partial FAM2)           GAACTCCATACAAAAAAAGAAAT--AATAAGAAAAAA-CATTTGACCAAATGATTTCAAGAAATGATGTG--AAT-GGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTT
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Donor                          TTTTTTATGATGATGATGATGATGTCAGTCCT-GC--TCCTCGGCCACGAAGT--GCACGCAGTTGCCGGCCGGGTCG-CGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGA
IV#9 (FAM1&2)                  TTTTTTATGATGATGATGATGATGTCAGTCCT-GC--TCCTCGGCCACGAAGT--GCACGCAGTTGCCGGCCGGGTCG-CGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGA
IV#13 (Partial FAM2)           TTTTTTATGATGATGATGATGATGTCAGTCCT-GC--TCCTCGGCCACGAAGT--GCACGCAGTTGCCGGCCGGGTCG-CGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGA
IV#17 (Partial FAM1-recovered) TTTTTTATGATGATGATGATGATGTCAGTCCT-GC--TCCTCGGCCACGAAGT--GCACGCAGTTGCCGGCCGGGTCG-CGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGA
IV#19 (Partial FAM1)           TTTTTTATGATGATGATGATGATGTCAGTCCT-GC--TCCTCGGCCACGAAGT--GCACGCAGTTGCCGGCCGGGTCG-CGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGA
IV#27 (FAM1&2)                 TTTTTTATGATGATGATGATGATGTCAGTCCT-GC--TCCTCGGCCACGAAGT--GCACGCAGTTGCCGGCCGGGTCG-CGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGA
IV#32 (Mutated)                TTTTTTATGATGATGATGATGATGTCAGTCCTGGC--TCCTCGGCCACGAAGT--GCACGCAGTTGCCGGCCGGGTCG-CGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGA
IV#39 (FAM1&2)                 TTTTTTATGATGATGATGATGATGTCAGTCCT-GC--TCCTCGGCCACGAAGT--GCACGCAGTTGCCGGCCGGGTCG-CGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGA
IV#45 (FAM1&2)                 TTTTTTATGATGATGATGATGATGTCAGTCCT-GC--TCCTCGGCCACGAAGT--GCACGCAGTTGCCGGCCGGGTCG-CGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGA
IV#46 (Partial FAM1)           TTTTTTATGATGATGATGATGATGTCAGTCCT-GC--TCCTCGGCCACGAAGT--GCACGCAGTTGCC-GCCGGGTCGCCGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGA
IV#54 (FAM1&2-recovered)       TTTTTTATGATGATGATGATGATGTCAGTCCT-GC--TCCTCGGCCACGAAGT--GCACGCAGTTGCCGGCCGGGTCG-CGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGA
IV#60 (Partial FAM1)           TTTTTTATGATGATGATGATGATGTCAGTCCT-GC--TCCTCGGCCACGAAGTGAGCACGCAGTTGCCGGCCGGGTCG-CGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGA
IV#68 (FAM1&2-recovered)       TTTTTTATGATGATGATGATGATGTCAGTCCT-GC--TCCTCGGCCACGAAGT--GCACGCAGTTGCCGGCCGGGTCG-CGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGA
IV#71 (Wild-type)              ------------------------------- -- ---------------- ------------------------ ------------------------------------
IV#75 (Partila FAM1)           TTTTTTATGATGATGATGATGATGTCAGTCCT-GC--TCCTCGGCCACGAAGT--GCACGCAGTTGCCGGCCGGGTCG-CGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGA
IV#76 (Partial FAM2)           TTTTTTATGATGATGATGATGATGTCAGTCCT-GC--TCCTCGGCCACGAAGT--GCACGCAGTTGCCGGCCGGGTCG-CGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGA
IV#79 (FAM1&2)                 TTTTTTATGATGATGATGATGATGTCAGTCCT-GC--TCCTCGGCCACGAAGT--GCACGCAGTTGCCGGCCGGGTCG-CGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGA
IV#80 (Partial FAM2)           TTTTTTATGATGATGATGATGATGTCAGTCCT-GC--TCCTCGGCCACGAAGT--GCACGCAGTTGCCGGCCGGGTCG-CGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGA
IV#83 (FAM1&2)                 TTTTTTATGATGATGATGATGATGTCAGTCCT-GC--TCCTCGGCCACGAAGT--GCACGCAGTTGCCGGCCGGGTCG-CGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGA
IV#85 (Partial FAM1)           TTTTTTATGATGATGATGATGATGTCAGTCCT-GC--TCCTCGGCCACGAAGT--GCACGCAGTTGCCGGCCGGGTCG-CGCGGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGA
IV#87 (Mutated)                TTTTTTATGATGATGATGATGATGTCAGTCCT-GCAATCCTCGGCCACGAAGT--GCACGCAGTTGCCGGCCGGGTCG-CGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGA
IV#90 (FAM1&2-recovered)       TTTTTTATGATGATGATGATGATGTCAGTCCT-GC--TCCTCGGCCACGAAGT--GCACGCAGTTGCCGGCCGGGTCG-CGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGA
IV#92 (Partial FAM2)           TTTTTTATGATGATGATGATGATGTCAGTCCT-GC--TCCTCGGCCACGAAGT--GCACGCAGTTGCCGGCCGGGTCG-CGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGA
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Donor                          TCT-CGGTCATGGCCGGCCC-GGAGGCGTC-CCGGAAGTTCGTGGA-CACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGC-GCACCCACACCCAGGCC-AGGGTGTTG
IV#9 (FAM1&2)                  TCT-CGGTCATGGCCGGCCC-GGAGGCGTC-CCGGAAGTTCGTGGA-CACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGC-GCACCCACACCCAGGCC-AGGGTGTTG
IV#13 (Partial FAM2)           TCT-CGGTCATGGCCGGCCC-GGAGGCGTC-CCGGAAGTTCGTGGA-CACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGC-GCACCCACACCCAGGCC-AGGGTGTTG
IV#17 (Partial FAM1-recovered) TCT-CGGTCATGGCCGGCCC-GGAGGCGTC-CCGGAAGTTCGTGGA-CACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGC-GCACCCACACCCAGGCC-AGGGTGTTG
IV#19 (Partial FAM1)           TCT-CGGTCATGGCCGGCCC-GGAGGCGT--CCGGAAGTTCGTGGA-CACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGC-GCACCCACACCCAGGCC-AGGGTGTTG
IV#27 (FAM1&2)                 TCT-CGGTCATGGCCGGCCC-GGAGGCGTC-CCGGAAGTTCGTGGA-CACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGC-GCACCCACACCCAGGCC-AGGGTGTTG
IV#32 (Mutated)                TCT-CGGTCATGGCCGGCCC-GGAGGCGTC-CCGGAAGTTCGTGGA-CACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGC-GCACCCACACCCAGGCC-AGGGTGTTG
IV#39 (FAM1&2)                 TCT-CGGTCATGGCCGGCCC-GGAGGCGTC-CCGGAAGTTCGTGGA-CACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGC-GCACCCACACCCAGGCC-AGGGTGTTG
IV#45 (FAM1&2)                 TCT-CGGTCATGGCCGGCCC-GGAGGCGTC-CCGGAAGTTCGTGGATCACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGC-GCACCCACACCCAGGCC-AGGGTGTTG
IV#46 (Partial FAM1)           TCT-CGGTCATGGCCGGCCC-GGAGGCGTC-CCGGAAGTTCGTGGA-CACGACCTCCGACCACTCGGCGTTCAGCTCGTCCAGGCCGC-GCACCCACACCCAGGCC-AGGGTGTTG
IV#54 (FAM1&2-recovered)       TCT-CGGTCATGGCCGGCCC-GGAGGCGTC-CCGGAAGTTCGTGGA-CACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGC-GCACCCACACCCAGGCC-AGGGTGTTG
IV#60 (Partial FAM1)           TCT-CGGTCATGGCCGGCCC-GGAGGCGTC-CCGGAAGTTCGTGGA-CACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGC-GCACCCACACCCAGGCC-AGGGTGTTG
IV#68 (FAM1&2-recovered)       TCT-CGGTCATGGCCGGCCC-GGAGGCGTC-CCGGAAGTTCGTGGA-CACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGC-GCACCCACACCCAGGCC-AGGGTGTTG
IV#71 (Wild-type)              TCT---------------- --------- --------------- ---------------------------------------- ----------------- ---------
IV#75 (Partila FAM1)           TCT-CGGTCATGGGCGGCCC-GGAGGCGTC-CCGGAAGTTCGTGGA-CACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGC-GCACCCACACCCAGGCCTAGGGTGTTG
IV#76 (Partial FAM2)           TCT-CGGTCATGGCCGGCCC-GGAGGCGTCGCCGGAAGTTCGTGGA-CACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGC-GCACCCACACCCAGGCC-AGGGTGTTG
IV#79 (FAM1&2)                 TCT-CGGTCATGGCCGGCCC-GGAGGCGTC-CCGGAAGTTCGTGGA-CACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGC-GCACCCACACCCAGGCC-AGGGTGTTG
IV#80 (Partial FAM2)           TCT-CGGTCATGGCCGGCCC-GGAGGCGTC-CCGGAAGTTCGTGGACCACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGC-CACCCACACCCAGGCC-AGGGTGTTG
IV#83 (FAM1&2)                 TCTCCGGTCATGGCCGGCCC-GGAGGCGTC-CCGGAAGTTCGTGGA-CACGACCTCCGACCACTCGGCGTACAGCTCGTACAGGCCGC-GCACCCACACCCAGGCC-AGGGTGTTG
IV#85 (Partial FAM1)           TCT-CGGTCATGGCCGGCCC-GGAGGCGTC-CCGGAAGTTCGTGGA-CACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGC-GCACCCACACCCAGGCC-AGGGTGTTG
IV#87 (Mutated)                TCT-CGGTCATGGCCGGCCC-GGAGGCGTC-CCGGAAGTTCGTGGA-CACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGCGGCACCCACACCCAGGCCAGCGGTGTTG
IV#90 (FAM1&2-recovered)       TCT-CGGTCATGGCCGGCCC-GGAGGCGTC-CCGGAAGTTCGTGGA-CACGACCTCCGACCACTCGGCGTACAGCTCGTCCAGGCCGC-GCACCCACACCCAGGCC-AGGGTGTTG
IV#92 (Partial FAM2)           TCT-CGGTCATGGCCGGCCCGGGAGGCGTC-CCGGAAGTTCGTGGA-CACGACCTCCGACCACTCGGCGT-CAGCTCGTCCAGGCCGC-GCACCCACACCCAGGCC-AGGGTGTTG
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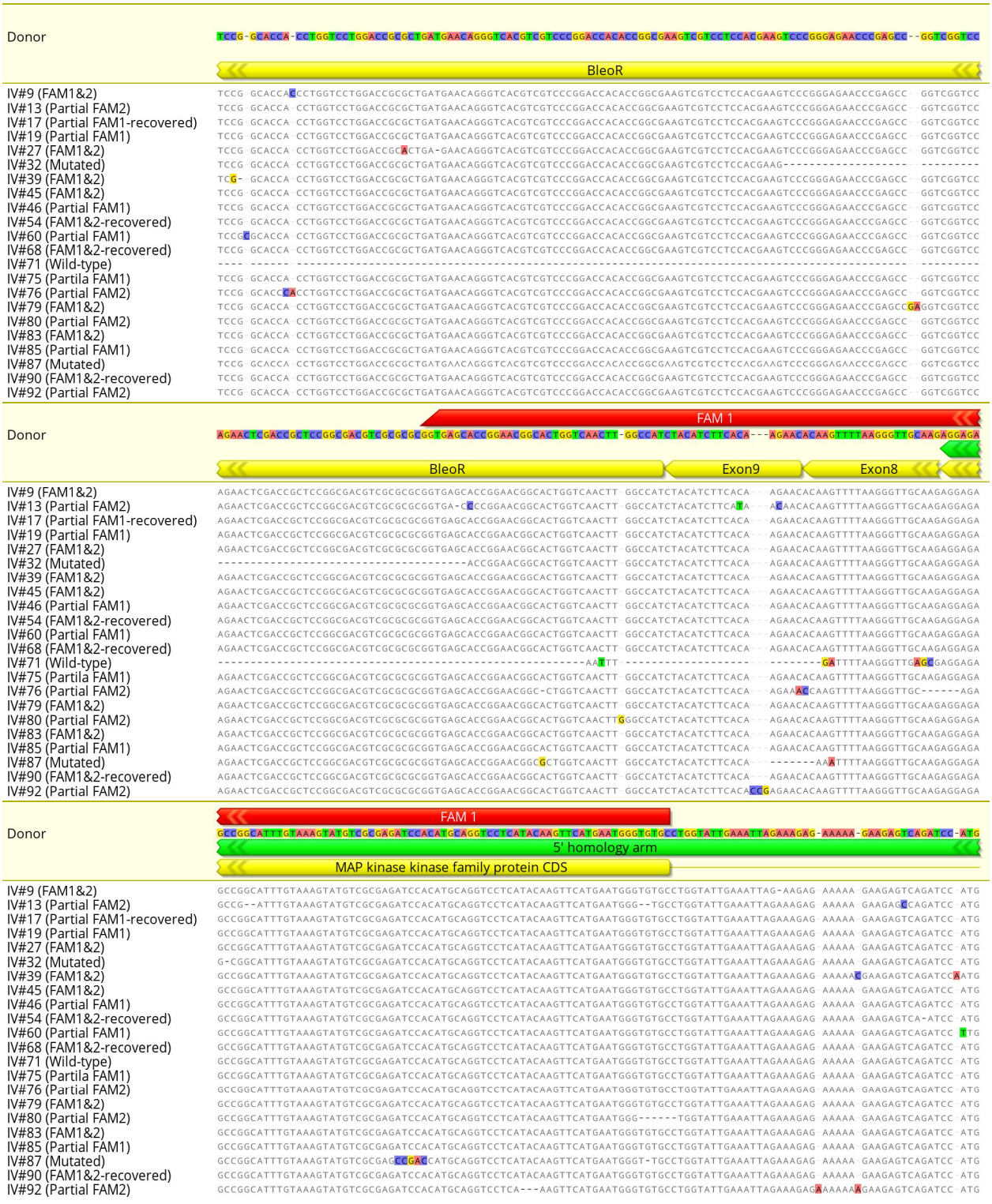
Donor
BleoR
IV#9 (FAM1&2)
IV#13 (Partial FAM2)
IV#17 (Partial FAM1-recovered)
IV#19 (Partial FAM1)
IV#27 (FAM1&2)
IV#32 (Mutated)
IV#39 (FAM1&2)
IV#45 (FAM1&2)
IV#46 (Partial FAM1)
IV#54 (FAM1&2-recovered)
IV#60 (Partial FAM1)
IV#68 (FAM1&2-recovered)
IV#71 (Wild-type)
IV#75 (Partila FAM1)
IV#76 (Partial FAM2)
IV#79 (FAM1&2)
IV#80 (Partial FAM2)
IV#83 (FAM1&2)
IV#85 (Partial FAM1)
IV#87 (Mutated)
IV#90 (FAM1&2-recovered)
IV#92 (Partial FAM2)
FAM 1
Donor
BleoR
Exon9
Exon8
IV#9 (FAM1&2)
IV#13 (Partial FAM2)
IV#17 (Partial FAM1-recovered)
IV#19 (Partial FAM1)
IV#27 (FAM1&2)
IV#32 (Mutated)
IV#39 (FAM1&2)
IV#45 (FAM1&2)
IV#46 (Partial FAM1)
IV#54 (FAM1&2-recovered)
IV#60 (Partial FAM1)
IV#68 (FAM1&2-recovered)
IV#71 (Wild-type)
IV#75 (Partila FAM1)
IV#76 (Partial FAM2)
IV#79 (FAM1&2)
IV#80 (Partial FAM2)
IV#83 (FAM1&2)
IV#85 (Partial FAM1)
IV#87 (Mutated)
IV#90 (FAM1&2-recovered)
IV#92 (Partial FAM2)
FAM 1
Donor
5' homology arm
MAP kinase kinase family protein CDS
IV#9 (FAM1&2)
IV#13 (Partial FAM2)
IV#17 (Partial FAM1-recovered)
IV#19 (Partial FAM1)
IV#27 (FAM1&2)
IV#32 (Mutated)
IV#39 (FAM1&2)
IV#45 (FAM1&2)
IV#46 (Partial FAM1)
IV#54 (FAM1&2-recovered)
IV#60 (Partial FAM1)
IV#68 (FAM1&2-recovered)
IV#71 (Wild-type)
IV#75 (Partila FAM1)
IV#76 (Partial FAM2)
IV#79 (FAM1&2)
IV#80 (Partial FAM2)
IV#83 (FAM1&2)
IV#85 (Partial FAM1)
IV#87 (Mutated)
IV#90 (FAM1&2-recovered)
IV#92 (Partial FAM2)

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Donor                                  -AGCGTCCACTAATAGCATACA-CAT-GTTTTGAACAT-ATTGAAAAG-AGGC---AAAAGAAGGG-TGGG--ATATTAGCAG---TCTGCTGAGTATTAATGACATTCCATATTG
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Supplementary 7: Alignment of events involved in experiment V.

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Donor                          TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
                                                                                 3' homology arm
V#3 (FAM1&2)                   TTTTGTGAAT-TGCTAATGGTTTGAAA-CCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#9 (FAM1&2)                   TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#18 (Partial FAM1)            TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#21 (FAM1&2-recovered)        TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#25 (FAM1&2-recovered)        TTTTGTGAATCTGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#29 (FAM1&2-recovered)        TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#32 (Partial FAM1-recovered)  TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAAGATGTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#33 (FAM1&2)                  TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#37 (Partial FAM2-recovered)  TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#39 (FAM1&2-recovered)        TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#48 (Partial FAM2)            TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#53 (Partial FAM1-recovered)  TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAAGGTGAATC-TTT
V#59 (Partial FAM1-recovered)  TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#64 (Partial FAM2)            TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#67 (FAM1&2)                  TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#73 (FAM1&2-recovered)        TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#75 (Partial FAM2)            TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#79 (FAM1&2)                  TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#80 (Mutated)                 TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATCTTTT
V#82 (Partial FAM1)            TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#85 (Partial FAM2)            TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#86 (Partial FAM1)            TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#88 (FAM1&2-recovered)        TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#89 (Partial FAM2)            TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#91 (FAM1&2-recovered)        TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCAC-ATG-ACAGTTAA---GAATC-TTT
V#92 (FAM1&2)                  TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#94 (FAM1&2-recovered)        TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATGAACAGTTAA---GAATC-TTT
V#95 (Partial FAM1)            TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#97 (Partial FAM1)            TTTTGTGAAT-TGCTAATGGTTTGAAACCCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#98 (Partial FAM2)            TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT
V#101 (FAM1&2)                 TTTTGTGAAT-TGCTAATGGTTTGAAAACCTCAGCCCTGGTCACTGTAATTTCAGCAA---GTTGATTTATTTCAAGCCACAATG-ACAGTTAA---GAATC-TTT

Donor                          CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
                                                                                 3' homology arm
V#3 (FAM1&2)                   CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#9 (FAM1&2)                   CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#18 (Partial FAM1)            CT--TCAGGCCTTCAAAATTTCAATAGATAACTCCC-- ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#21 (FAM1&2-recovered)        CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#25 (FAM1&2-recovered)        CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#29 (FAM1&2-recovered)        CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#32 (Partial FAM1-recovered)  CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#33 (FAM1&2)                  CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#37 (Partial FAM2-recovered)  CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#39 (FAM1&2-recovered)        CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#48 (Partial FAM2)            CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#53 (Partial FAM1-recovered)  CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#59 (Partial FAM1-recovered)  CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#64 (Partial FAM2)            CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#67 (FAM1&2)                  CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTC-ACTCTAAA-GTACA--
V#73 (FAM1&2-recovered)        CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#75 (Partial FAM2)            CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#79 (FAM1&2)                  CTCATCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#80 (Mutated)                 CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#82 (Partial FAM1)            CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#85 (Partial FAM2)            CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#86 (Partial FAM1)            CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTC-AACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#88 (FAM1&2-recovered)        CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCCAGATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#89 (Partial FAM2)            CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#91 (FAM1&2-recovered)        CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#92 (FAM1&2)                  CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAAGGTACAGC
V#94 (FAM1&2-recovered)        CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#95 (Partial FAM1)            CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTTTTTCAACTCTAAA-GTACA--
V#97 (Partial FAM1)            CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#98 (Partial FAM2)            CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAG--TATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
V#101 (FAM1&2)                 CT--TCAGGCCTTCAAAATTTCAATAGATAACTTCCC--ATAACTCTCAAGAGTCTGATATAGTCTATCTGCACTTGTCAAACACAATGGCTTAAATTCAACTCTAAA-GTACA--
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Donor                                  TGAATTC-TCATAAGAGTTATGGTCGACATGGTAAATGCATTAATTGC-AT--AGACAC---AGGC-GAACTATTAAATGA-TTAATAAGACTTGGATTATGCAACTACATCT-TC
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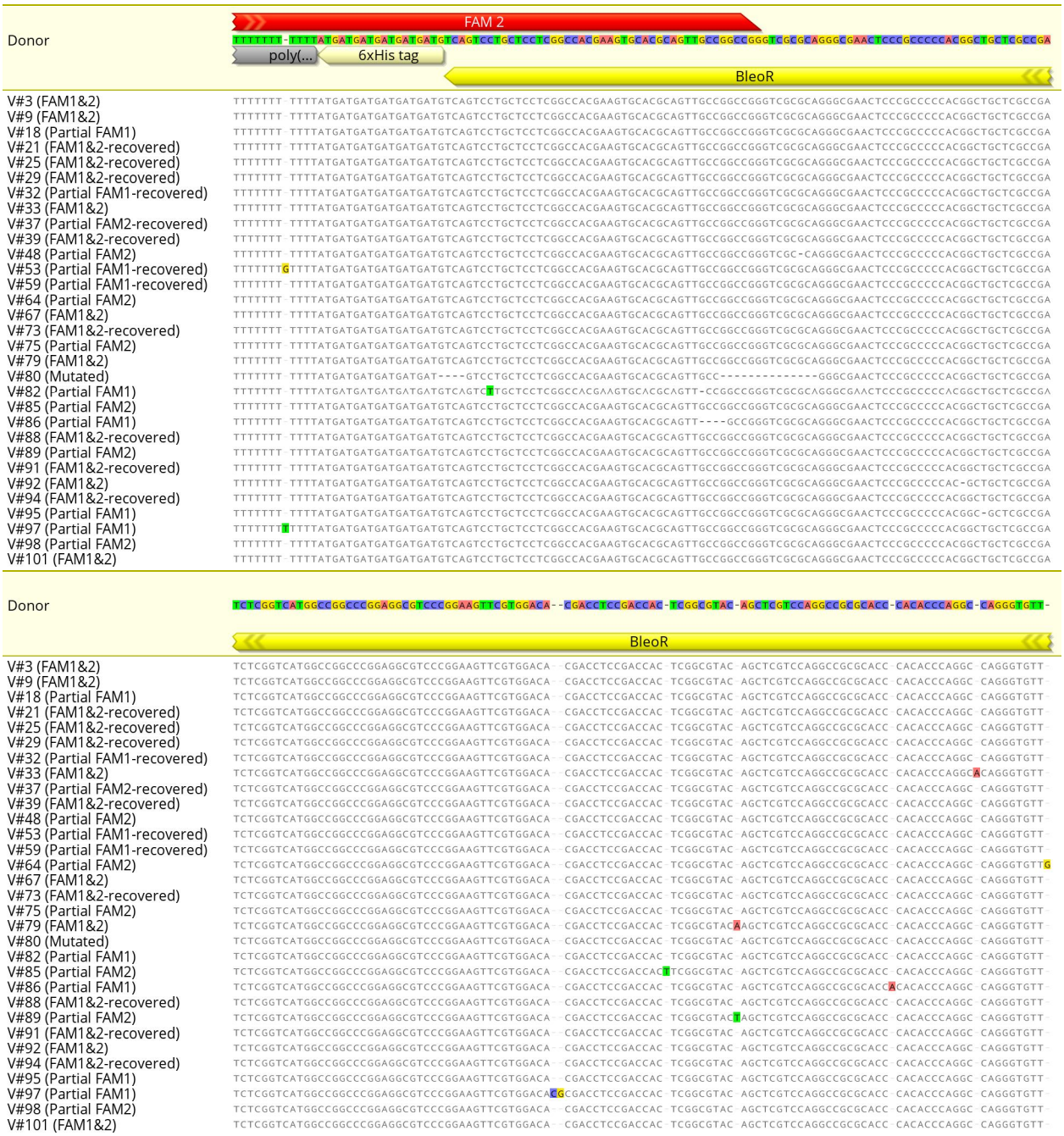
Donor
FAM 2
poly(...
6xHis tag
BleoR
V#3 (FAM1&2)
V#9 (FAM1&2)
V#18 (Partial FAM1)
V#21 (FAM1&2-recovered)
V#25 (FAM1&2-recovered)
V#29 (FAM1&2-recovered)
V#32 (Partial FAM1-recovered)
V#33 (FAM1&2)
V#37 (Partial FAM2-recovered)
V#39 (FAM1&2-recovered)
V#48 (Partial FAM2)
V#53 (Partial FAM1-recovered)
V#59 (Partial FAM1-recovered)
V#64 (Partial FAM2)
V#67 (FAM1&2)
V#73 (FAM1&2-recovered)
V#75 (Partial FAM2)
V#79 (FAM1&2)
V#80 (Mutated)
V#82 (Partial FAM1)
V#85 (Partial FAM2)
V#86 (Partial FAM1)
V#88 (FAM1&2-recovered)
V#89 (Partial FAM2)
V#91 (FAM1&2-recovered)
V#92 (FAM1&2)
V#94 (FAM1&2-recovered)
V#95 (Partial FAM1)
V#97 (Partial FAM1)
V#98 (Partial FAM2)
V#101 (FAM1&2)
Donor
BleoR
V#3 (FAM1&2)
V#9 (FAM1&2)
V#18 (Partial FAM1)
V#21 (FAM1&2-recovered)
V#25 (FAM1&2-recovered)
V#29 (FAM1&2-recovered)
V#32 (Partial FAM1-recovered)
V#33 (FAM1&2)
V#37 (Partial FAM2-recovered)
V#39 (FAM1&2-recovered)
V#48 (Partial FAM2)
V#53 (Partial FAM1-recovered)
V#59 (Partial FAM1-recovered)
V#64 (Partial FAM2)
V#67 (FAM1&2)
V#73 (FAM1&2-recovered)
V#75 (Partial FAM2)
V#79 (FAM1&2)
V#80 (Mutated)
V#82 (Partial FAM1)
V#85 (Partial FAM2)
V#86 (Partial FAM1)
V#88 (FAM1&2-recovered)
V#89 (Partial FAM2)
V#91 (FAM1&2-recovered)
V#92 (FAM1&2)
V#94 (FAM1&2-recovered)
V#95 (Partial FAM1)
V#97 (Partial FAM1)
V#98 (Partial FAM2)
V#101 (FAM1&2)

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Donor                      GTCCGGC-ACCACCTGGTCCTGGACCGCGCTGATGA---ACAGGGTCACGTCGTCCC---GGACCA--CACCGGCG---AAGTCGTCCTCCA-CGAAGTCCCGGGAGAACCCGAGC

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Donor                 FAM 1
                      TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
                      5' homology arm
                      MAP kinase kinase family protein CDS
V#3 (FAM1&2)          TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#9 (FAM1&2)          TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#18 (Partial FAM1)   TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#21 (FAM1&2-recovered)  TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#25 (FAM1&2-recovered)  TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#29 (FAM1&2-recovered)  TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#32 (Partial FAM1-recovered)  TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#33 (FAM1&2)         TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#37 (Partial FAM2-recovered)  TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#39 (FAM1&2-recovered)  TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#48 (Partial FAM2)   TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCGGCAAGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#53 (Partial FAM1-recovered)  TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#59 (Partial FAM1-recovered)  TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#64 (Partial FAM2)   TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCCTGACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#67 (FAM1&2)         TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#73 (FAM1&2-recovered)  TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#75 (Partial FAM2)   TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#79 (FAM1&2)         TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#80 (Mutated)        TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG CCAGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#82 (Partial FAM1)   TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#85 (Partial FAM2)   TTGCAAGAGGAG-GCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#86 (Partial FAM1)   TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#88 (FAM1&2-recovered)  TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#89 (Partial FAM2)   TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#91 (FAM1&2-recovered)  TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#92 (FAM1&2)         TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#94 (FAM1&2-recovered)  TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#95 (Partial FAM1)   TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#97 (Partial FAM1)   TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#98 (Partial FAM2)   TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGATTCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG
V#101 (FAM1&2)        TTGCAAGAGGAGAGCCGGCATTTGTAAAGTATGTCGCG---AGA-TCC--ACATGCAGGTCCTCATACAAGTTCATGAATGGGTGTGCCTGGTATTGAAATTAGAAAGAGAAAAAG

Donor                 AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
                      5' homology arm
V#3 (FAM1&2)          AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#9 (FAM1&2)          AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#18 (Partial FAM1)   AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#21 (FAM1&2-recovered)  AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#25 (FAM1&2-recovered)  AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#29 (FAM1&2-recovered)  AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG--CATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#32 (Partial FAM1-recovered)  AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#33 (FAM1&2)         AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#37 (Partial FAM2-recovered)  AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACATGGTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#39 (FAM1&2-recovered)  AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTGAACAACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAAGTGAC
V#48 (Partial FAM2)   AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#53 (Partial FAM1-recovered)  AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#59 (Partial FAM1-recovered)  AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#64 (Partial FAM2)   AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#67 (FAM1&2)         AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#73 (FAM1&2-recovered)  -AGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#75 (Partial FAM2)   AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#79 (FAM1&2)         AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#80 (Mutated)        AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#82 (Partial FAM1)   AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#85 (Partial FAM2)   AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#86 (Partial FAM1)   AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAACGAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#88 (FAM1&2-recovered)  AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#89 (Partial FAM2)   AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#91 (FAM1&2-recovered)  AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGCTCTATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#92 (FAM1&2)         AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#94 (FAM1&2-recovered)  AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#95 (Partial FAM1)   AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#97 (Partial FAM1)   AAGAGTCAGATCCATGAGCGTCCACTAATCGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#98 (Partial FAM2)   AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
V#101 (FAM1&2)        AAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT-GTTTTG---AACATATTGAAAAGAGGCAAAA-GAAGGGTGGG---ATATTAGCAGTCTGCTGAGTATTAA-TGAC
```

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Donor                   ATTCCATATTGATAGAGAGGAGAAAAGAGTAAA--GGACGTGGAGTGCCAGTAACAGGCAG---ACAGCTAATTGCCCCACCCAGTTTAACAATCAT------AGGACTTC-AAAT
                        <<<
```

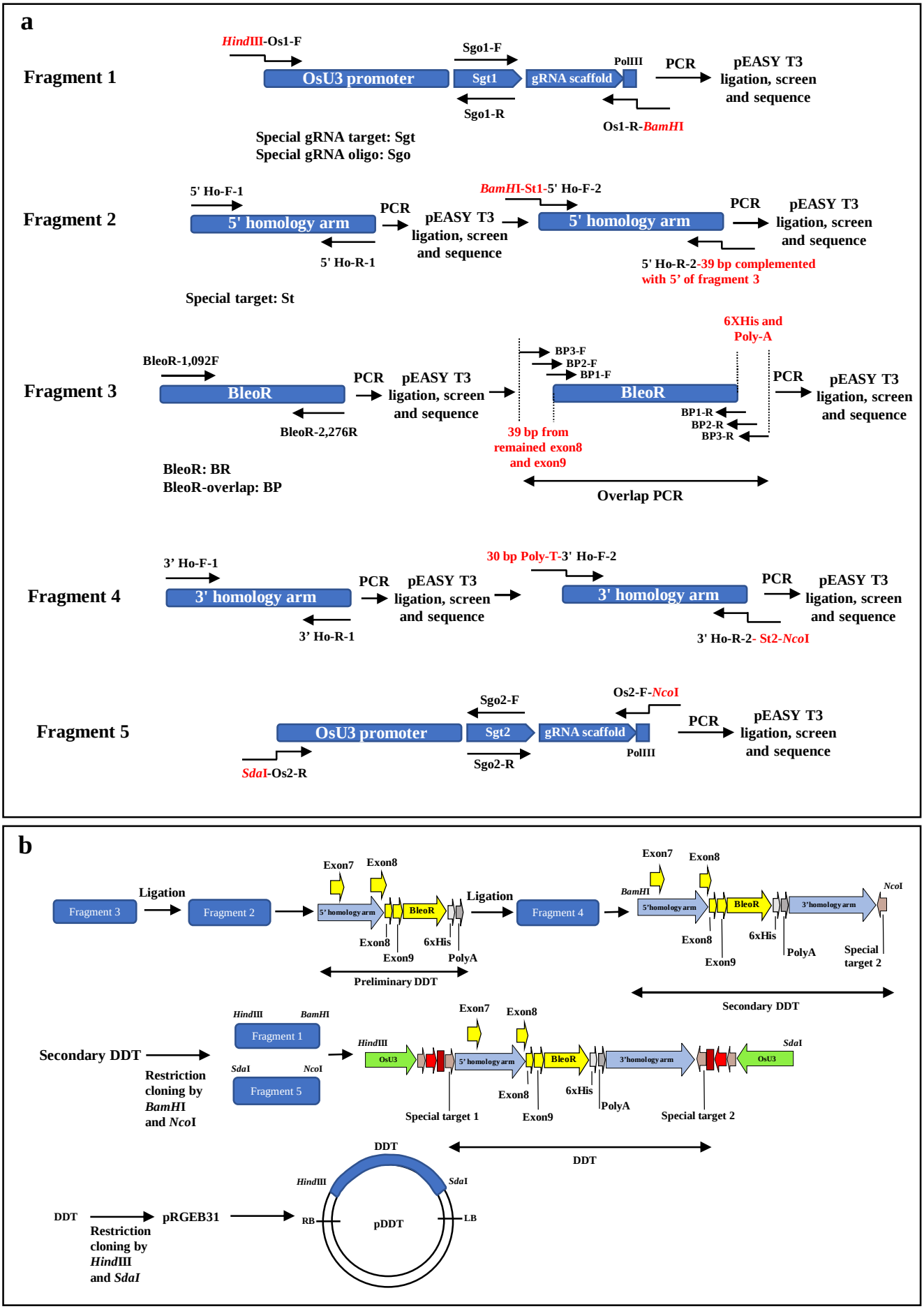
a

	Ex.I	Ex.II	Ex.III	Ex.IV	Ex.V
Event-1	0.001341	0.218214	0.222401	0.224571	0.212052
Event-2	0.000479	-0.003374	-0.005283	0.232881	0.218487
Event-3	0.005560	-0.003572	-0.001727	0.228651	0.211959
Event-4	0.000002	-0.005070	-0.004172	0.219351	0.207729
Event-5	-0.002166	-0.001216	-0.007625	0.001762	0.215642
Event-6	0.007921	-0.005845	-0.002696	-0.002184	0.223132
Event-7	-0.004246	0.002081	0.006539	0.002051	0.211527
Event-8	-0.002188	0.001357	0.001354	0.001351	0.226069
Event-9	0.004493	-0.006539	-0.001964	-0.000494	0.210693
Event-10	-0.000359	-0.010235	-0.000999	0.003170	0.213876
Event-11	-0.002152	-0.006556	-0.006290	-0.001712	0.210325
Event-12	0.006629	0.000466	-0.002540	0.006862	0.212543

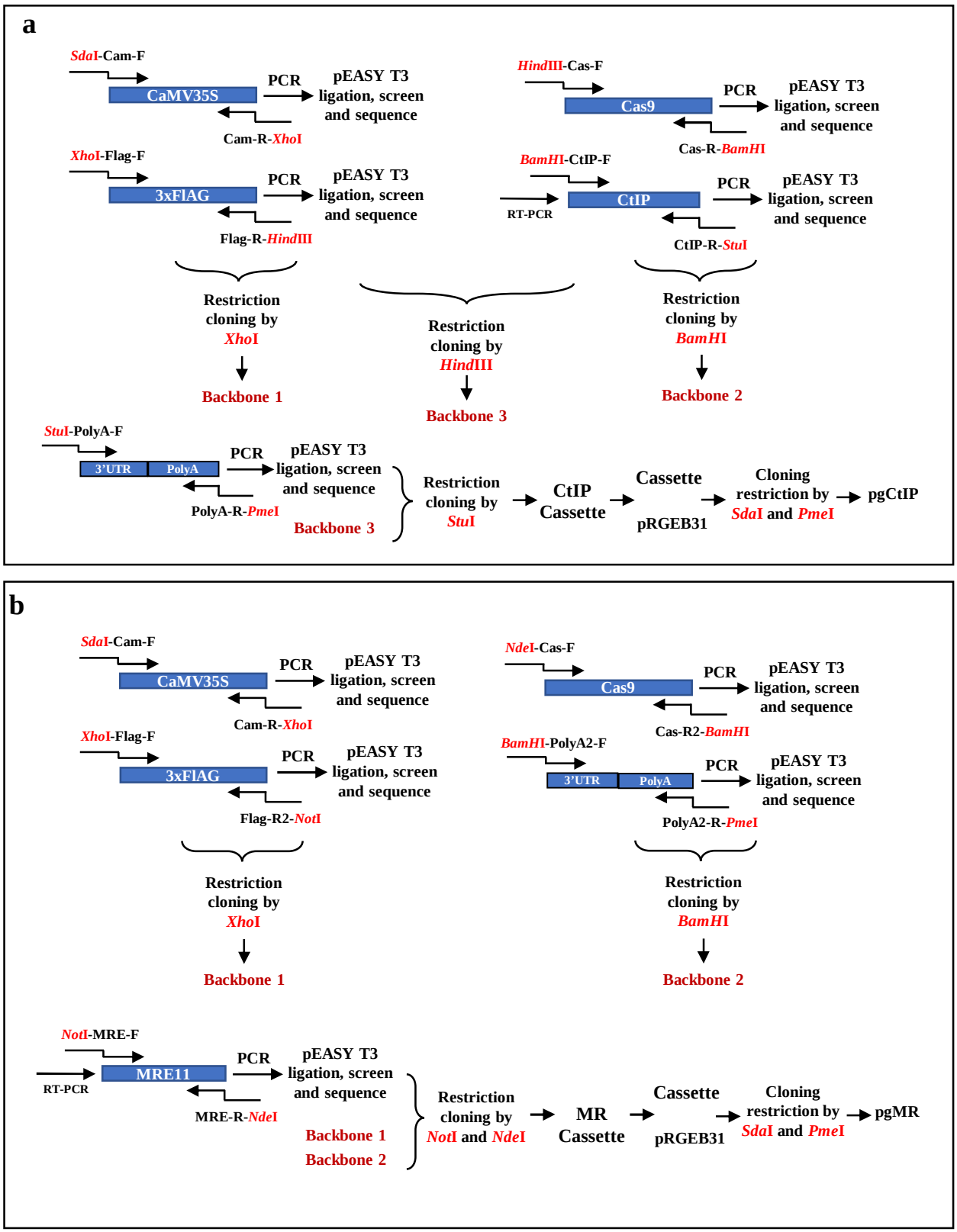
b

	Mean	Standard Deviation	SE of Mean
Ex.I	0.00128	0.00396	0.00114
Ex.II	0.01498	0.06411	0.01851
Ex.III	0.01642	0.06497	0.01876
Ex.IV	0.07636	0.11085	0.032
EX.V	0.2145	0.00547	0.00158

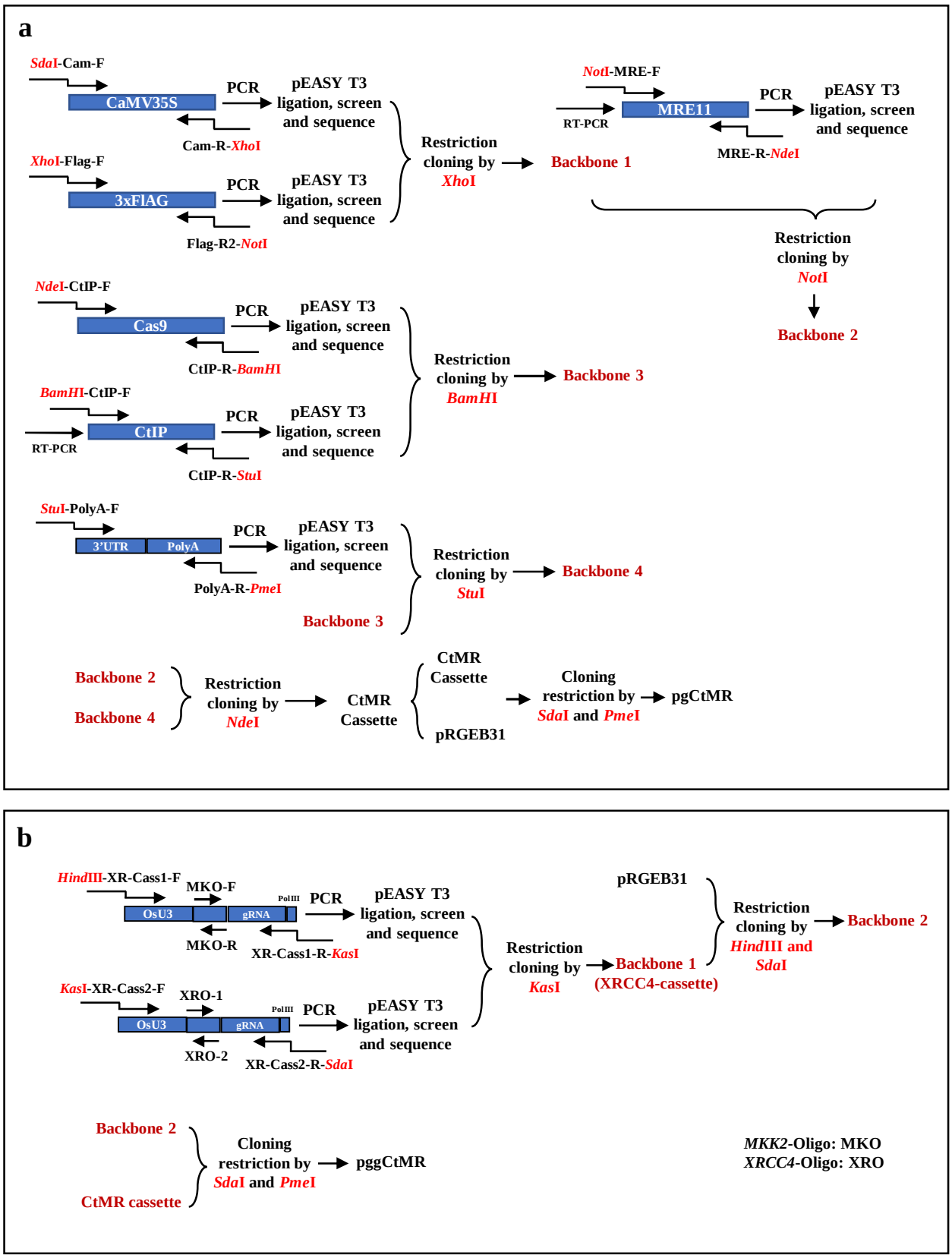
Supplementary 8: The raw data of real-time PCR to evaluate percentage of delta-delta C_t mean from *BleoR* in the all experiments. **a**, Delta-delta C_t mean raw data calculated from 12 biological replicates with three technical repeats. **b**, Descriptive statistic table of raw data calculated by ANOVA-One way.



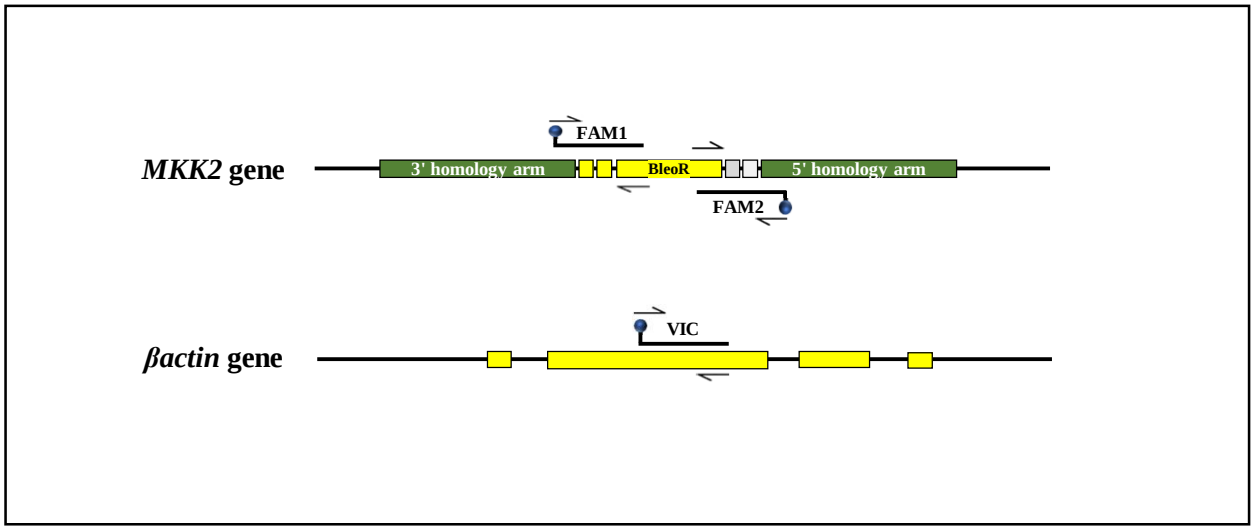
Supplementary 9: Schematic construction of DDT and pDDT fragments, primers and oligos.



Supplementary 10: Schematic construction of cassettes (CtIP and MR) and vectors (pgCtIP and pgMR) and their primers.

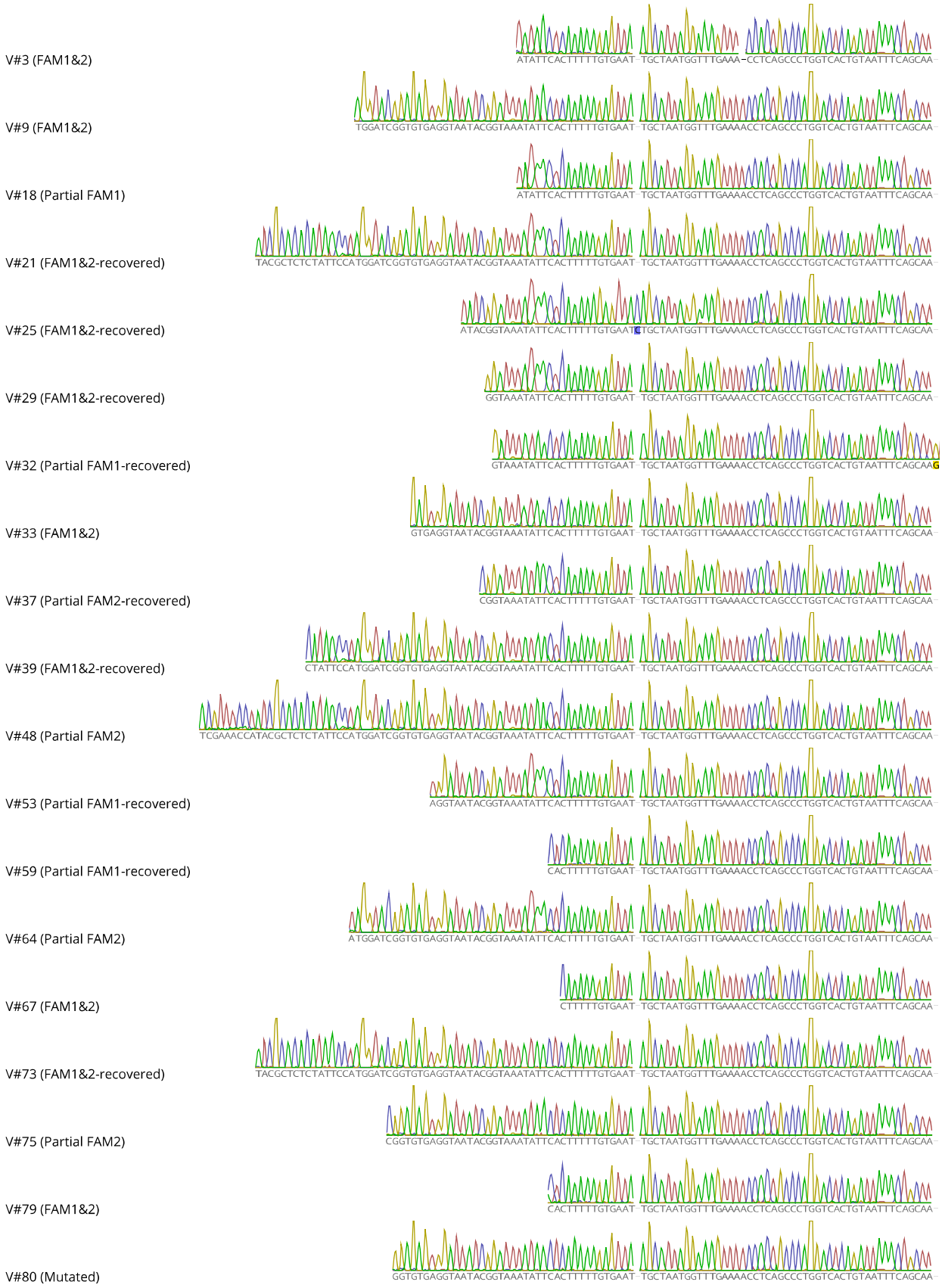


Supplementary 11: Schematic construction of cassettes (CtMR, XRCC4) and vectors (pgCtMR and pggCtMR) and their primers.

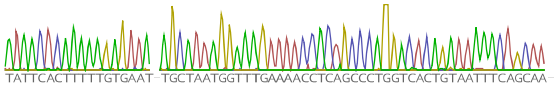


Supplementary 12: Schematic of TaqMan real-time PCR FAM and VIC target assays in this study. Yellow rectangles exhibited CDS.

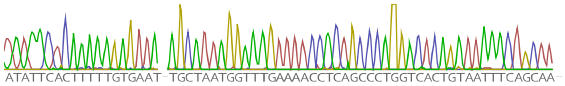
Supplementary 13: Chromatogram allignments of events included in experiment V.



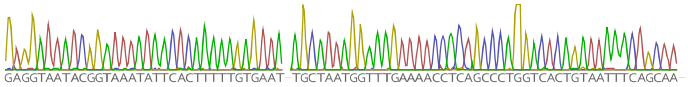
V#82 (Partial FAM1)



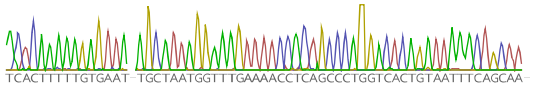
V#85 (Partial FAM2)



V#86 (Partial FAM1)



V#88 (FAM1&2-recovered)



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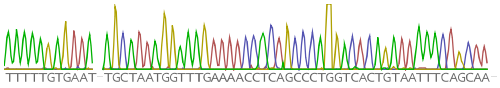
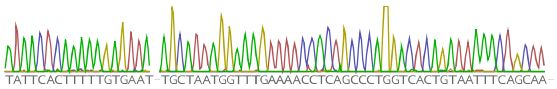
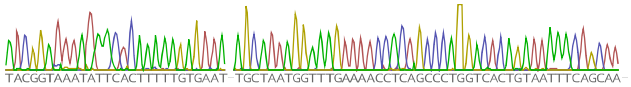


V#91 (FAM1&2-recovered)



V#92 (FAM1&2)



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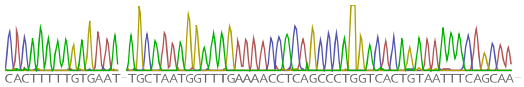

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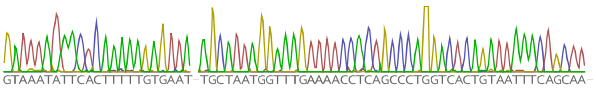

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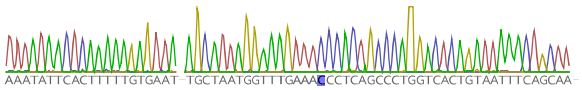

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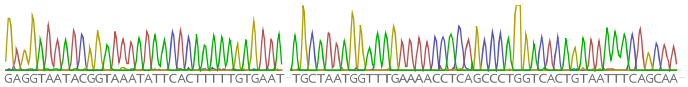
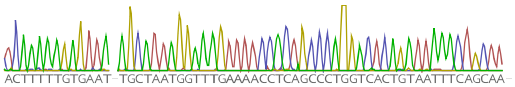
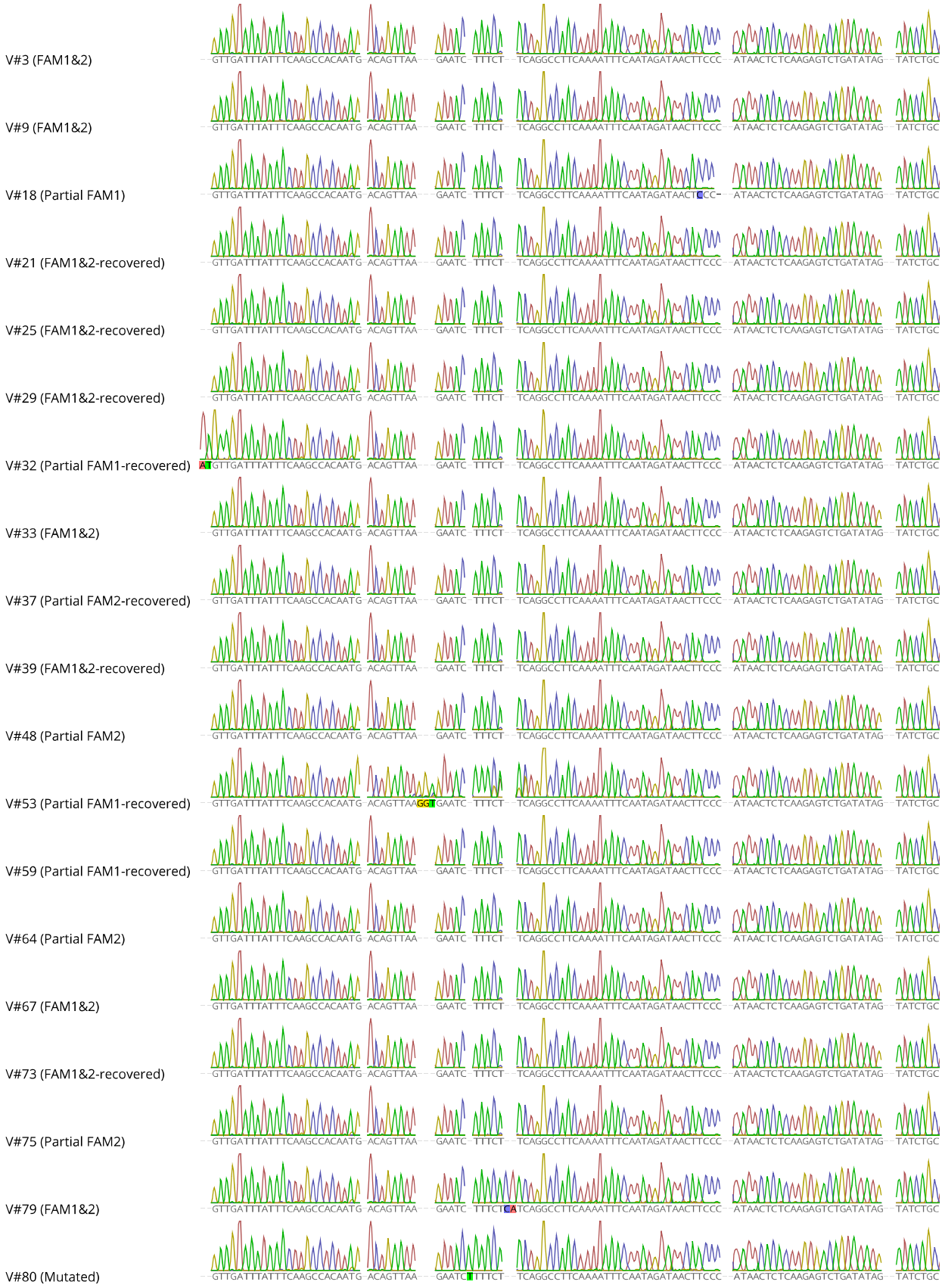


V#101 (FAM1&2)




V#3 (FAM1&2)
V#9 (FAM1&2)
V#18 (Partial FAM1)
V#21 (FAM1&2-recovered)
V#25 (FAM1&2-recovered)
V#29 (FAM1&2-recovered)
V#32 (Partial FAM1-recovered)
V#33 (FAM1&2)
V#37 (Partial FAM2-recovered)
V#39 (FAM1&2-recovered)
V#48 (Partial FAM2)
V#53 (Partial FAM1-recovered)
V#59 (Partial FAM1-recovered)
V#64 (Partial FAM2)
V#67 (FAM1&2)
V#73 (FAM1&2-recovered)
V#75 (Partial FAM2)
V#79 (FAM1&2)
V#80 (Mutated)
GTTGATTTTATTTCAAGCCACAATG
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GAATC
TTTCT
TCAGGCCTTCAAAATTTCAATAGATAACTTCCC
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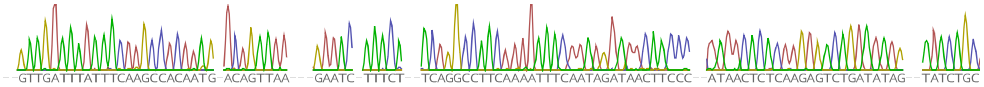
TATCTGC

V#82 (Partial FAM1)



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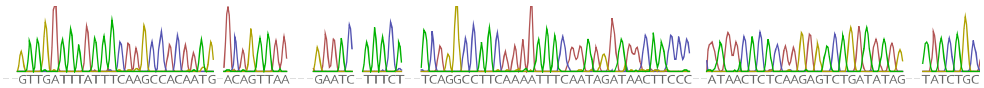

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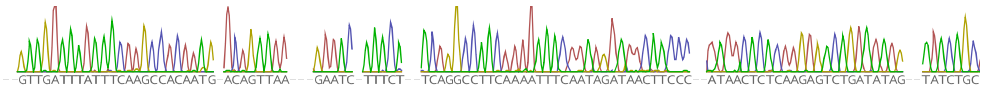
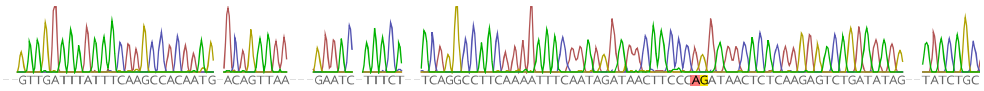
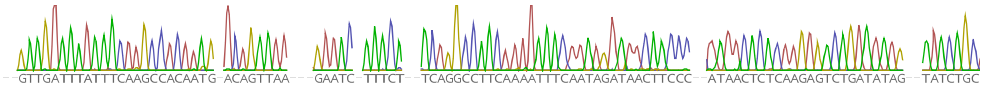


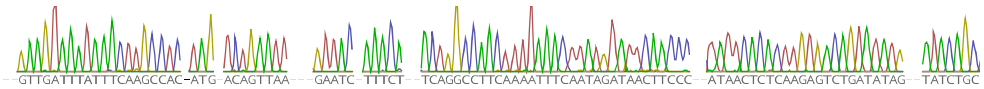
V#88 (FAM1&2-recovered)



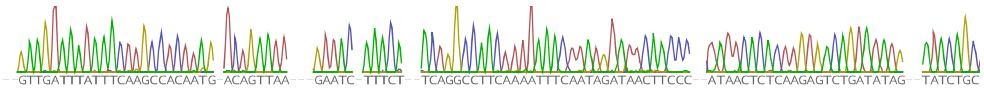
V#89 (Partial FAM2)



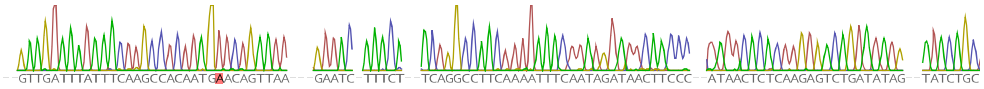
V#91 (FAM1&2-recovered)



V#92 (FAM1&2)



V#94 (FAM1&2-recovered)



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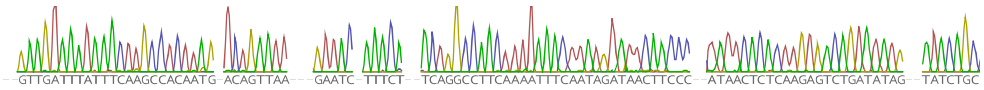

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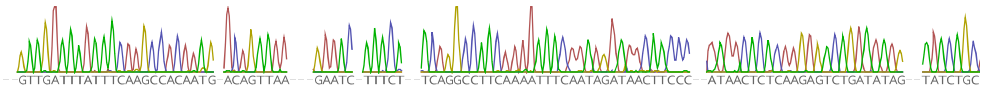

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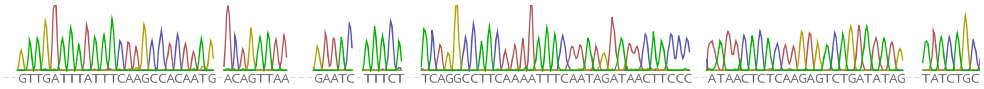
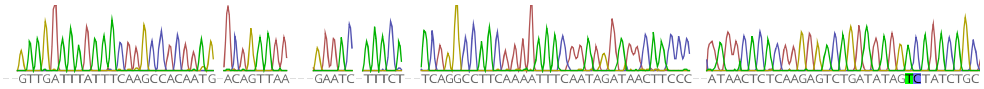


V#101 (FAM1&2)



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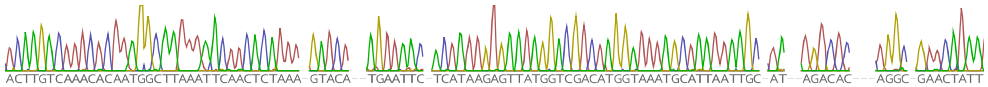
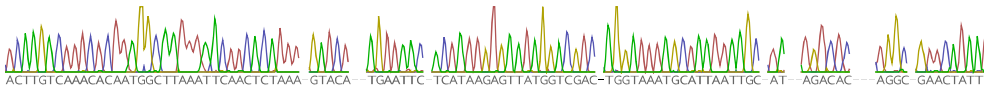


V#9 (FAM1&2)



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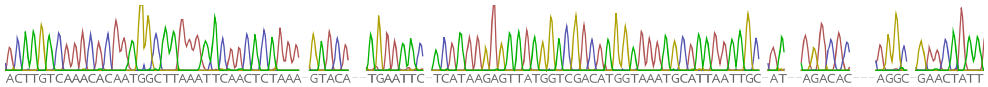
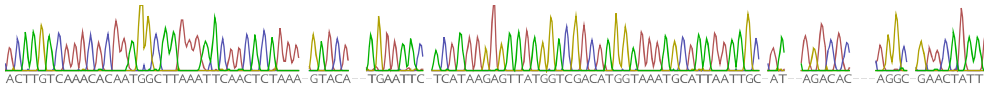


V#21 (FAM1&2-recovered)



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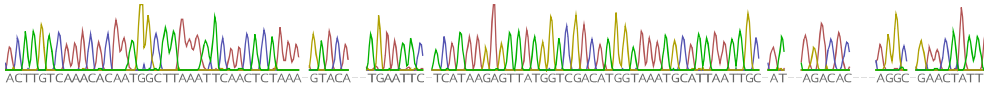
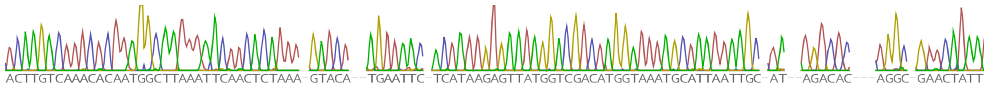


V#29 (FAM1&2-recovered)



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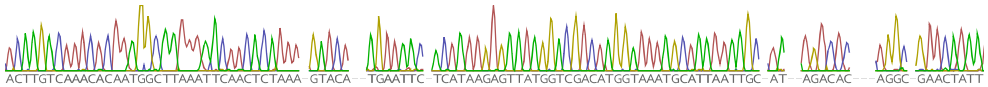
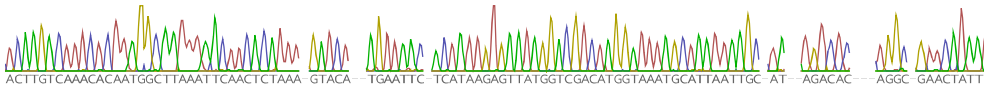
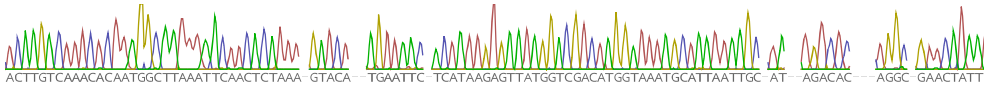


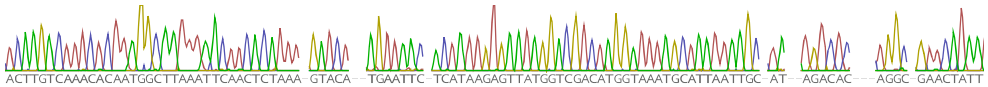
V#33 (FAM1&2)



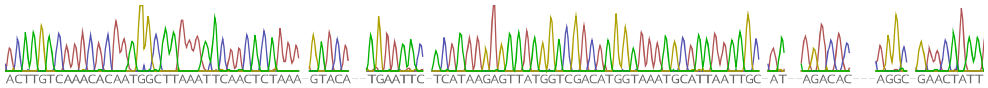
V#37 (Partial FAM2-recovered)



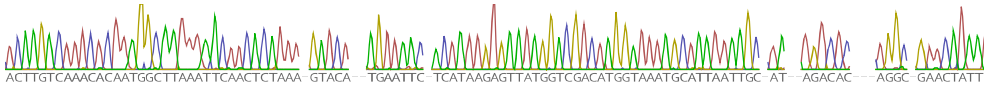
V#39 (FAM1&2-recovered)



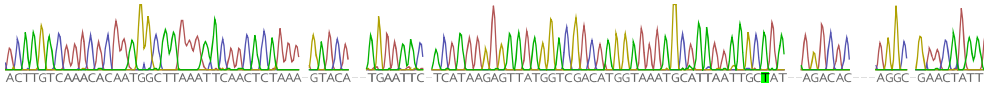
V#48 (Partial FAM2)



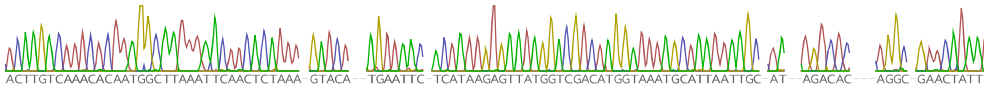
V#53 (Partial FAM1-recovered)



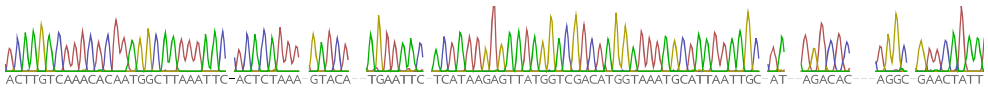
V#59 (Partial FAM1-recovered)



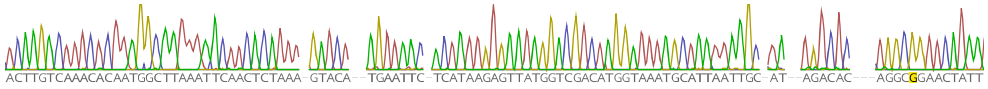
V#64 (Partial FAM2)



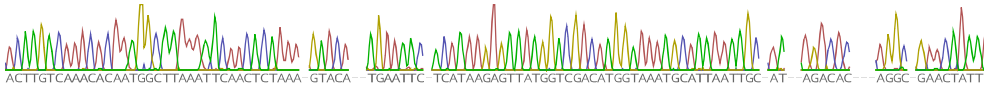
V#67 (FAM1&2)



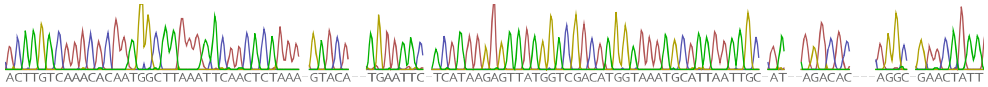
V#73 (FAM1&2-recovered)



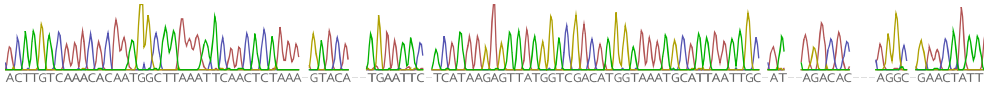
V#75 (Partial FAM2)



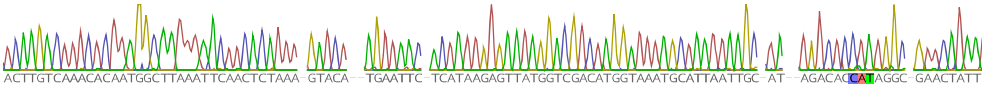
V#79 (FAM1&2)



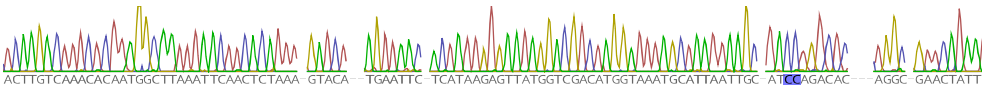
V#80 (Mutated)



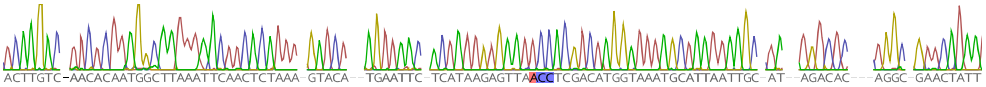
V#82 (Partial FAM1)



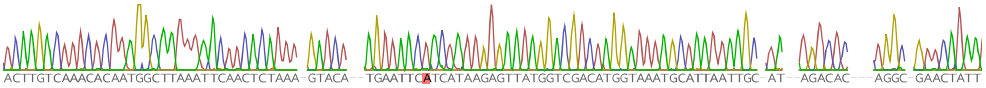
V#85 (Partial FAM2)



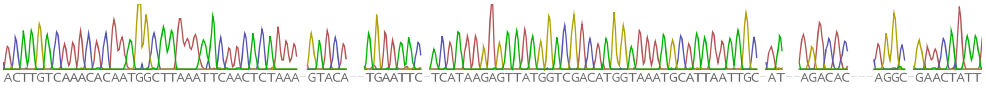
V#86 (Partial FAM1)



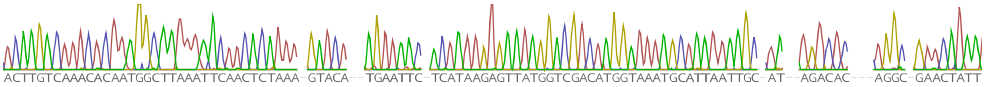
V#88 (FAM1&2-recovered)



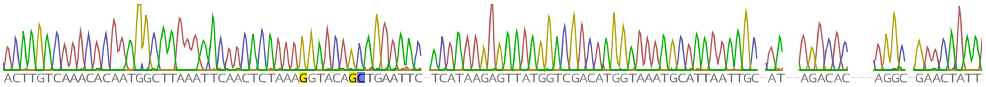
V#89 (Partial FAM2)



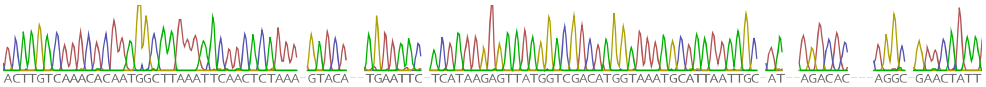
V#91 (FAM1&2-recovered)



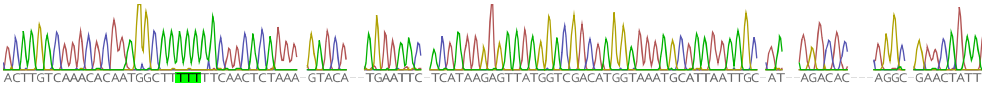
V#92 (FAM1&2)



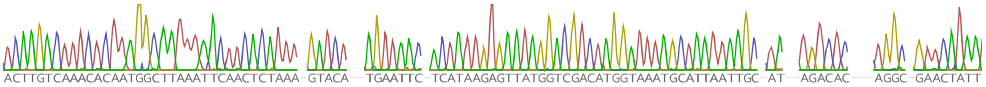
V#94 (FAM1&2-recovered)



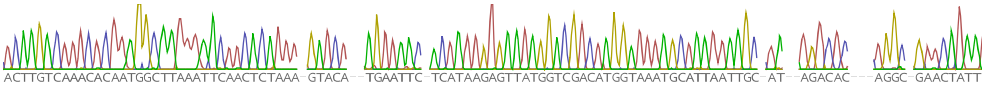
V#95 (Partial FAM1)



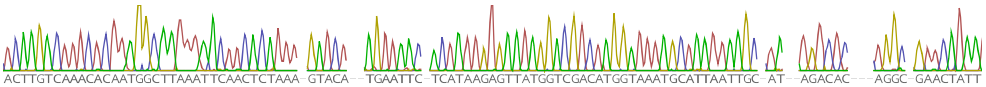
V#97 (Partial FAM1)



V#98 (Partial FAM2)



V#101 (FAM1&2)



V#3 (FAM1&2)
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V#9 (FAM1&2)
AAATGA TTAATAAGACTTGGATTATGCAACTACATCT TCACAAGAACTCCATAC AAAAAAAGAAATAATAAGAAAAAACATTTGACC AAATGATTTCAAGAAATGAT GTG
V#18 (Partial FAM1)
AAATGA TTAATAAGACTTGGATTATGCAACTACATCT TCACAAGAACTCCATAC AAAAAAAGAAATAATAAGAAAAAACATTTGACC AAATGATTTCAAGAAATGATGGTG
V#21 (FAM1&2-recovered)
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V#25 (FAM1&2-recovered)
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V#29 (FAM1&2-recovered)
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V#32 (Partial FAM1-recovered)
AAATGATTTAATAAGACTTGGATTATGCAACTACATCT TCACAAGAACTCCATAC AAAAAAAGAAATAATAAGAAAAAACATTTGACC -AATGATTTCAAGAAATGAT GTG
V#33 (FAM1&2)
AAATGA TTAATAAGACTTGGATTATGCAACTACATCT TCACAAGAACTCCATAC AAAAAAAGAAATAATAAGAAAAAACATTTGACC AAATGATTTCAAGAAATGAT GTG
V#37 (Partial FAM2-recovered)
AAATGA TTAATAAGACTTGGATTATGCAACTACATCT TCACAAGAACTCCATAC AAAAAAAGAAATAATAAGAAAAAACATTTGACC AAATGATTTCAAGAAATGAT GTG
V#39 (FAM1&2-recovered)
AAATGA TTAATAAGACTTGGATTATGCAACTACATCT TCAC-AGAACTCCATAC AAAAAAAGAAATAATAAGAAAAAACATTTGACC AAATGATTTCAAGAAATGAT GTG
V#48 (Partial FAM2)
AAATGA TTAATAAGACTTGGATTATGCAACTACATCTGTCACAAGAACTCCATAC AAAAAAAGAAATAATAAGAAAAAACATTTGACC AAATGATTTCAAGAAATGAT GTG
V#53 (Partial FAM1-recovered)
AAATGA TTAATAAGACTTGGATTATGCAACTACATCT TCACAAGAACTCCATAC AAAAAAAGAAATAATAAGAAAAAACATTTGACC AAATGATTTCAAGAAATGAT GTG
V#59 (Partial FAM1-recovered)
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V#64 (Partial FAM2)
AAATGA TTAATAAGACTTGGATTATGCAACTACATCT TCACAAGAACTCCATAC AAAAAAAGAAATAATAAGAAAAAACATTTGACC AAATGATTTCAAGAAATGAT GTG
V#67 (FAM1&2)
AAATGA TTAATAAGACTTGGATTATGCAACTACATCT TCACAAGAACTCCATAC AAAAAAAGAAATAATAAGAAAAAACATTTGACC AAATGATTTCAAGAAATGAT GTG
V#73 (FAM1&2-recovered)
AAATGA TTAATAAGACTTGGATTATGCAACTACATCT TCACAAGAACTCCATAC AAAAAAAGAAATAATAAGAAAAAACATTTGACC AAATGATTTCAAGAAATGAT GTG
V#75 (Partial FAM2)
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V#79 (FAM1&2)
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V#80 (Mutated)
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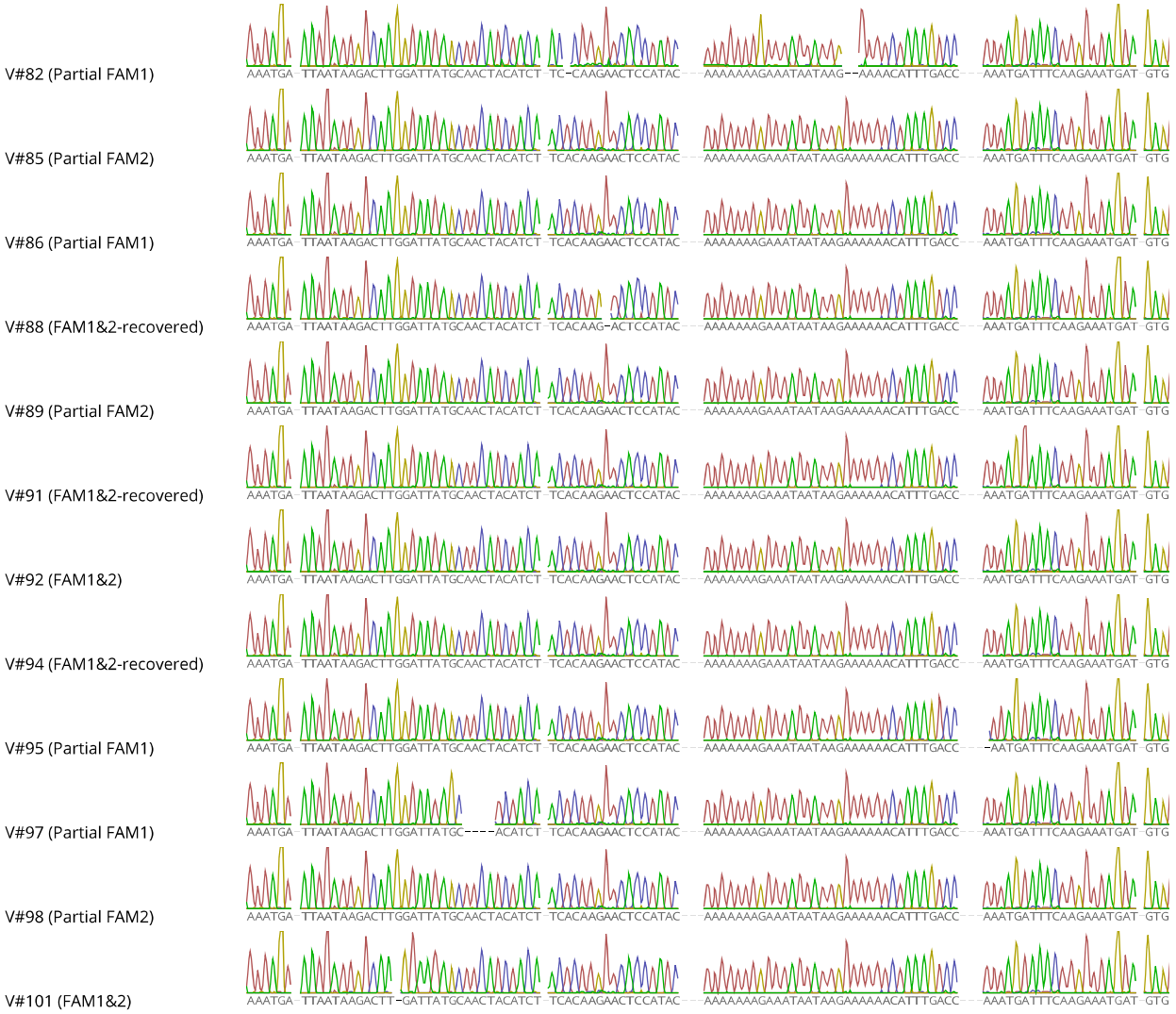
V#82 (Partial FAM1)
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V#85 (Partial FAM2)
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V#86 (Partial FAM1)
AAATGA TTAATAAGACTTGGATTATGCAACTACATCT TCACAAGAACTCCATAC AAAAAAAGAAATAATAAGAAAAAACATTTGACC AAATGATTTCAAGAAATGAT GTG
V#88 (FAM1&2-recovered)
AAATGA TTAATAAGACTTGGATTATGCAACTACATCT TCACAAG-ACTCCATAC AAAAAAAGAAATAATAAGAAAAAACATTTGACC AAATGATTTCAAGAAATGAT GTG
V#89 (Partial FAM2)
AAATGA TTAATAAGACTTGGATTATGCAACTACATCT TCACAAGAACTCCATAC AAAAAAAGAAATAATAAGAAAAAACATTTGACC AAATGATTTCAAGAAATGAT GTG
V#91 (FAM1&2-recovered)
AAATGA TTAATAAGACTTGGATTATGCAACTACATCT TCACAAGAACTCCATAC AAAAAAAGAAATAATAAGAAAAAACATTTGACC AAATGATTTCAAGAAATGAT GTG
V#92 (FAM1&2)
AAATGA TTAATAAGACTTGGATTATGCAACTACATCT TCACAAGAACTCCATAC AAAAAAAGAAATAATAAGAAAAAACATTTGACC AAATGATTTCAAGAAATGAT GTG
V#94 (FAM1&2-recovered)
AAATGA TTAATAAGACTTGGATTATGCAACTACATCT TCACAAGAACTCCATAC AAAAAAAGAAATAATAAGAAAAAACATTTGACC AAATGATTTCAAGAAATGAT GTG
V#95 (Partial FAM1)
AAATGA TTAATAAGACTTGGATTATGCAACTACATCT TCACAAGAACTCCATAC AAAAAAAGAAATAATAAGAAAAAACATTTGACC -AATGATTTCAAGAAATGAT GTG
V#97 (Partial FAM1)
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V#98 (Partial FAM2)
AAATGA TTAATAAGACTTGGATTATGCAACTACATCT TCACAAGAACTCCATAC AAAAAAAGAAATAATAAGAAAAAACATTTGACC AAATGATTTCAAGAAATGAT GTG
V#101 (FAM1&2)
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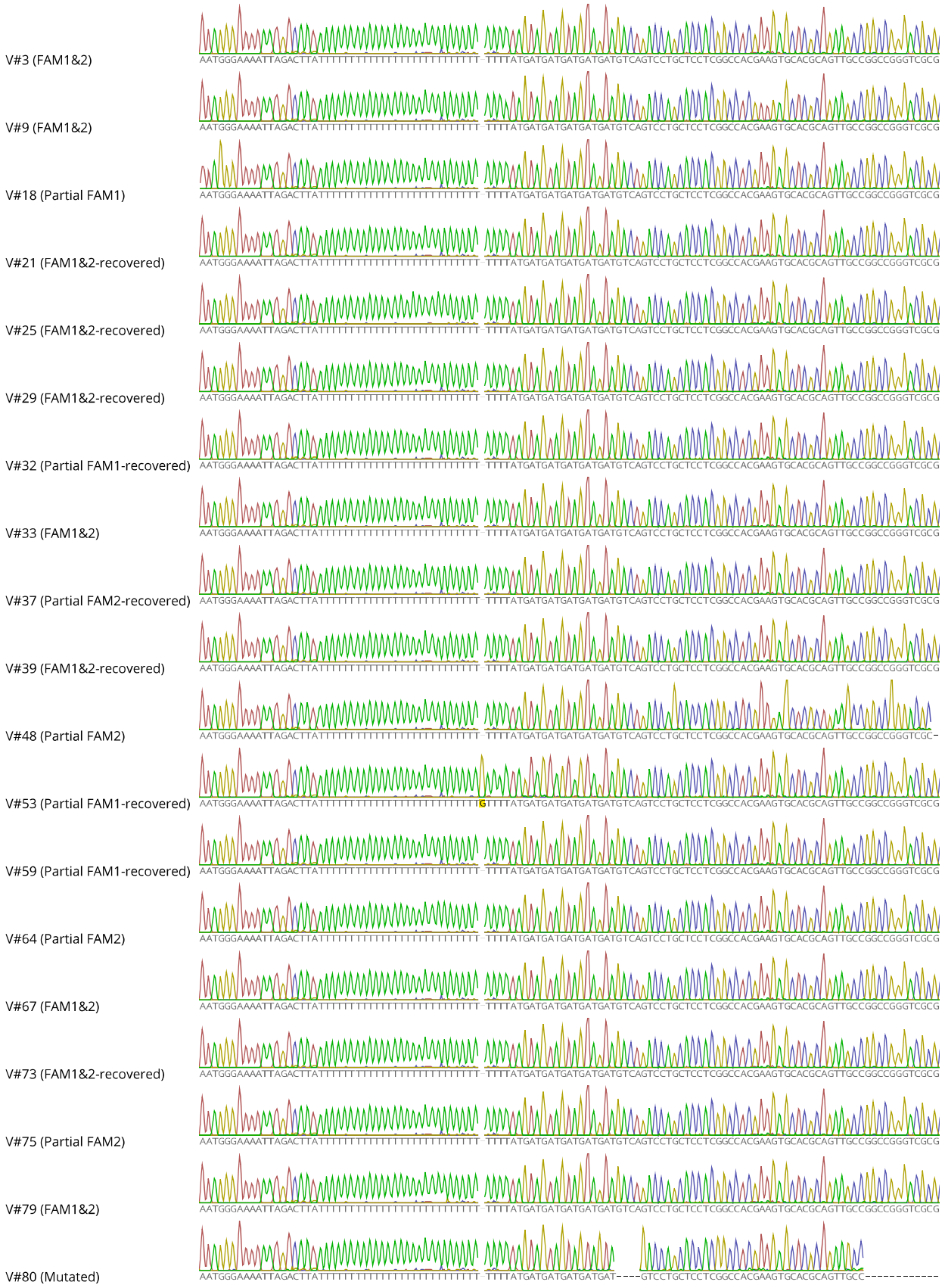
V#3 (FAM1&2)
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V#9 (FAM1&2)
AATGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCTGCTCCTCGGCCACGAAGTGCACGCAGTTGCCGGCCGGGTCGCG
V#18 (Partial FAM1)
AATGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCTGCTCCTCGGCCACGAAGTGCACGCAGTTGCCGGCCGGGTCGCG
V#21 (FAM1&2-recovered)
AATGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCTGCTCCTCGGCCACGAAGTGCACGCAGTTGCCGGCCGGGTCGCG
V#25 (FAM1&2-recovered)
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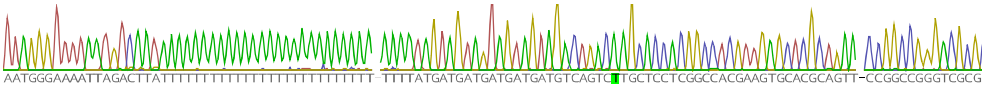
V#29 (FAM1&2-recovered)
AATGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCTGCTCCTCGGCCACGAAGTGCACGCAGTTGCCGGCCGGGTCGCG
V#32 (Partial FAM1-recovered)
AATGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCTGCTCCTCGGCCACGAAGTGCACGCAGTTGCCGGCCGGGTCGCG
V#33 (FAM1&2)
AATGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCTGCTCCTCGGCCACGAAGTGCACGCAGTTGCCGGCCGGGTCGCG
V#37 (Partial FAM2-recovered)
AATGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCTGCTCCTCGGCCACGAAGTGCACGCAGTTGCCGGCCGGGTCGCG
V#39 (FAM1&2-recovered)
AATGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCTGCTCCTCGGCCACGAAGTGCACGCAGTTGCCGGCCGGGTCGCG
V#48 (Partial FAM2)
AATGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCTGCTCCTCGGCCACGAAGTGCACGCAGTTGCCGGCCGGGTCGC-
V#53 (Partial FAM1-recovered)
AATGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTGTTTTATGATGATGATGATGATGTCAGTCCTGCTCCTCGGCCACGAAGTGCACGCAGTTGCCGGCCGGGTCGCG
V#59 (Partial FAM1-recovered)
AATGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCTGCTCCTCGGCCACGAAGTGCACGCAGTTGCCGGCCGGGTCGCG
V#64 (Partial FAM2)
AATGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCTGCTCCTCGGCCACGAAGTGCACGCAGTTGCCGGCCGGGTCGCG
V#67 (FAM1&2)
AATGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCTGCTCCTCGGCCACGAAGTGCACGCAGTTGCCGGCCGGGTCGCG
V#73 (FAM1&2-recovered)
AATGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCTGCTCCTCGGCCACGAAGTGCACGCAGTTGCCGGCCGGGTCGCG
V#75 (Partial FAM2)
AATGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCTGCTCCTCGGCCACGAAGTGCACGCAGTTGCCGGCCGGGTCGCG
V#79 (FAM1&2)
AATGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATGTCAGTCCTGCTCCTCGGCCACGAAGTGCACGCAGTTGCCGGCCGGGTCGCG
V#80 (Mutated)
AATGGGAAAATTAGACTTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGAT----GTCCTGCTCCTCGGCCACGAAGTGCACGCAGTTGCC----------

V#82 (Partial FAM1)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V#3 (FAM1&2)
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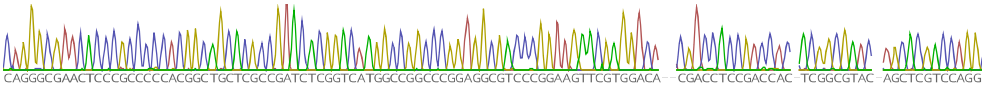
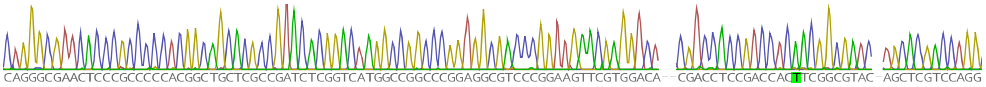
V#9 (FAM1&2)
CAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCGTCCCGGAAGTTCGTGGACA CGACCTCCGACCAC TCGGCGTAC AGCTCGTCCAGG
V#18 (Partial FAM1)
CAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCGTCCCGGAAGTTCGTGGACA CGACCTCCGACCAC TCGGCGTAC AGCTCGTCCAGG
V#21 (FAM1&2-recovered)
CAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCGTCCCGGAAGTTCGTGGACA CGACCTCCGACCAC TCGGCGTAC AGCTCGTCCAGG
V#25 (FAM1&2-recovered)
CAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCGTCCCGGAAGTTCGTGGACA CGACCTCCGACCAC TCGGCGTAC AGCTCGTCCAGG
V#29 (FAM1&2-recovered)
CAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCGTCCCGGAAGTTCGTGGACA CGACCTCCGACCAC TCGGCGTAC AGCTCGTCCAGG
V#32 (Partial FAM1-recovered)
CAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCGTCCCGGAAGTTCGTGGACA CGACCTCCGACCAC TCGGCGTAC AGCTCGTCCAGG
V#33 (FAM1&2)
CAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCGTCCCGGAAGTTCGTGGACA CGACCTCCGACCAC TCGGCGTAC AGCTCGTCCAGG
V#37 (Partial FAM2-recovered)
CAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCGTCCCGGAAGTTCGTGGACA CGACCTCCGACCAC TCGGCGTAC AGCTCGTCCAGG
V#39 (FAM1&2-recovered)
CAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCGTCCCGGAAGTTCGTGGACA CGACCTCCGACCAC TCGGCGTAC AGCTCGTCCAGG
V#48 (Partial FAM2)
CAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCGTCCCGGAAGTTCGTGGACA CGACCTCCGACCAC TCGGCGTAC AGCTCGTCCAGG
V#53 (Partial FAM1-recovered)
CAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCGTCCCGGAAGTTCGTGGACA CGACCTCCGACCAC TCGGCGTAC AGCTCGTCCAGG
V#59 (Partial FAM1-recovered)
CAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCGTCCCGGAAGTTCGTGGACA CGACCTCCGACCAC TCGGCGTAC AGCTCGTCCAGG
V#64 (Partial FAM2)
CAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCGTCCCGGAAGTTCGTGGACA CGACCTCCGACCAC TCGGCGTAC AGCTCGTCCAGG
V#67 (FAM1&2)
CAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCGTCCCGGAAGTTCGTGGACA CGACCTCCGACCAC TCGGCGTAC AGCTCGTCCAGG
V#73 (FAM1&2-recovered)
CAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCGTCCCGGAAGTTCGTGGACA CGACCTCCGACCAC TCGGCGTAC AGCTCGTCCAGG
V#75 (Partial FAM2)
CAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCGTCCCGGAAGTTCGTGGACA CGACCTCCGACCAC TCGGCGTAC AGCTCGTCCAGG
V#79 (FAM1&2)
CAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCGTCCCGGAAGTTCGTGGACA CGACCTCCGACCAC TCGGCGTACAAGCTCGTCCAGG
V#80 (Mutated)
--GGGCGAACTCCCGCCCCCACGGCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCGTCCCGGAAGTTCGTGGACA CGACCTCCGACCAC TCGGCGTAC AGCTCGTCCAGG

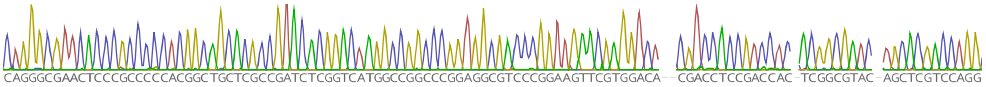
V#82 (Partial FAM1)



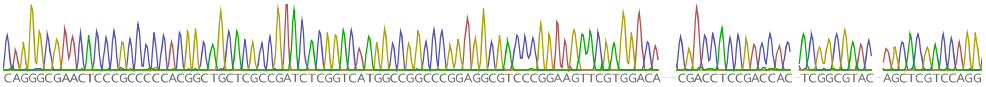
V#85 (Partial FAM2)



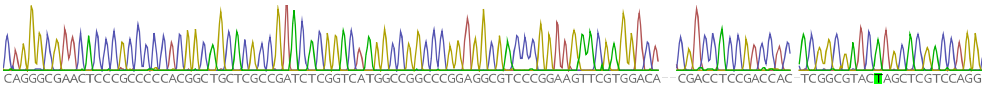
V#86 (Partial FAM1)



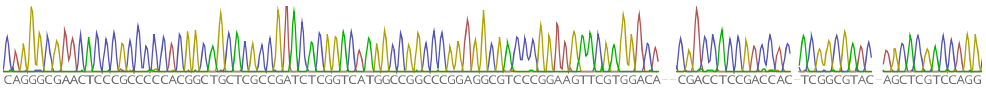
V#88 (FAM1&2-recovered)



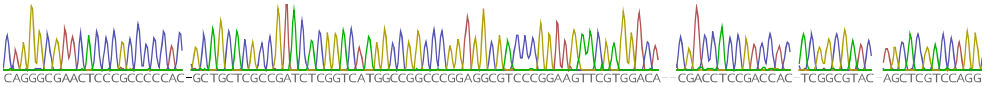
V#89 (Partial FAM2)



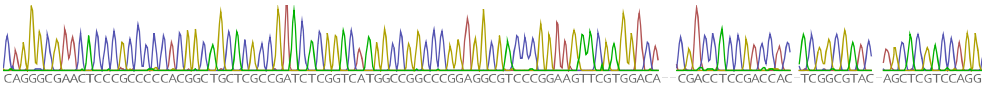
V#91 (FAM1&2-recovered)



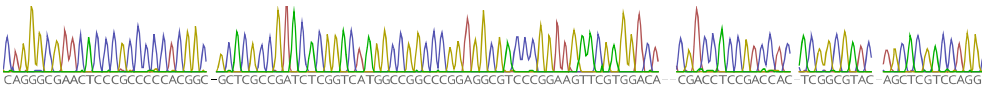
V#92 (FAM1&2)



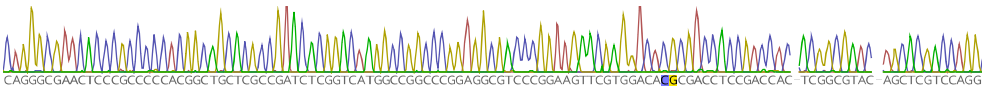
V#94 (FAM1&2-recovered)



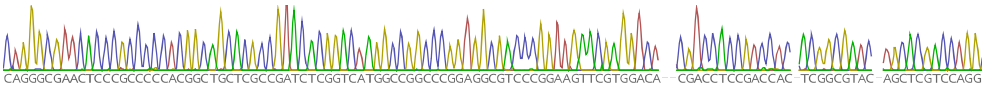
V#95 (Partial FAM1)



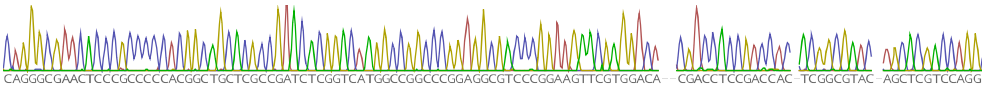
V#97 (Partial FAM1)



V#98 (Partial FAM2)

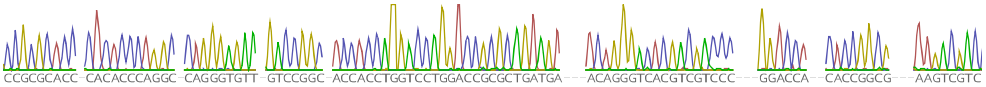


V#101 (FAM1&2)

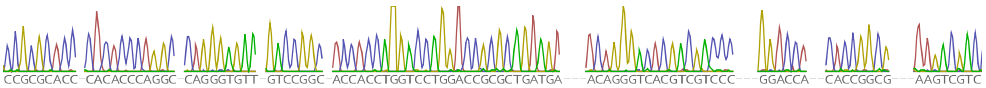


V#3 (FAM1&2)
CCGCGCACC CACACCCAGGC CAGGGTGTT GTCCGGC ACCACCTGGTCCTGGACCGCGCTGATGATCCACAGGGTCACGTCGTCCC GGACCA CACCGGCG AAGTCGTC
V#9 (FAM1&2)
CCGCGCACC CACACCCAGGC CAGGGTGTT GTCCGGC ACCACCTGGTCCTGGACCGCGCTGATGA ACAGGGTCACGTCGTCCC GGACCA CACCGGCGATAAAGTCGTC
V#18 (Partial FAM1)
CCGCGCACC CACACCCAGGC CAGGGTGTT GTCCGGC ACCACCTGGTCCTGGACCGCGCTGATGA ACAGGGTCACGTCGTCCCTCGGGACCA CACCGGCG AAGTCGTC
V#21 (FAM1&2-recovered)
CCGCGCACC CACACCCAGGC CAGGGTGTT GTCCGGC ACCACCTGGTCCTGGACCGCGCTGATGA ACAGGGTCACGTCGTCCC GGACCA CACCGGCG AAGTCGTC
V#25 (FAM1&2-recovered)
CCGCGCACC CACACCCAGGC CAGGGTGTT GTCCGGC ACCACCTGGTCCTGGACCGCGCTGATGA ACAGGGTCACGTCGTCCC GGACCA CACCGGCG AAGTCGTC
V#29 (FAM1&2-recovered)
CCGCGCACC CACACCCAGGC CAGGGTGTT GTCCGGC ACCACCTGGTCCTGGACCGCGCTGATGA ACAGGGTCACGTCGTCCC GGACCA CACCGGCG AAGTCGTC
V#32 (Partial FAM1-recovered)
CCGCGCACC CACACCCAGGC CAGGGTGTT GTCCGGC ACCACCTGGTCCTGGACCGCGCTGATGA ACAGGGTCACGTCGTCCC GGACCA CACCGGCG AAGTCGTC
V#33 (FAM1&2)
CCGCGCACC CACACCCAGGCACAGGGTGTT GTCCGGC ACCACCTGGTCCTGGACCGCGCTGATGA ACAGGGTCACGTCGTCCC GGACCA CACCGGCG AAGTCGTC
V#37 (Partial FAM2-recovered)
CCGCGCACC CACACCCAGGC CAGGGTGTT GTCCGGC ACCACCTGGTCCTGGACCGCGCTGATGA ACAGGGTCACGTCGTCCC GGACCA CACCGGCG AAGTCGTC
V#39 (FAM1&2-recovered)
CCGCGCACC CACACCCAGGC CAGGGTGTT GTCCGGC ACCACCTGGTCCTGGACCGCGCTGATGA ACAGGGTCACGTCGTCCC GGACCA CACCGGCG AAGTCGTC
V#48 (Partial FAM2)
CCGCGCACC CACACCCAGGC CAGGGTGTT GTCCGGC ACCACCTGGTCCTGGACCGCGCTGATGA ACAGGGTCACGTCGTCCC GGACCA CACCGGCG AAGTCGTC
V#53 (Partial FAM1-recovered)
CCGCGCACC CACACCCAGGC CAGGGTGTT GTCCGGC ACCACCTGGTCCTGGACCGCGCTGATGA ACAGGGTCACGTCGTCCC GGACCA CACCGGCG AAGTCGTC
V#59 (Partial FAM1-recovered)
CCGCGCACC CACACCCAGGC CAGGGTGTT GTCCGGC ACCACCTGGTCCTGGACCGCGCTGATGA ACAGGGTCACGTCGTCCC GGACCA CACCGGCG AAGTCGTC
V#64 (Partial FAM2)
CCGCGCACC CACACCCAGGC CAGGGTGTTGGTCCGGC ACCACCTGGTCCTGGACCGCGCTGATGA ACAGGGTCACGTCGTCCC GGACCA CACCGGCG AAGTCGTC
V#67 (FAM1&2)
CCGCGCACC CACACCCAGGC CAGGGTGTT GTCCGGC ACCACCTGGTCCTGGACCGCGCTGATGA ACAGGGTCACGTCGTCCC GGACCATTCACCGGCG AAGTCGTC
V#73 (FAM1&2-recovered)
CCGCGCACC CACACCCAGGC CAGGGTGTT GTCCGGC ACCACCTGGTCCTGGACCGCGCTGATGA ACAGGGTCACGTCGTCCC GGACCA CACCGGCG AAGTCGTC
V#75 (Partial FAM2)
CCGCGCACC CACACCCAGGC CAGGGTGTT GTCCGGCAACCACCTGGTCCTGGACCGCGCTGATGA ACAGGGTCACGTCGTCCC GGACCA CACCGGCG AAGTCGTC
V#79 (FAM1&2)
CCGCGCACC CACACCCAGGC CAGGGTGTT GTCCGGC ACCACCTGGTCCTGGACCGCGCTGATGA ACAGGGTCACGTCGTCCC -GACCA CACCGGCG AAGTCGTC
V#80 (Mutated)
CCGCGCACC CACACCCAGGC CAGGGTGTT GTCCGGC ACCACCTGGTCCTGGACCGCGCTGATGA ACAGGGTCACGTCGTCCC GGACCA CACCGGCG AAGTCGTC

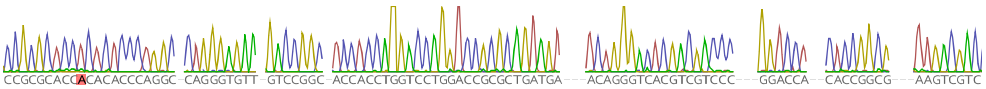
V#82 (Partial FAM1)



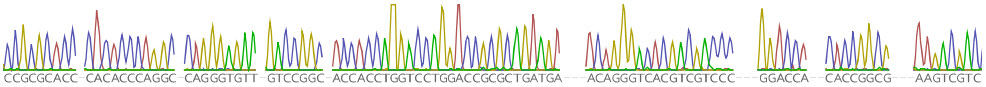
V#85 (Partial FAM2)



V#86 (Partial FAM1)



V#88 (FAM1&2-recovered)



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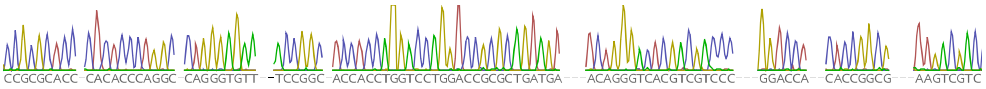
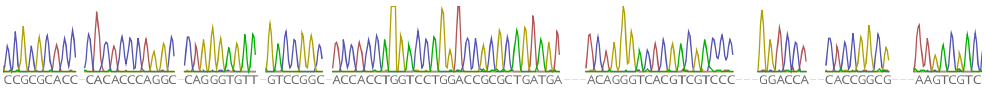
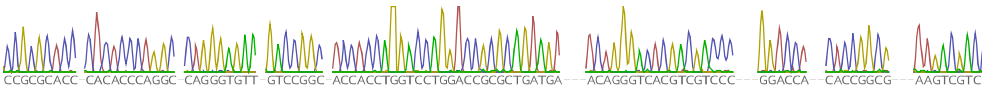


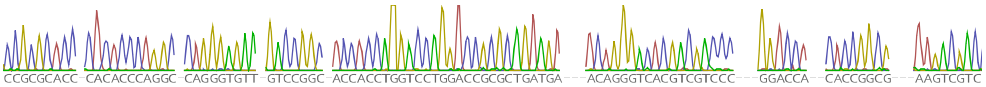
V#91 (FAM1&2-recovered)



V#92 (FAM1&2)



V#94 (FAM1&2-recovered)



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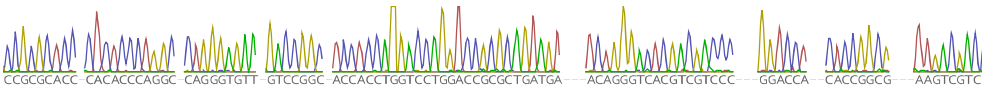
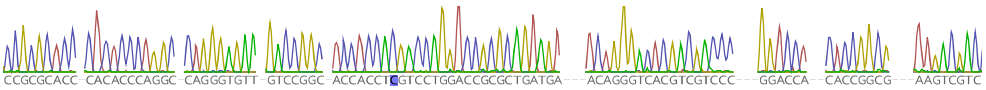
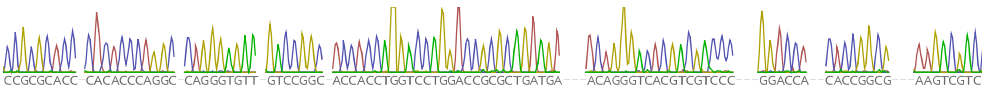


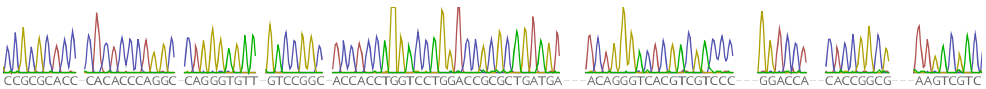
V#97 (Partial FAM1)



V#98 (Partial FAM2)



V#101 (FAM1&2)



V#3 (FAM1&2)
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V#9 (FAM1&2)
CTCCA CGAAGTCCCGGGAGAACCCGAGCCGGTC GGTCCAGAA CTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGC ACCGGAACGGCACTGGTCAACTTGGCCATCTAC AT
V#18 (Partial FAM1)
CTCCA CGAAGTCCCGGGAGAACCCGAGCCGGTC GGTCCAGAA CTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGC ACCGGAACGGCACTGGTCAACTTGGCCATCTAC AT
V#21 (FAM1&2-recovered)
CTCCA CGAAGTCCCGGGAGAACCCGAGCCGGTC GGTCCAGAA CTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGC ACCGGAACGGCACTGGTCAACTTGGCCATCTAC AT
V#25 (FAM1&2-recovered)
CTCCA CGAAGTCCCGGGAGAACCCGAGCCGGTC GGTCCAGAA CTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGC ACCGGAACGGCACTGGTCAACTTGGCCATCTAC AT
V#29 (FAM1&2-recovered)
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V#32 (Partial FAM1-recovered)
CTCCA CGAAGTCCCGGGAGAACCCGAGCCGGTC GGTCCAGAA CTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGC ACCGGAACGGCACTGGTCAACTTGGCCATCTAC AT
V#33 (FAM1&2)
CTCCA CGAAGTCCCGGGAGAACCCGAGCCGGTC GGTCCAGAA CTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGC ACCGGAACGGCACTGGTCAACTTGGCCATCTAC AT
V#37 (Partial FAM2-recovered)
CTCCA CGAAGTCCCGGGAGAACCCGAGCCGGTC GGTCCAGAA CTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGC ACCGGAACGGCACTGGTCAACTTGGCCATCTACTAAT
V#39 (FAM1&2-recovered)
CTCCA CGAAGTCCCGGGAGAACCCGAGCCGGTC GGTCCAGAA CTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGC ACCGGAACGGCACTGGTCAACTTGGCCATCTAC AT
V#48 (Partial FAM2)
CTCCA CGAAGTCCCGGGAGAACCCGAGCCGGTC GGTCCAGAA CTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGC ACCGGAACGGCACTGGTCAACTTGGCCATCTAC AT
V#53 (Partial FAM1-recovered)
CTCCA CGAAGTCCCGGGAGAACCCGAGCCGGTC GGTCCAGAA CTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGC ACCGGAACGGCACTGGTCAACTTGGCCATCTAC AT
V#59 (Partial FAM1-recovered)
CTCCA CGAAGTCCCGGGAGAACCCGAGCCGGTC GGTCCAGAA CTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGC ACCGGAACGGCACTGGTCAACTTGGCCATCTAC AT
V#64 (Partial FAM2)
CT-CA CGAAGTCCCGGGAGAACCCGAGCCGGTC GGTCCAGAA CTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGC ACCGGAACGGCACTGGTCAACTTGGCCATCTAC AT
V#67 (FAM1&2)
CTCCA CGAAGTCCCGGGAGAACCCGAGCCGGTC GGTCCAGAA CTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGC ACCGGAACGGCACTGGTCAACTTGGCCATCTAC AT
V#73 (FAM1&2-recovered)
CTCCA CGAAGTCCCGGGAGAACCCGAGCCGGTC GGTCCAGAA CTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGC ACCGGAACGGCACTGGTCAACTTGGCCATCTAC AT
V#75 (Partial FAM2)
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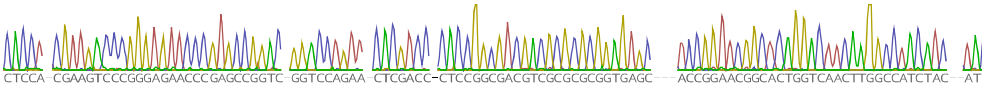
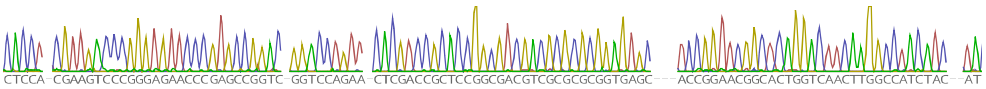
V#79 (FAM1&2)
CTCCA CGAAGTCCCGGGAGAACCCGAGCCGGTC GGTCCAGAA CTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGC ACCGGAACGGCACTGGTCAACTTGGCCATCTAC AT
V#80 (Mutated)
CTCCA CGAAGTCCCGGGAGAACCCGAGCCGGTC GGTCCAGAA CTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGC ACCGGAACGGCACTGGTCAACTTGGCCAC----AT

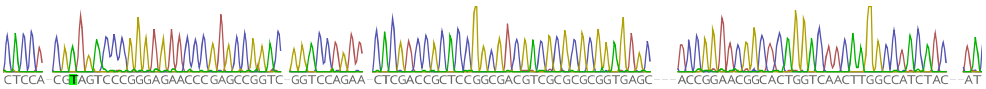
V#82 (Partial FAM1)



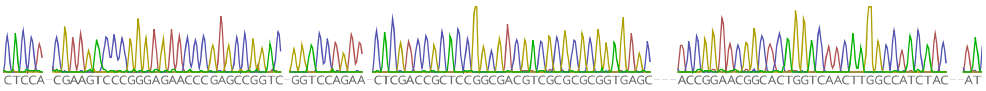
V#85 (Partial FAM2)



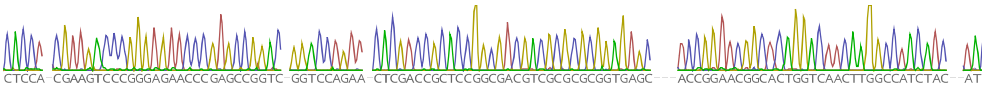
V#86 (Partial FAM1)



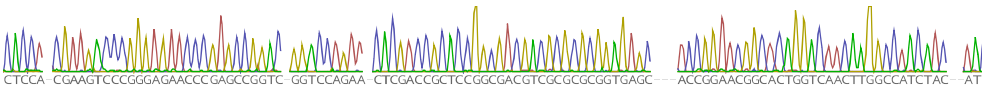
V#88 (FAM1&2-recovered)



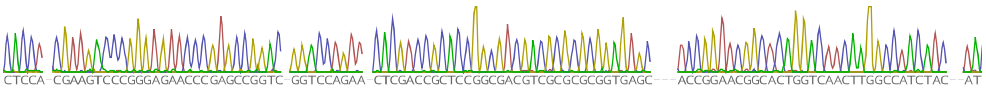
V#89 (Partial FAM2)



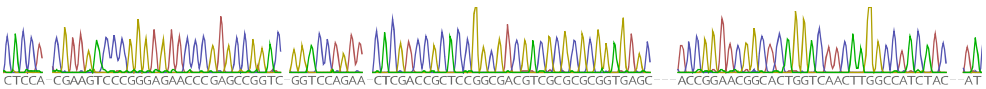
V#91 (FAM1&2-recovered)



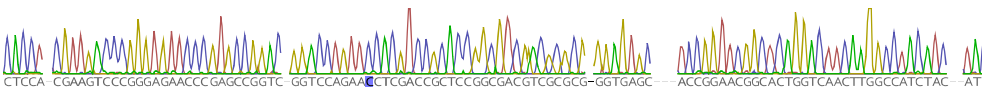
V#92 (FAM1&2)



V#94 (FAM1&2-recovered)



V#95 (Partial FAM1)



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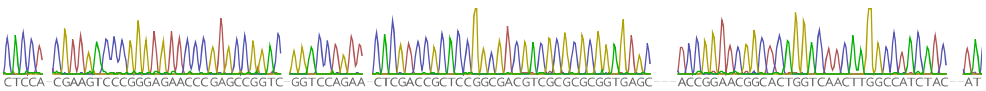
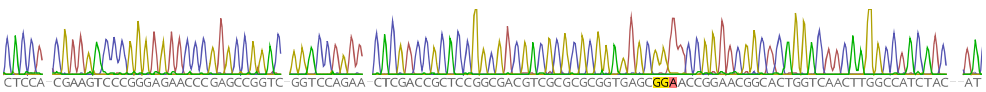
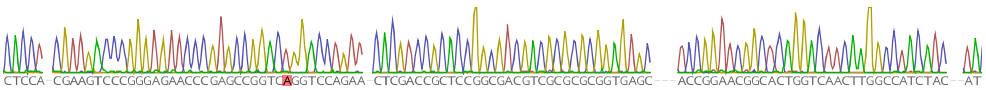


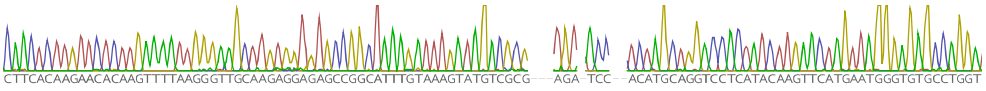
V#98 (Partial FAM2)



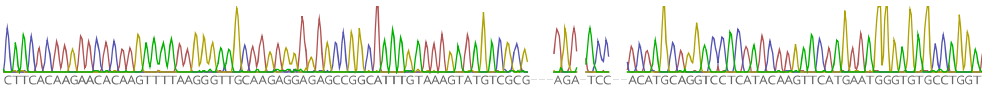
V#101 (FAM1&2)



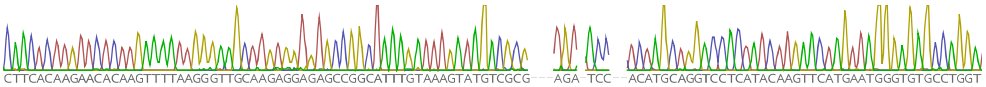
V#3 (FAM1&2)



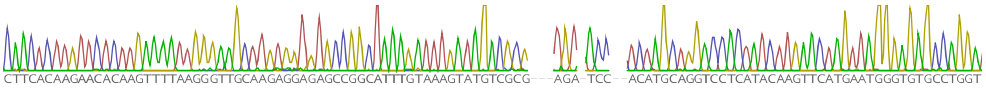
V#9 (FAM1&2)



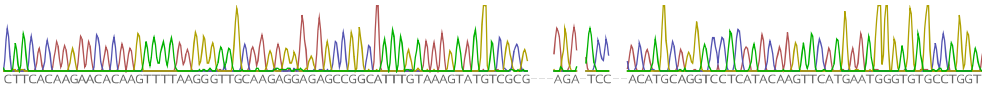
V#18 (Partial FAM1)



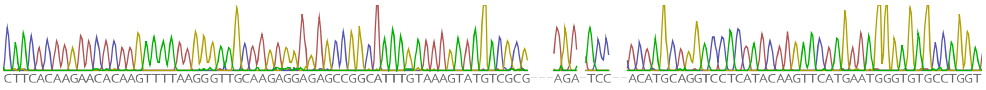
V#21 (FAM1&2-recovered)



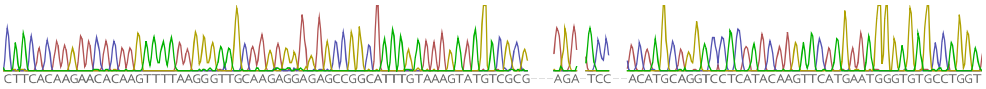
V#25 (FAM1&2-recovered)



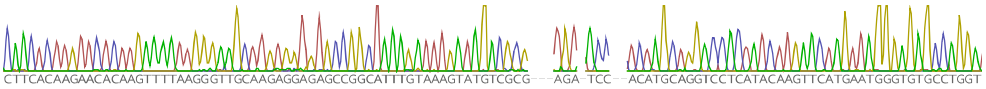
V#29 (FAM1&2-recovered)



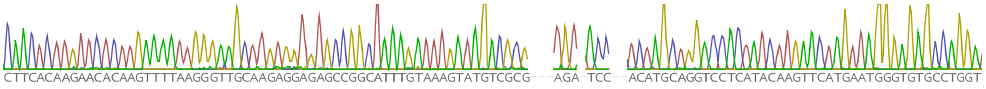
V#32 (Partial FAM1-recovered)



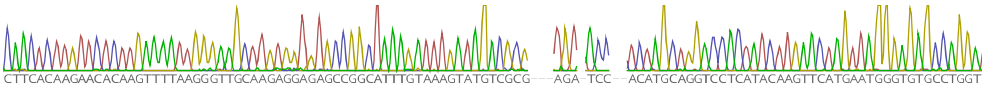
V#33 (FAM1&2)



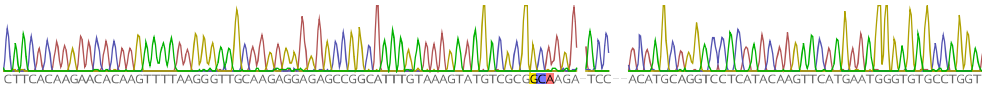
V#37 (Partial FAM2-recovered)



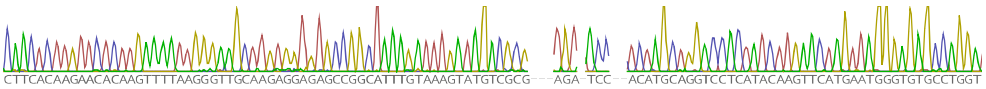
V#39 (FAM1&2-recovered)



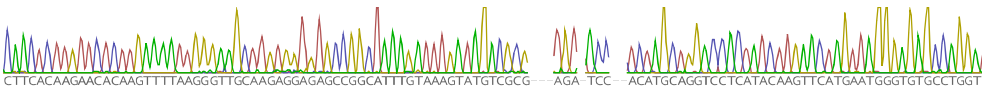
V#48 (Partial FAM2)



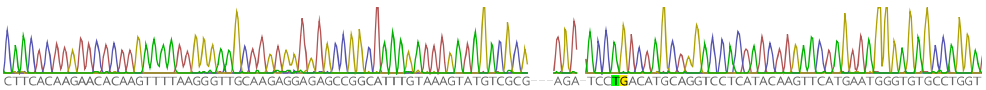
V#53 (Partial FAM1-recovered)



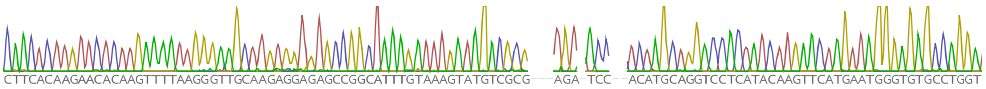
V#59 (Partial FAM1-recovered)



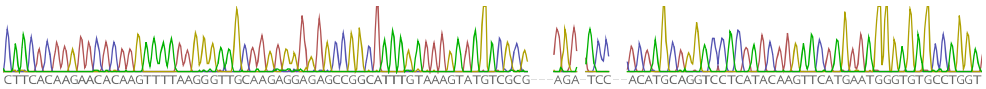
V#64 (Partial FAM2)



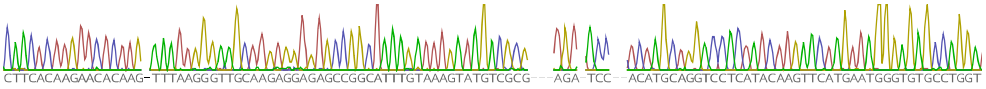
V#67 (FAM1&2)



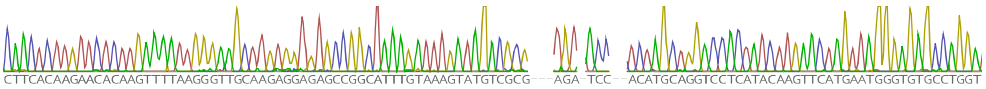
V#73 (FAM1&2-recovered)



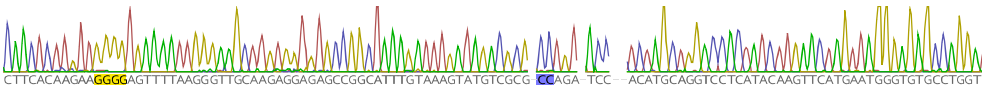
V#75 (Partial FAM2)



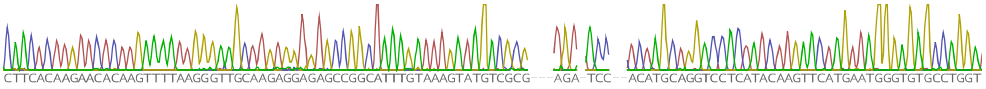
V#79 (FAM1&2)



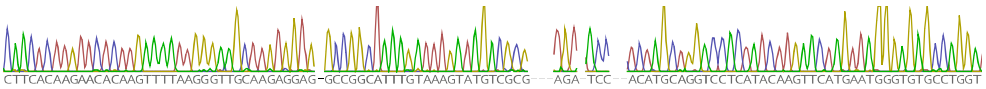
V#80 (Mutated)



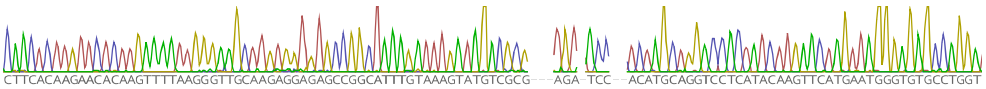
V#82 (Partial FAM1)



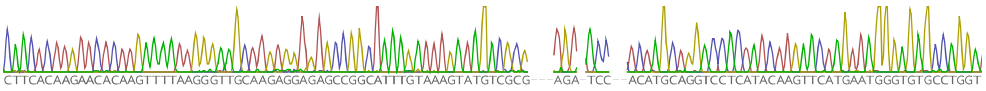
V#85 (Partial FAM2)



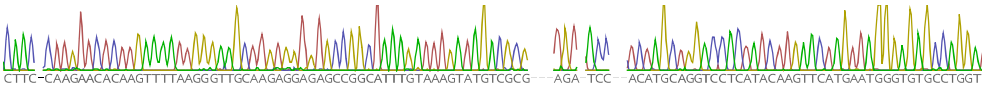
V#86 (Partial FAM1)



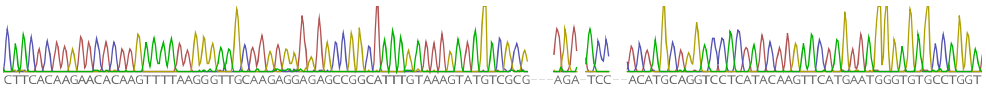
V#88 (FAM1&2-recovered)



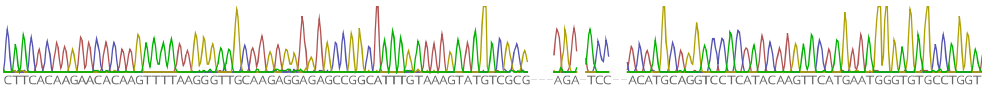
V#89 (Partial FAM2)



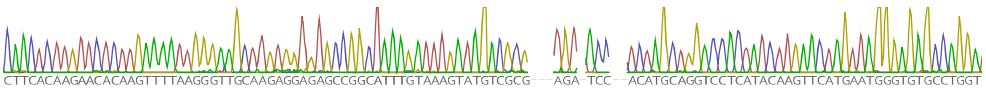
V#91 (FAM1&2-recovered)



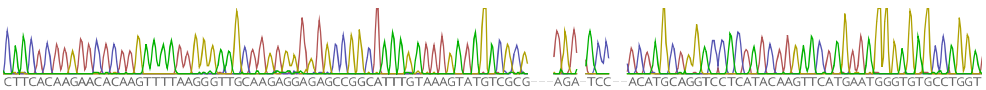
V#92 (FAM1&2)



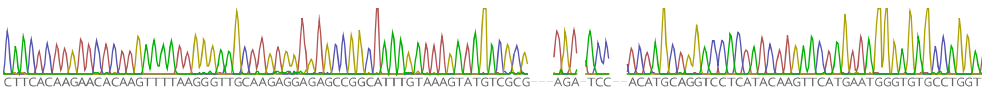
V#94 (FAM1&2-recovered)



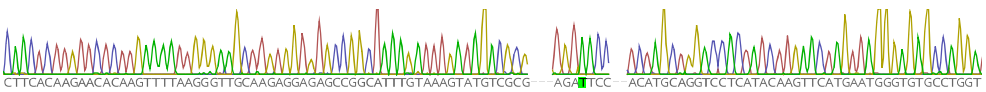
V#95 (Partial FAM1)



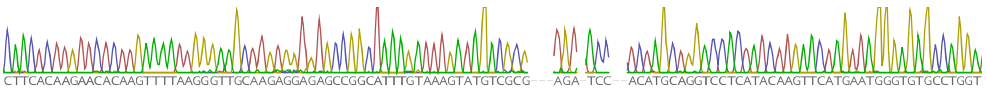
V#97 (Partial FAM1)

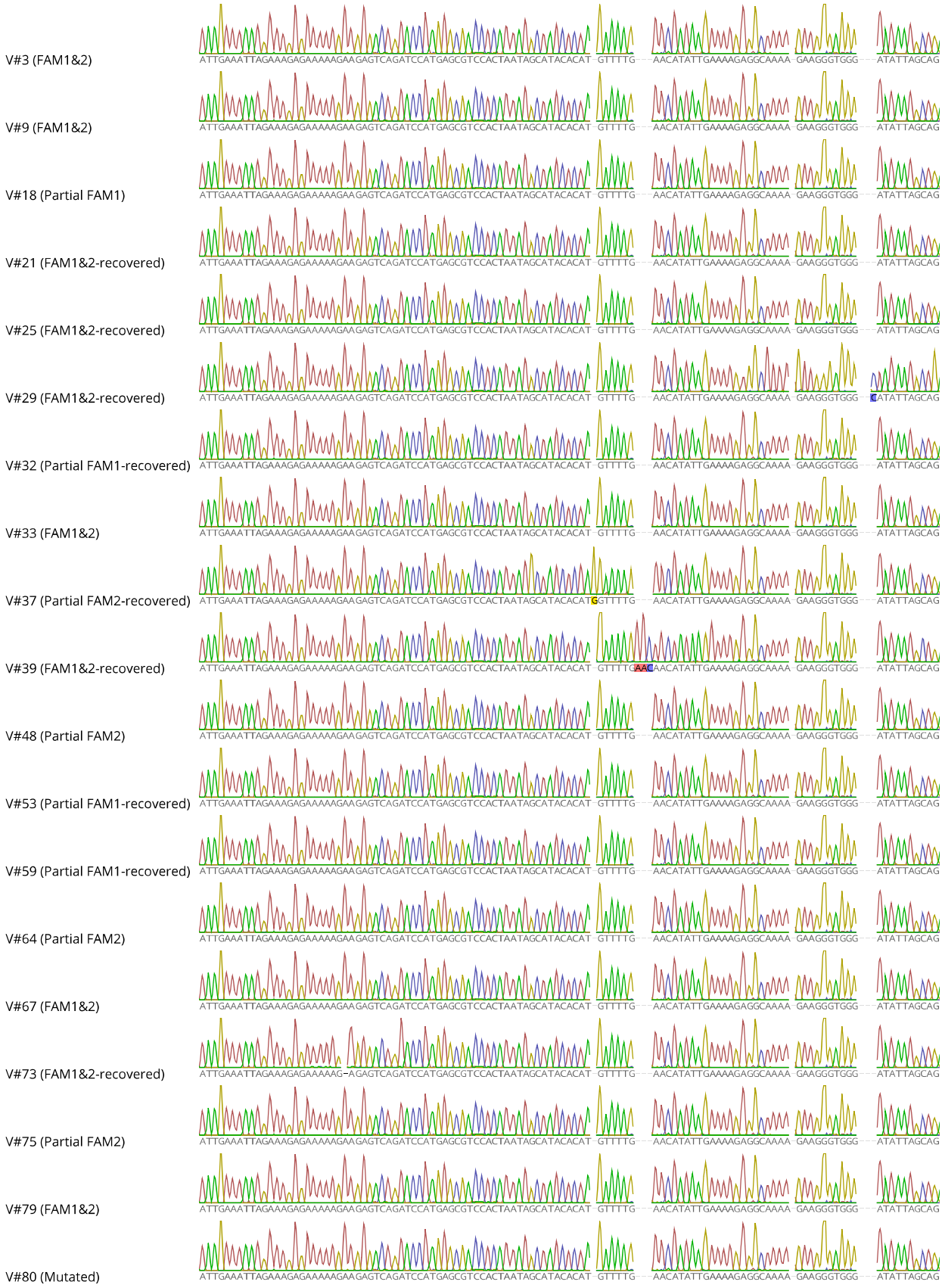


V#98 (Partial FAM2)



V#101 (FAM1&2)




V#3 (FAM1&2)
ATTGAAATTAGAAAGAGAAAAAGAAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT GTTTTG AACATATTGAAAAGAGGCAAAA GAAGGGTGGG ATATTAGCAG
V#9 (FAM1&2)
ATTGAAATTAGAAAGAGAAAAAGAAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT GTTTTG AACATATTGAAAAGAGGCAAAA GAAGGGTGGG ATATTAGCAG
V#18 (Partial FAM1)
ATTGAAATTAGAAAGAGAAAAAGAAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT GTTTTG AACATATTGAAAAGAGGCAAAA GAAGGGTGGG ATATTAGCAG
V#21 (FAM1&2-recovered)
ATTGAAATTAGAAAGAGAAAAAGAAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT GTTTTG AACATATTGAAAAGAGGCAAAA GAAGGGTGGG ATATTAGCAG
V#25 (FAM1&2-recovered)
ATTGAAATTAGAAAGAGAAAAAGAAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT GTTTTG AACATATTGAAAAGAGGCAAAA GAAGGGTGGG ATATTAGCAG
V#29 (FAM1&2-recovered)
ATTGAAATTAGAAAGAGAAAAAGAAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT GTTTTG AACATATTGAAAAGAGGCAAAA GAAGGGTGGG CATATTAGCAG
V#32 (Partial FAM1-recovered)
ATTGAAATTAGAAAGAGAAAAAGAAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT GTTTTG AACATATTGAAAAGAGGCAAAA GAAGGGTGGG ATATTAGCAG
V#33 (FAM1&2)
ATTGAAATTAGAAAGAGAAAAAGAAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT GTTTTG AACATATTGAAAAGAGGCAAAA GAAGGGTGGG ATATTAGCAG
V#37 (Partial FAM2-recovered)
ATTGAAATTAGAAAGAGAAAAAGAAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACATGGTTTTG AACATATTGAAAAGAGGCAAAA GAAGGGTGGG ATATTAGCAG
V#39 (FAM1&2-recovered)
ATTGAAATTAGAAAGAGAAAAAGAAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT GTTTTGAACAACATATTGAAAAGAGGCAAAA GAAGGGTGGG ATATTAGCAG
V#48 (Partial FAM2)
ATTGAAATTAGAAAGAGAAAAAGAAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT GTTTTG AACATATTGAAAAGAGGCAAAA GAAGGGTGGG ATATTAGCAG
V#53 (Partial FAM1-recovered)
ATTGAAATTAGAAAGAGAAAAAGAAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT GTTTTG AACATATTGAAAAGAGGCAAAA GAAGGGTGGG ATATTAGCAG
V#59 (Partial FAM1-recovered)
ATTGAAATTAGAAAGAGAAAAAGAAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT GTTTTG AACATATTGAAAAGAGGCAAAA GAAGGGTGGG ATATTAGCAG
V#64 (Partial FAM2)
ATTGAAATTAGAAAGAGAAAAAGAAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT GTTTTG AACATATTGAAAAGAGGCAAAA GAAGGGTGGG ATATTAGCAG
V#67 (FAM1&2)
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V#73 (FAM1&2-recovered)
ATTGAAATTAGAAAGAGAAAAAG-AGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT GTTTTG AACATATTGAAAAGAGGCAAAA GAAGGGTGGG ATATTAGCAG
V#75 (Partial FAM2)
ATTGAAATTAGAAAGAGAAAAAGAAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT GTTTTG AACATATTGAAAAGAGGCAAAA GAAGGGTGGG ATATTAGCAG
V#79 (FAM1&2)
ATTGAAATTAGAAAGAGAAAAAGAAGAGTCAGATCCATGAGCGTCCACTAATAGCATACACAT GTTTTG AACATATTGAAAAGAGGCAAAA GAAGGGTGGG ATATTAGCAG
V#80 (Mutated)
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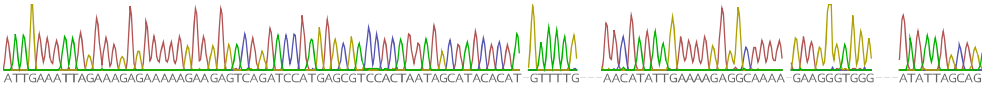
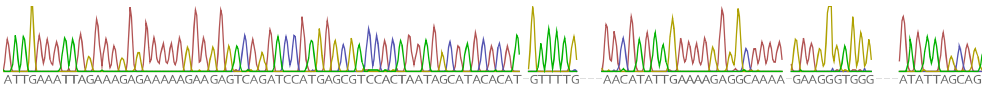
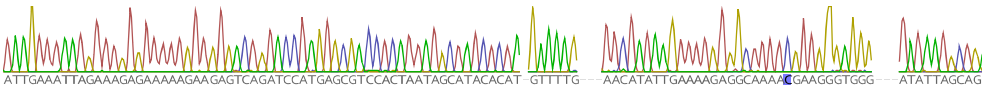
V#82 (Partial FAM1)



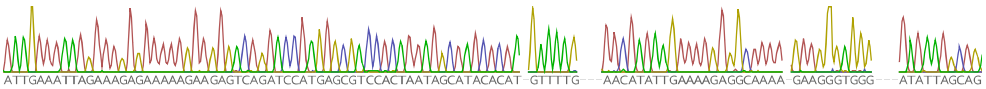
V#85 (Partial FAM2)



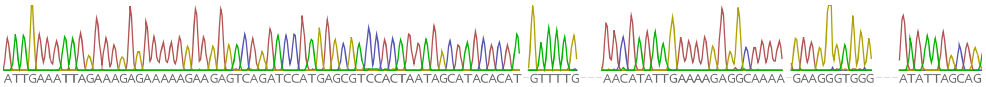
V#86 (Partial FAM1)



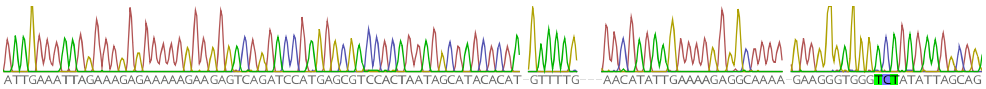
V#88 (FAM1&2-recovered)



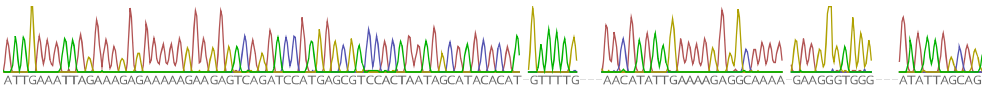
V#89 (Partial FAM2)



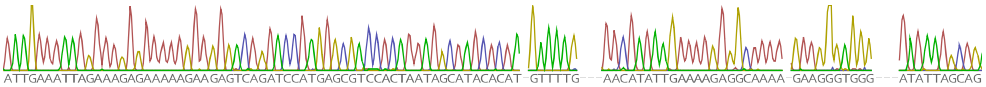
V#91 (FAM1&2-recovered)



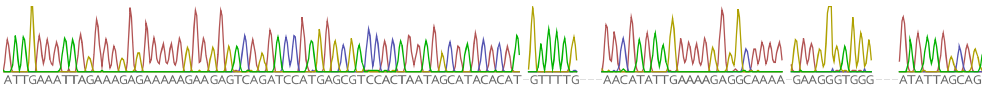
V#92 (FAM1&2)



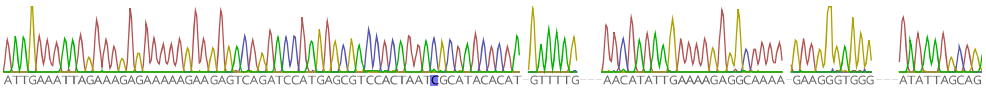
V#94 (FAM1&2-recovered)



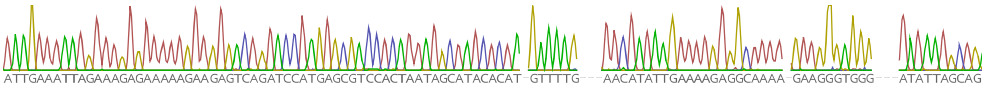
V#95 (Partial FAM1)



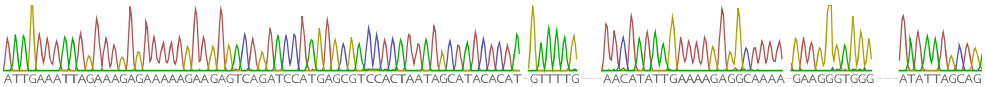
V#97 (Partial FAM1)

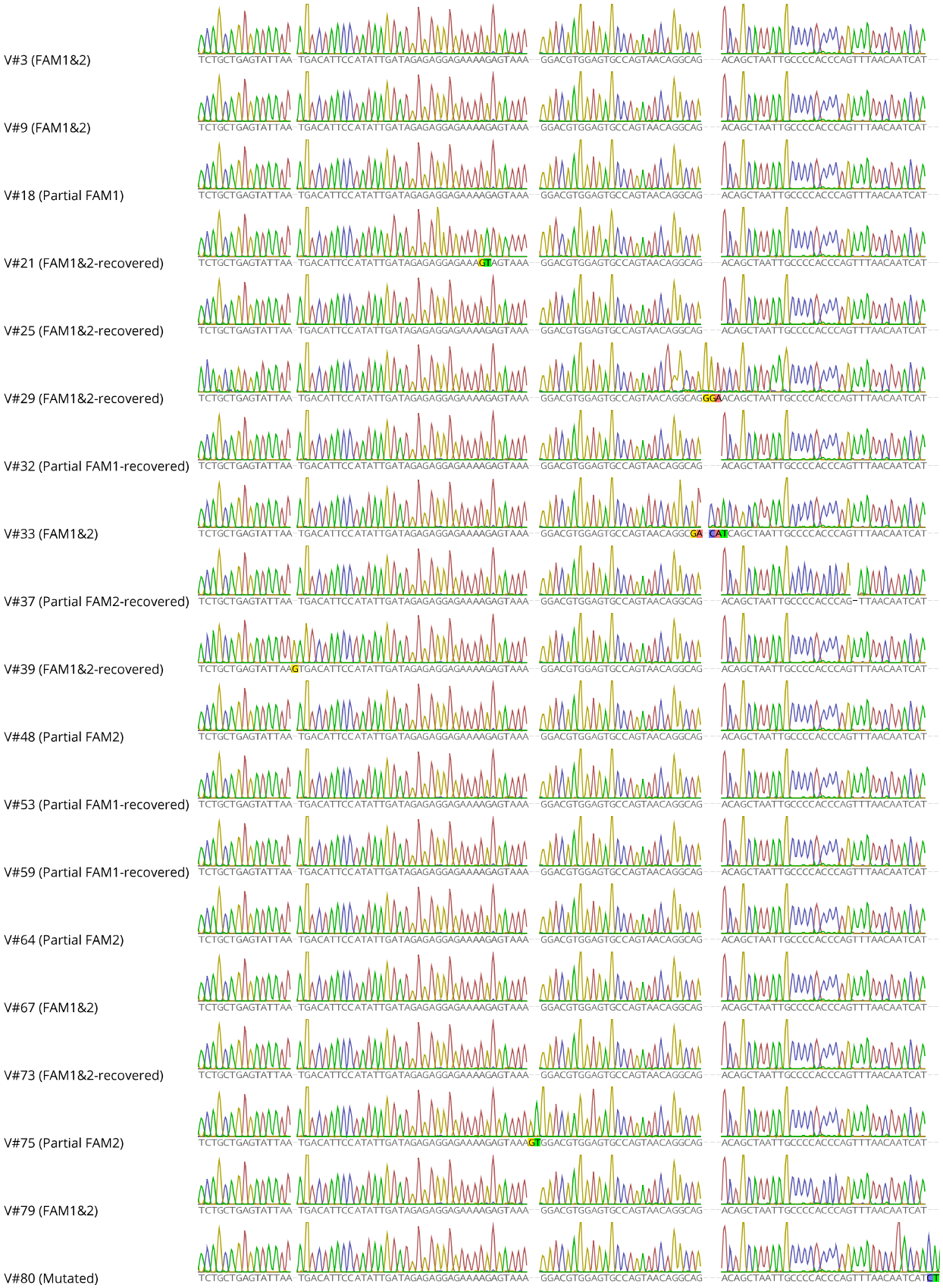


V#98 (Partial FAM2)



V#101 (FAM1&2)




V#3 (FAM1&2)
TCTGCTGAGTATTAA TGACATTCCATATTGATAGAGAGGAGAAAAGAGTAAA GGACGTGGAGTGCCAGTAACAGGCAG ACAGCTAATTGCCCCACCCAGTTTAACAATCAT
V#9 (FAM1&2)
TCTGCTGAGTATTAA TGACATTCCATATTGATAGAGAGGAGAAAAGAGTAAA GGACGTGGAGTGCCAGTAACAGGCAG ACAGCTAATTGCCCCACCCAGTTTAACAATCAT
V#18 (Partial FAM1)
TCTGCTGAGTATTAA TGACATTCCATATTGATAGAGAGGAGAAAAGAGTAAA GGACGTGGAGTGCCAGTAACAGGCAG ACAGCTAATTGCCCCACCCAGTTTAACAATCAT
V#21 (FAM1&2-recovered)
TCTGCTGAGTATTAA TGACATTCCATATTGATAGAGAGGAGAAAGTAGTAAA GGACGTGGAGTGCCAGTAACAGGCAG ACAGCTAATTGCCCCACCCAGTTTAACAATCAT
V#25 (FAM1&2-recovered)
TCTGCTGAGTATTAA TGACATTCCATATTGATAGAGAGGAGAAAAGAGTAAA GGACGTGGAGTGCCAGTAACAGGCAG ACAGCTAATTGCCCCACCCAGTTTAACAATCAT
V#29 (FAM1&2-recovered)
TCTGCTGAGTATTAA TGACATTCCATATTGATAGAGAGGAGAAAAGAGTAAA GGACGTGGAGTGCCAGTAACAGGCAGGGAACAGCTAATTGCCCCACCCAGTTTAACAATCAT
V#32 (Partial FAM1-recovered)
TCTGCTGAGTATTAA TGACATTCCATATTGATAGAGAGGAGAAAAGAGTAAA GGACGTGGAGTGCCAGTAACAGGCAG ACAGCTAATTGCCCCACCCAGTTTAACAATCAT
V#33 (FAM1&2)
TCTGCTGAGTATTAA TGACATTCCATATTGATAGAGAGGAGAAAAGAGTAAA GGACGTGGAGTGCCAGTAACAGGCGA CATCAGCTAATTGCCCCACCCAGTTTAACAATCAT
V#37 (Partial FAM2-recovered)
TCTGCTGAGTATTAA TGACATTCCATATTGATAGAGAGGAGAAAAGAGTAAA GGACGTGGAGTGCCAGTAACAGGCAG ACAGCTAATTGCCCCACCCAG-TTAACAATCAT
V#39 (FAM1&2-recovered)
TCTGCTGAGTATTAAGTGACATTCCATATTGATAGAGAGGAGAAAAGAGTAAA GGACGTGGAGTGCCAGTAACAGGCAG ACAGCTAATTGCCCCACCCAGTTTAACAATCAT
V#48 (Partial FAM2)
TCTGCTGAGTATTAA TGACATTCCATATTGATAGAGAGGAGAAAAGAGTAAA GGACGTGGAGTGCCAGTAACAGGCAG ACAGCTAATTGCCCCACCCAGTTTAACAATCAT
V#53 (Partial FAM1-recovered)
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V#59 (Partial FAM1-recovered)
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V#64 (Partial FAM2)
TCTGCTGAGTATTAA TGACATTCCATATTGATAGAGAGGAGAAAAGAGTAAA GGACGTGGAGTGCCAGTAACAGGCAG ACAGCTAATTGCCCCACCCAGTTTAACAATCAT
V#67 (FAM1&2)
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V#73 (FAM1&2-recovered)
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V#75 (Partial FAM2)
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V#79 (FAM1&2)
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V#80 (Mutated)
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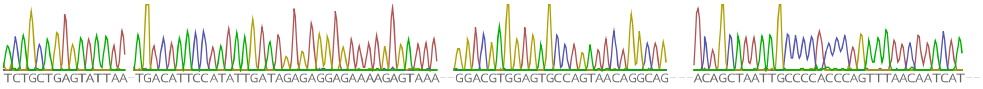
V#82 (Partial FAM1)



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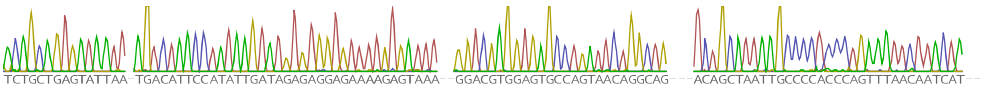
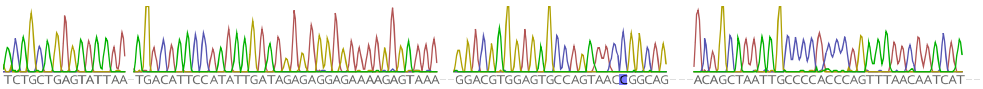
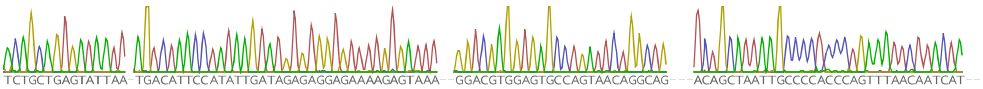


V#86 (Partial FAM1)



V#88 (FAM1&2-recovered)



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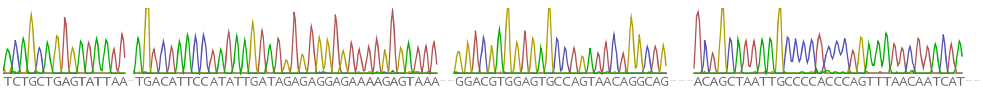

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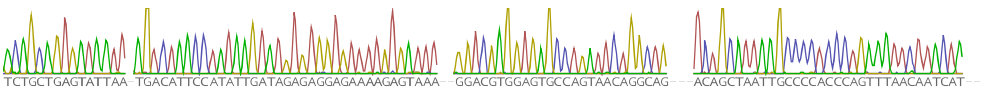
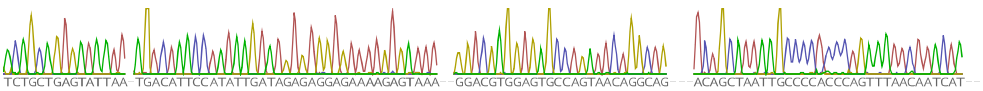
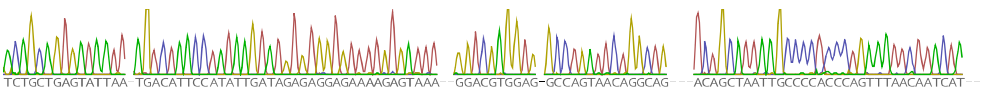


V#92 (FAM1&2)



V#94 (FAM1&2-recovered)



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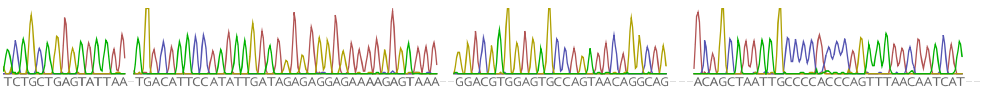

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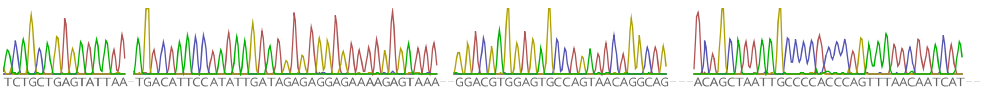

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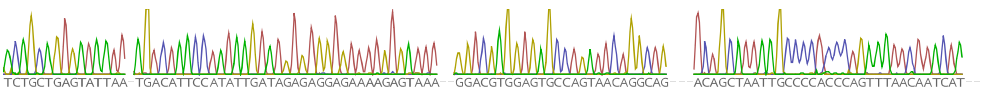
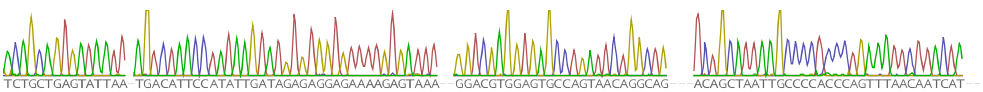


V#101 (FAM1&2)



V#3 (FAM1&2)
AGGACTTC AAATACC ATCAGTTCATGTGCTGCCTGTCTATCCTTTGGATCTTT CTGCACACT GGAAG AAGAC AGAACCACAGAATGAAAATCAGTAACTTCACAAA
V#9 (FAM1&2)
AGGACTTC AAATACC ATCAGTTCATGTGCTGCCTGTCTATCCTTTGGATCTTT CTGCACACT GGAAG AAGAC AGAACCACAGAATGAAAATCAGTAACTTCACAAA
V#18 (Partial FAM1)
AGGACTTC AAATACC ATCAGTTCATGTGCTGCCTGTCTATCCTTTGGATCTTT CTGCACACT GGAAG AAGAC AGAACCACAGAATGAAAATCAGTAACTTCACAAA
V#21 (FAM1&2-recovered)
AGGACTTC AAATACC ATCAGTTCATGTGCTGCCTGTCTATCCTTTGGATCTTT CTGCACACT GGAAG AAGACAGAGAACCACAGAATGAAAATCAGTAACTTCACAAA
V#25 (FAM1&2-recovered)
AGGACTTC AAATACC ATCAGTTCATGTGCTGCCTGTCTATCCTTTGGATCTTT CTGCACACT GGAAG AAGAC AGAACCACAGAATGAAAATCAGTAACTTCACAAA
V#29 (FAM1&2-recovered)
AGGACTTC AAATACC ATCAGTTCATGTGCTGCCTGTCTATCCTTTGGATCTTT CTGCACACT GGAAG AAGAC AGAACCACAGAATGAAAATCAGTAACTTCACAAA
V#32 (Partial FAM1-recovered)
AGGACTTC AAATACC ATCAGTTCATGTGCTGCCTGTCTATCCTTTGGATCTTT CTGCACACT GGAAG AAGAC AGAACCACAGAATGAAAATCAGTAACTTCACAAA
V#33 (FAM1&2)
AGGACTTC AAATACC ATCAGTTCATGTGCTGCCTGTCTATCCTTTGGATCTTT CTGCACACT GGAAG AAGAC AGAACCACAGAATGAAAATCAGTAACTTCACAAA
V#37 (Partial FAM2-recovered)
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V#39 (FAM1&2-recovered)
AGGACTTC AAATACC ATCAGTTCATGTGCTGCCTGTCTATCCTTTGGATCTTT CTGCACACT GGAAG AAGAC AGAACCACAGAATGAAAATCAGTAACTTCACAAA
V#48 (Partial FAM2)
AGGACTTC AAATACC ATCAGTTCATGTGCTGCCTGTCTATCCTTTGGATCTTT CTGCACACT GGAAG AAGAC AGAACCACAGAATGAAAATCAGTAACTTCACAAA
V#53 (Partial FAM1-recovered)
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V#59 (Partial FAM1-recovered)
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V#64 (Partial FAM2)
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V#67 (FAM1&2)
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V#73 (FAM1&2-recovered)
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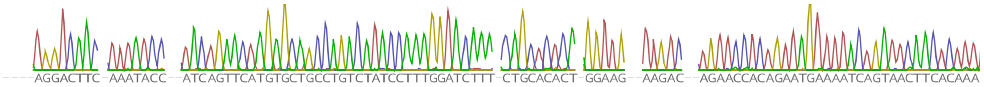
V#75 (Partial FAM2)
AGGACTTC AAATACC ATCAGTTCATGTGCTGCCTGTCTATCCTTTGGATCTTT CTGCACACT GGAAG AAGAC AGAACCACAGAATGAAAATCAGTAACTTCACAAA
V#79 (FAM1&2)
AGGACTTC AAATACC ATCAGTTCATGTGCTGCCTGTCTATCCTTTGGATCTTT CTGCACACT GGAAG AAGAC AGAACCACAGAATGAAAATCAGTAACTTCA
V#80 (Mutated)
TCAAAGGACTTC AAATACC ATCAGTTCATGTGCTGCCTGTCTATCCTTTGGATTTT- CTGCACACT GGAAG AAGAC AGAACCACAGAATGAAAATCAGTAACTTCACAAA

V#82 (Partial FAM1)



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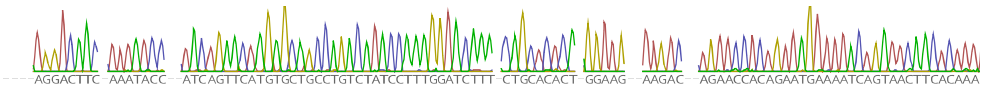

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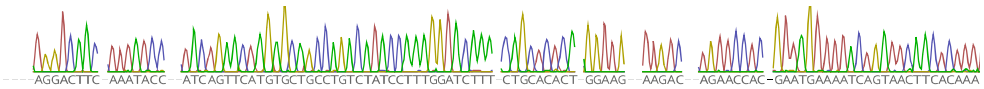
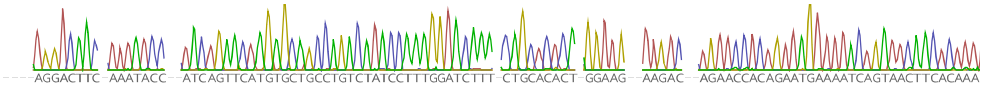


V#88 (FAM1&2-recovered)



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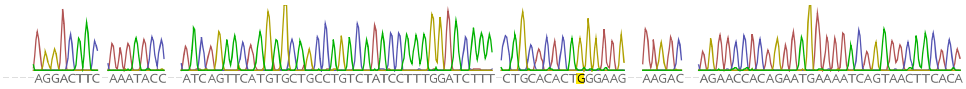
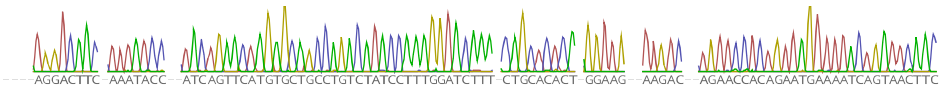
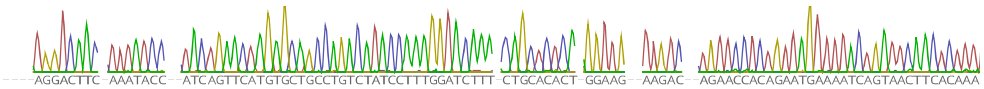


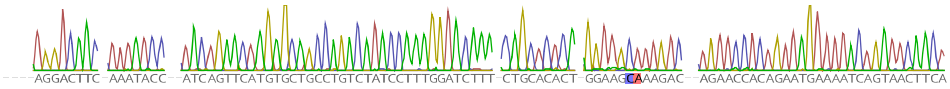
V#91 (FAM1&2-recovered)



V#92 (FAM1&2)



V#94 (FAM1&2-recovered)



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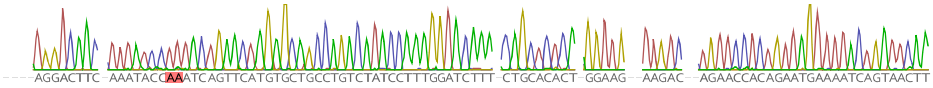

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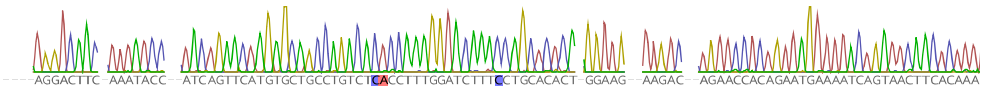

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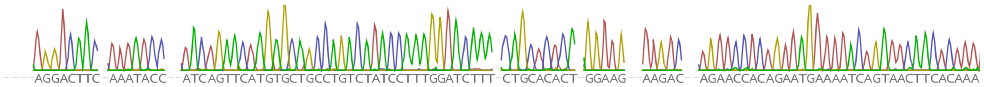
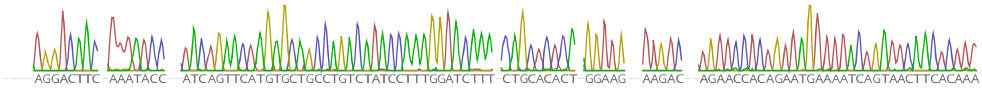
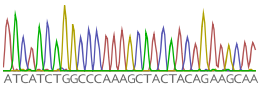


V#101 (FAM1&2)

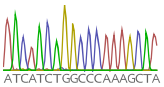


V#3 (FAM1&2)



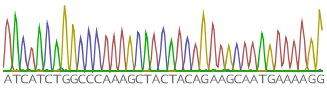
V#9 (FAM1&2)

V#18 (Partial FAM1)



V#21 (FAM1&2-recovered)

V#25 (FAM1&2-recovered)



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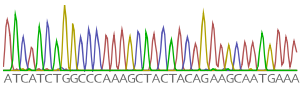
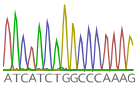
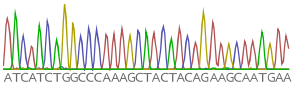


V#32 (Partial FAM1-recovered)

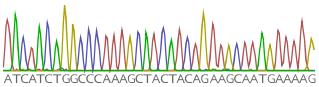
V#33 (FAM1&2)



V#37 (Partial FAM2-recovered)



V#39 (FAM1&2-recovered)



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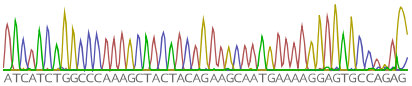
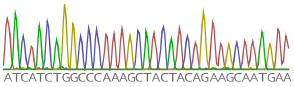
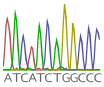


V#53 (Partial FAM1-recovered)



V#59 (Partial FAM1-recovered)



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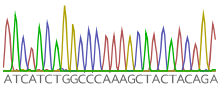
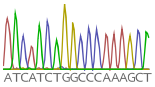


V#67 (FAM1&2)

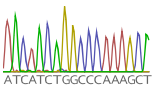


V#73 (FAM1&2-recovered)

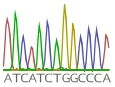
V#75 (Partial FAM2)

V#79 (FAM1&2)

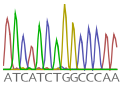
V#80 (Mutated)



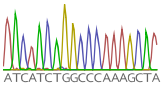
V#82 (Partial FAM1)



V#85 (Partial FAM2)



V#86 (Partial FAM1)



V#88 (FAM1&2-recovered)

V#89 (Partial FAM2)

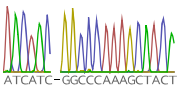
V#91 (FAM1&2-recovered)

V#92 (FAM1&2)

V#94 (FAM1&2-recovered)

V#95 (Partial FAM1)

V#97 (Partial FAM1)



V#98 (Partial FAM2)

V#101 (FAM1&2)

Name	Length	Direction	# Off-target Sites	Doench (2014) Activity Score	Protospacer Adjacent Motif (PAM)	Zhang (2013) Specificity Score	Target Sequence
CRISPR guide 3	23	forward	57 (1 in CDS)	0.237	AGG	32.44%	AAGTTCCTCAAGAGTTTGAA
CRISPR guide 4	23	reverse	140 (1 in CDS)	0.063	TGG	48.14%	TTATTATTTCTTTTTTTGTA
CRISPR guide 6	23	reverse	3 (0 in CDS)	0.26	AGG	77.76%	ATAGAGAGCGTATGGTTTCG
CRISPR guide 7	23	forward	3 (0 in CDS)	0.126	TGG	78.25%	TGGTTTGAAAACCTCAGCCC
CRISPR guide 11	23	reverse	7 (0 in CDS)	0.067	AGG	81.71%	GTTATCTATTGAAATTTTGA
CRISPR guide 12	23	reverse	2 (0 in CDS)	0.631	TGG	81.72%	TATTACCTCACACCGATCCA
CRISPR guide 13	23	forward	10 (0 in CDS)	0.091	CGG	82.08%	ACAATAAAATCACTTTATTT
CRISPR guide 15	23	reverse	4 (1 in CDS)	0.099	AGG	82.80%	GCATCAAACTCCTGTTTGAA
CRISPR guide 16	23	forward	3 (0 in CDS)	0.217	AGG	82.94%	TATATTGACACCTTTCAAAC
CRISPR guide 20	23	forward	2 (0 in CDS)	0.371	CGG	83.09%	TGGATCGGTGTGAGGTAATA
CRISPR guide 22	23	forward	21 (2 in CDS)	0.112	TGG	83.15%	GAAAAGAGGCAAAAGAAGGG
CRISPR guide 25	23	forward	1 (0 in CDS)	0.031	AGG	83.33%	ACAGTTAAGAATCTTTCTTC
CRISPR guide 27	23	reverse	1 (1 in CDS)	0.122	AGG	83.33%	CTCTTTCTAATTTCAATACC
CRISPR guide 28	23	forward	1 (0 in CDS)	0.289	AGG	83.33%	CTATTCCATGGATCGGTGTG
CRISPR guide 30	23	reverse	1 (0 in CDS)	0.55	AGG	83.33%	AATTACAGTGACCAGGGCTG
CRISPR guide 31	23	reverse	1 (0 in CDS)	0.107	TGG	83.33%	TCGAGGCTTTTGATTTGTGA
CRISPR guide 36	23	forward	2 (1 in CDS)	0.137	GGG	84.30%	CCTCATACAAGTTCATGAAT
CRISPR guide 42	23	forward	1 (0 in CDS)	0.139	AGG	89.21%	AAGAGACATCAGATCGTAAG
CRISPR guide 43	23	forward	14 (1 in CDS)	0.449	GGG	89.43%	ATTGAAAAGAGGCAAAAGAA
CRISPR guide 44	23	forward	2 (2 in CDS)	0.085	TGG	89.48%	TCCTCATACAAGTTCATGAA
CRISPR guide 48	23	reverse	4 (1 in CDS)	0.052	AGG	91.10%	TTGATTTGTGATGGATGTCC
CRISPR guide 50	23	reverse	4 (0 in CDS)	0.075	AGG	92.63%	TTTGACCTTTCAAACTCTTG
CRISPR guide 51	23	forward	8 (0 in CDS)	0.081	TGG	92.73%	ATTTCAAGAAATGATGTGAA
CRISPR guide 52	23	reverse	3 (2 in CDS)	0.104	TGG	92.76%	TCCATGGAATAGAGAGCGTA
CRISPR guide 54	23	reverse	8 (0 in CDS)	0.215	TGG	93.33%	CATCATTTCTTGAAATCATT
CRISPR guide 55	23	reverse	2 (0 in CDS)	0.027	AGG	93.40%	TTGCTGAAATTACAGTGACC
CRISPR guide 57	23	forward	9 (2 in CDS)	0.057	GGG	93.66%	ATTCTTACTATTCTCCAATT
CRISPR guide 60	23	forward	4 (1 in CDS)	0.515	GGG	94.19%	AGACTTACCACAAGTTTTAA
CRISPR guide 64	23	reverse	1 (1 in CDS)	0.22	CGG	94.59%	GCGACATACTTTACAAATGC
CRISPR guide 65	23	forward	6 (0 in CDS)	0.017	TGG	94.59%	TATACAGAAAACTATTTTCC
CRISPR guide 66	23	forward	6 (1 in CDS)	0.363	AGG	94.63%	GTTTTGAACATATTGAAAAG
CRISPR guide 67	23	forward	3 (0 in CDS)	0.13	TGG	94.67%	CACTTTTTGTGAATTGCTAA
CRISPR guide 72	23	reverse	6 (0 in CDS)	0.006	TGG	95.21%	AAGTGATTTTATTGTTTGTC
CRISPR guide 77	23	reverse	2 (1 in CDS)	0.279	CGG	95.85%	TGGAGAATAGTAAGAATTTG
CRISPR guide 78	23	reverse	3 (0 in CDS)	0.111	TGG	95.98%	TTACGATCTGATGTCTCTTT
CRISPR guide 80	23	forward	1 (1 in CDS)	0.268	AGG	96.24%	ATGTCGCGAGATCCACATGC
CRISPR guide 82	23	reverse	2 (1 in CDS)	0.12	GGG	96.43%	ATCAGACTCTTGAGAGTTAT
CRISPR guide 87	23	forward	1 (1 in CDS)	0.158	TGG	96.67%	AGTTCATGAATGGGTGTGCC
CRISPR guide 89	23	reverse	3 (1 in CDS)	0.065	TGG	96.81%	TCTTTTGGGTGGCCACGAGG
CRISPR guide 90	23	forward	2 (0 in CDS)	0.087	TGG	96.84%	ATGAATTCTCATAAGAGTTA
CRISPR guide 93	23	reverse	1 (0 in CDS)	0.447	GGG	96.94%	TGCTGAAATTACAGTGACCA
CRISPR guide 94	23	reverse	3 (1 in CDS)	0.223	AGG	96.99%	CCCATTCATGAACTTGTATG
CRISPR guide 95	23	reverse	3 (1 in CDS)	0.133	AGG	97.09%	AGAATTTGCGGATCAAGAAA
CRISPR guide 96	23	reverse	1 (1 in CDS)	0.15	TGG	97.12%	CTTGTATGAGGACCTGCATG
CRISPR guide 97	23	forward	9 (0 in CDS)	0.196	GGG	97.19%	AAAAGAGGCAAAAGAAGGGT
CRISPR guide 100	23	forward	2 (2 in CDS)	0.19	TGG	97.48%	ACCATACGCTCTCTATTCCA
CRISPR guide 102	23	reverse	1 (0 in CDS)	0.374	TGG	97.55%	GATCTGATGTCTCTTTTGGG
CRISPR guide 104	23	forward	6 (0 in CDS)	0.139	TGG	97.70%	ATTAAATGATTAATAAGACT
CRISPR guide 108	23	forward	5 (0 in CDS)	0.278	AGG	98.08%	TATTGAAAAGAGGCAAAAGA
CRISPR guide 111	23	reverse	3 (2 in CDS)	0.107	TGG	98.34%	AAACATGTGTATGCTATTAG
CRISPR guide 116	23	forward	3 (1 in CDS)	0.113	GGG	98.59%	TTTCAAGAAATGATGTGAAT
CRISPR guide 117	23	reverse	1 (0 in CDS)	0.224	AGG	98.73%	GTCTCTTTTGGGTGGCCACG
CRISPR guide 118	23	reverse	2 (0 in CDS)	0.075	GGG	98.79%	TACGATCTGATGTCTCTTTT
CRISPR guide 120	23	forward	2 (0 in CDS)	0.127	TGG	98.80%	AATTCTTACTATTCTCCAAT
CRISPR guide 123	23	forward	3 (0 in CDS)	0.159	CGG	98.98%	AAGGGTTGCAAGAGGAGAGC
CRISPR guide 125	23	forward	1 (0 in CDS)	0.26	CGG	99.06%	ACGCTCTCTATTCCATGGAT
CRISPR guide 126	23	forward	1 (1 in CDS)	0.103	AGG	99.13%	TGCATTAATTGCATAGACAC
CRISPR guide 137	23	forward	2 (0 in CDS)	0.308	TGG	99.41%	TCTGCACTTGTCAAACACAA
CRISPR guide 138	23	forward	1 (0 in CDS)	0.401	TGG	99.44%	GTCAGGGAAAAACCACCTCG
CRISPR guide 139	23	forward	1 (0 in CDS)	0.403	AGG	99.52%	CAAGTTTTAAGGGTTGCAAG
CRISPR guide 140	23	reverse	2 (0 in CDS)	0.02	TGG	99.53%	AAGATTCTTAACTGTCATTG
CRISPR guide 148	23	forward	1 (0 in CDS)	0.238	TGG	99.78%	CATAAGAGTTATGGTCGACA
CRISPR guide 162	23	forward	0 (0 in CDS)	0.072	AGG	100.00%	TCTCCAATTGGGAATCAGTC
CRISPR guide 163	23	forward	0 (0 in CDS)	0.175	GGG	100.00%	CTCCAATTGGGAATCAGTCA
CRISPR guide 164	23	forward	0 (0 in CDS)	0.014	AGG	100.00%	TAGACTTACCACAAGTTTTA
CRISPR guide 179	23	reverse	0 (0 in CDS)	0.084	TGG	100.00%	ATGCTATTAGTGGACGCTCA
CRISPR guide 180	23	reverse	0 (0 in CDS)	0.243	TGG	100.00%	CTTGCAACCCTTAAAACTTG
CRISPR guide 181	23	reverse	0 (0 in CDS)	0.069	TGG	100.00%	TATCAGACTCTTGAGAGTTA
CRISPR guide 182	23	reverse	0 (0 in CDS)	0.241	TGG	100.00%	TTCCCTGACTGATTCCCAAT

Supplementary Table 1: CRISPR sites located on 3' region of *MKK2*. Yellow highlight reveals the selected CRISPR target in this study.

Supplemntary Table 2 : Variant nucleotides happened from experiment I

Variant events	Polymorphism type	Variant genotyping	Protein effect	Nucleotide genotyping
I#11	T	Deletion	Frame Shift	CCG
I#11	T	Deletion	Frame Shift	A--------CAAGAAC
I#11	T	Insertion (tandem repeat)		-
I#11	T	SNP (transition)		C
I#11	T	Insertion (tandem repeat)		-
I#11	G	Insertion		-
I#11	G	SNP	None	--------G
I#11	G	Insertion		-
I#11	C	Deletion	Frame Shift	GCCGATCTCGGTCATGGCCGGCCGGAGGCGTCCCG GAAGTTCGTGGACACGACCTCCGACCACTC
I#11	C	Deletion	Frame Shift	TC
I#11	C	Deletion	Frame Shift	TC
I#11	C	Insertion		-
I#11	C	Insertion		-
I#11	C	SNP (transversion)		A
I#11	C	Insertion		-
I#11	A	Deletion	Truncation	GTCCTCCCGAAGTCCCGG-GA
I#11	A	Insertion		-
I#11	A	Insertion		-
I#11	A	SNP (transversion)		T
I#11	A	Insertion		-
I#11	A	Insertion		-
I#11		Deletion		A
I#11		Deletion		C
I#11		Deletion	Frame Shift	CCCA
I#11		Deletion	Frame Shift	C
I#11		Deletion	Frame Shift	GTACAGCTCG---------T-CCAGGCCGCGCACCCACACCCAGGCCAGGGTGTTG TCCGGCACCACCTGGTCCTGGACCGCGCTGATGAA CA
I#11		Deletion	Frame Shift	AT
I#11		Deletion	Frame Shift	AT
I#11		Deletion	Frame Shift	C
I#11		Deletion	Frame Shift	C
I#11, I#19	A	Insertion	Frame Shift	-
I#11, I#19, I#23		Deletion	Frame Shift	A
I#11, I#19, I#23, I#27, I#35, I#4, I#41, I#5, I#7	C	Insertion		-

I#11, I#19, I#23, I#27, I#35, I#4, I#5, I#7		Deletion		C
I#11, I#19, I#23, I#27, I#4, I#5	A	Insertion		-
I#11, I#19, I#23, I#27, I#5		Deletion		T
I#11, I#19, I#23, I#35, I#4, I#41, I#5, I#7		Deletion		A
I#11, I#19, I#27		Deletion	Deletion	ACAAGTTTTAAGGGTTGCAAG
I#11, I#19, I#27		Deletion	Deletion	GCC
I#11, I#19, I#27		Deletion	Deletion	GCC
I#11, I#19, I#27		Deletion	Deletion	GGC
I#11, I#19, I#27		Deletion	Deletion	GGC
I#11, I#19, I#27		Deletion	Deletion	CAC
I#11, I#19, I#27		Deletion	Deletion	CAC
I#11, I#19, I#27		Deletion	Deletion	ATG
I#11, I#19, I#27		Deletion	Deletion	ATG
I#11, I#19, I#27		Deletion	Deletion	CAG
I#11, I#19, I#27		Deletion	Deletion	CAG
I#11, I#19, I#27		Deletion	Deletion	GTC
I#11, I#19, I#27		Deletion	Deletion	GTC
I#11, I#19, I#27, I#35		Deletion	Deletion	AGG
I#11, I#19, I#27, I#35		Deletion	Deletion	AGG
I#11, I#19, I#27, I#35		Deletion	Deletion	AGA
I#11, I#19, I#27, I#35		Deletion	Deletion	AGA
I#11, I#19, I#35		Deletion (tandem repeat)		A
I#11, I#19, I#35, I#41	T	SNP	None	-------T
I#11, I#23	TA	Insertion (tandem repeat)		--
I#11, I#23	T	Insertion (tandem repeat)		-
I#11, I#23	C	Insertion		-
I#11, I#23	A	Insertion		-
I#11, I#23, I#35		Deletion		AATAAGACTTGGATT
I#11, I#23, I#35, I#4, I#41, I#5		Deletion		C
I#11, I#27		Deletion	Deletion	GGTCACGTCGTCCCGGACCACACCGGCGAAGTC
I#11, I#27, I#35		Deletion	Deletion	CGGCTGCTC
I#11, I#27, I#35, I#5		Deletion (tandem repeat)		TTTTTT
I#11, I#27, I#35, I#5		Deletion		TTTTTTTTTATGATGATGATGATGATG
I#11, I#27, I#35, I#5		Deletion	Extension	TCAGTCCTGCTCCTCGGCCACGAAGTGCACGCAGT TGCCGGCCGGGTCGCGCAGGGCGAA
I#11, I#35		Deletion		A
I#11, I#35		Deletion		T

I#11, I#35		Deletion		GCAACTACATCTTCACAAGAACTCCATACAAAAAA AGAAATAATAA
I#11, I#35		Deletion (tandem repeat)		A
I#11, I#35		Deletion		AAAA
I#11, I#35		Deletion		A
I#11, I#35		Deletion		TTGA
I#11, I#35		Deletion		AA
I#11, I#35		Deletion		ATGATTTCAAGAAATGATGTGAATGGGAAAATTAG ACTTA
I#11, I#35, I#4		Deletion (tandem repeat)		T
I#11, I#35, I#5		Deletion		C
I#11, I#35, I#5		Deletion (tandem repeat)		TTTTTTTTTTTTTT
I#11, I#35, I#5		Deletion	Deletion	CTC
I#11, I#4, I#5	C	Insertion		-
I#11, I#41	A	Insertion		-
I#19	T	SNP	None	-T
I#19	T	SNP (transversion)	None	G
I#19	T	SNP (transversion)	None	G
I#19	T	Deletion	Frame Shift	AA
I#19	T	Deletion	Frame Shift	AA
I#19	G	Deletion	Extension	CTACATCTTCA--------CAAGAAC
I#19	G	Insertion		-
I#19	A	Insertion (tandem repeat)		-
I#19	A	Insertion		-
I#19		Deletion		TAAATTC
I#19		Deletion	Frame Shift	GTCACGTCGTCCCGGACCACACCGGCGAAGTC
I#19		Deletion	Frame Shift	CG
I#19		Deletion	Frame Shift	CG
I#19		Deletion		ATAGC
I#19		Deletion		C
I#19		Deletion		A
I#19		Deletion		CAT
I#19		Deletion		TGA
I#19		Deletion		A
I#19		Deletion (tandem repeat)		A
I#19, I#23, I#27, I#35, I#4, I#41, I#5, I#7		Deletion		C
I#19, I#23, I#27, I#35, I#41	C	Insertion		-
I#19, I#27		Deletion	Deletion	ATT
I#19, I#27		Deletion	Deletion	ATT

I#19, I#27		Deletion	Deletion	TGT
I#19, I#27		Deletion	Deletion	TGT
I#19, I#27		Deletion	Deletion	AAA
I#19, I#27		Deletion	Deletion	AAA
I#19, I#27		Deletion	Deletion	GTA
I#19, I#27		Deletion	Deletion	GTA
I#19, I#27		Deletion	Deletion	TGT
I#19, I#27		Deletion	Deletion	TGT
I#19, I#27		Deletion	Deletion	ATC
I#19, I#27		Deletion	Deletion	ATC
I#19, I#27		Deletion	Deletion	CTC
I#19, I#27		Deletion	Deletion	CTC
I#19, I#27		Deletion		AAATTAGAA
I#19, I#27		Deletion		AGAAAAA
I#19, I#27		Deletion		AGAGTCAGATCCATG
I#19, I#27		Deletion		TCCACTA
I#19, I#27		Deletion		ATA
I#19, I#27		Deletion		TTT
I#19, I#27		Deletion		CATAT
I#19, I#27		Deletion		GA
I#19, I#27, I#4		Deletion	Deletion	GAA
I#19, I#27, I#4		Deletion	Deletion	GAA
I#19, I#27, I#4, I#41		Deletion		A
I#19, I#27, I#4, I#5		Deletion	Deletion	TGG
I#19, I#27, I#4, I#5		Deletion	Deletion	TGG
I#19, I#27, I#4, I#5		Deletion	Deletion	GTG
I#19, I#27, I#4, I#5		Deletion	Deletion	GTG
I#19, I#27, I#4, I#5		Deletion	Deletion	TGC
I#19, I#27, I#4, I#5		Deletion	Deletion	TGC
I#19, I#27, I#4, I#5		Deletion		C
I#19, I#27, I#5		Deletion	Deletion	GTCCTCCACGAAGTCCCGG-GA
I#19, I#27, I#5		Deletion	Deletion	GAACCCG------AGCCGGTCGGTCCAGAACTCGACC-------GCTCCGGCGACGTCGCGCGCGGTGAG
I#19, I#27, I#5		Deletion	Start Codon Loss	CACCGGAACGGCACTGGTCAACTTGGCCAT
I#19, I#27, I#5		Deletion	Deletion	CAA
I#19, I#27, I#5		Deletion	Deletion	CAA
I#19, I#27, I#5		Deletion	Deletion	GTT
I#19, I#27, I#5		Deletion	Deletion	GTT
I#19, I#27, I#5		Deletion	Deletion	CAT
I#19, I#27, I#5		Deletion	Deletion	CAT

I#19, I#27, I#5		Deletion		TATTG
I#19, I#35		Deletion		AACTCTAAAG
I#19, I#4, I#5		Deletion		TG
I#19, I#5		Deletion		G
I#23	T	Deletion	Extension	CTACATCTTCA--------CAAGAAC
I#23	T	Insertion		-
I#23	T	Insertion (tandem repeat)		-
I#23	GTCCTG	Insertion		------
I#23	G	SNP	None	---------G
I#23	G	Insertion		-
I#23	G	Insertion		-
I#23	G	Insertion		-
I#23	CCGG	Insertion	Frame Shift	----
I#23	CCGG	Insertion	Frame Shift	----
I#23	C	SNP	None	------C
I#23	C	Insertion		-
I#23	ACATTCCCCCT	Insertion	Frame Shift	---------T-
I#23	A	Insertion		-
I#23	A	Insertion (tandem repeat)		-
I#23	A	SNP (transversion)		T
I#23	A	Insertion		-
I#23	A	Insertion	Frame Shift	-
I#23		Deletion		G
I#23		Deletion	Frame Shift	ACAAGTTTTAAGGGTT
I#23, I#27	T	SNP	None	------T
I#23, I#5	T	Insertion (tandem repeat)		-
I#23, I#7	C	Insertion (tandem repeat)		-
I#27	TCCG	Insertion		----
I#27	GGGCGAA	Insertion		-------
I#27	G	Insertion		-
I#27	G	Insertion		-
I#27	G	SNP (transition)		A
I#27	C	Insertion (tandem repeat)		-
I#27	C	Insertion (tandem repeat)		-
I#27	C	SNP (transversion)		A
I#27	C	SNP (transversion)		A
I#27	C	Insertion		-
I#27	C	Insertion	Frame Shift	-
I#27	AT	Insertion	Frame Shift	---------
I#27	A	Insertion (tandem repeat)		-

I#27	A	Insertion		-
I#27	A	Insertion		-
I#27	A	Insertion		-
I#27	A	Insertion		-
I#27	A	SNP (transversion)		C
I#27	A	Deletion	Extension	CTACATCTTCCAAGAAC
I#27		Deletion	Frame Shift	T-CCAGGCCGCGCACCCACACCCAGGCCAGGGTGTTGTCCGGCACCACCTGGTCCTGGACCGCGC
I#27		Deletion	Frame Shift	TGAACAG
I#27		Deletion	Deletion	CGC
I#27		Deletion	Deletion	CGC
I#27		Deletion	Deletion	GAG
I#27		Deletion	Deletion	GAG
I#27		Deletion		AG
I#27		Deletion		G
I#27		Deletion		AGCG
I#27		Deletion (tandem repeat)		A
I#27, I#35, I#41		Deletion	Frame Shift	A--T
I#27, I#35, I#41, I#7	A	Insertion		-
I#27, I#35, I#41, I#7		Deletion		A
I#27, I#41, I#7	C	Insertion (tandem repeat)		-
I#27, I#5		Deletion	Deletion	CCG
I#27, I#5		Deletion	Deletion	CCCCCA
I#27, I#5		Deletion	Deletion	ATA
I#27, I#5		Deletion	Deletion	ATA
I#27, I#7	A	Insertion		-
I#35	TTTGTAA	Insertion		-------
I#35	T	Insertion	Frame Shift	-
I#35	GAAA	Insertion	Frame Shift	----
I#35	AAAA	Insertion	Frame Shift	----
I#35	AAAA	Insertion	Frame Shift	----
I#35	A	Deletion	Frame Shift	GTACAGCTCG---------T-CCAGGCCGCGCA
I#35	A	SNP (transition)	None	G
I#35		Deletion		TACA
I#35		Deletion		T
I#35		Deletion		G
I#35		Deletion		AATTCTCATAAGAGT
I#35		Deletion		T
I#35		Deletion		ATGGTCGACATGGTAAATGCATTA

I#35		Deletion		ATTG
I#35		Deletion		C
I#35		Deletion		ATAGACA
I#35		Deletion		GAACTAT
I#35		Deletion		T
I#35		Deletion		AAATGATT
I#35		Deletion		G
I#35		Deletion	Frame Shift	CC
I#35		Deletion	Frame Shift	CCCCA
I#35		Deletion	Frame Shift	G
I#35		Deletion	Frame Shift	TCCAGAACTCGACC--------- GCTCCGGCGACGTCGCGCGCGGTGAG
I#35		Deletion	Deletion	CCGGAACGGCACTGG
I#35		Deletion	Start Codon Loss	AACTTGGCCAT
I#35		Deletion	Frame Shift	G
I#35		Deletion	Frame Shift	GC
I#35		Deletion	Frame Shift	GC
I#35, I#4, I#41	A	Insertion (tandem repeat)		-
I#35, I#41	AT	Insertion	Frame Shift	--------
I#35, I#41	A	Insertion		-
I#35, I#41, I#5, I#7	T	Insertion	Frame Shift	-
I#35, I#41, I#5, I#7	T	Insertion	Frame Shift	-
I#35, I#41, I#5, I#7		Deletion	Frame Shift	T
I#35, I#41, I#5, I#7		Deletion	Frame Shift	T
I#35, I#5		Deletion	Deletion	GCCGATCTCGGTCATGGCCGGC------ CCGGAGGCGTCCCGGAAGTTCGTGGACACGACCTC CGACCACTC
I#4	TTTATCGCA	Insertion	Truncation	A--------
I#4	TCCTAA	Insertion	Truncation	------
I#4	T	SNP	None	T-
I#4	G	Insertion (tandem repeat)	Frame Shift	-
I#4	G	Insertion		-
I#4	G	Insertion		-
I#4	CCACAC	Insertion		------
I#4	A	Insertion		-
I#4	A	SNP	None	A-
I#4		Deletion		AACAGGCAG
I#4		Deletion		A
I#4		Deletion		CAGCTA
I#4, I#7	T	SNP	None	T-

I#4, I#7	C	Insertion (tandem repeat)		-
I#41	T	SNP	None	--------T
I#41	GG	Insertion	Frame Shift	--
I#41	CTGTTCGAC	Insertion	Insertion	---------
I#41	C	Insertion	Frame Shift	-
I#41	C	Insertion	Frame Shift	-
I#41	AAGAACACA	Insertion		---------
I#41	A	Insertion		-
I#41		Deletion		A
I#41		Deletion	Frame Shift	G
I#41		Deletion	Frame Shift	C
I#41		Deletion	Frame Shift	C
I#41		Deletion	Deletion	TGC
I#5	T	SNP (transversion)		G
I#5	T	SNP (transversion)		A
I#5	T	SNP (transition)		C
I#5	G	SNP (transversion)		T
I#5	G	SNP (transversion)		T
I#5	G	SNP (transversion)		C
I#5	CT	Insertion		--
I#5	C	SNP (transition)		T
I#5	C	SNP (transversion)		A
I#5	A	Deletion	Frame Shift	GGTCCGTCGTCCCGGACCACACCGGCGAAGTC
I#5		Deletion		CCC
I#5		Deletion	Frame Shift	GGCTGCTC
I#5		Deletion	Deletion	GGC
I#5		Deletion	Frame Shift	GTACAGCTCG---------T-CCAGGCCGCGCACC
I#5		Deletion	Frame Shift	CCCAGGCCAGGGTGTTGTCCGGCACCACCTGGTCC TGGACCGCGCTGATGAACAG
I#5		Deletion	Extension	CTACATCTTCA--------CAAGAAC
I#5		Deletion	Frame Shift	TC
I#5		Deletion	Frame Shift	TC
I#5		Deletion	Frame Shift	AA
I#5		Deletion	Frame Shift	AA
I#5		Deletion	Deletion	AC-A
I#5		Deletion		CTGG
I#7	T	Insertion (tandem repeat)		-
I#7	T	Insertion		-
I#7	T	Insertion		-
I#7	T	Insertion		-

I#7	GA	Insertion	Frame Shift	--
I#7	G	Insertion		-
I#7	C	Insertion (tandem repeat)		-
I#7	C	Insertion (tandem repeat)		-
I#7	C	Insertion		-
I#7	AGTTCGAGTATGC	Insertion	Frame Shift	----------
I#7	AATAAT	Insertion	Insertion	------
I#7	AAACCTCAGCCCTGGTT	Insertion	Frame Shift	----------
I#7	A	Insertion		-
I#7		Deletion	Frame Shift	GGCACCACCT
I#7		Deletion		G

Supplemntary Table 2 : Variant nucleotides happened from experiment II

Variant events	Polymorphism type	Variant genotyping	Protein effect	Nucleotide genotyping
II#11	G	SNP (transversion)	Substitution	T
II#11	G	SNP (transversion)	Substitution	T
II#11	C	SNP (transversion)	Substitution	A
II#11	C	Insertion		-
II#11	AC	Insertion		--
II#11	A	Insertion	Frame Shift	-
II#11, II#23		Deletion		ATACACA
II#13	T	Insertion	Frame Shift	-
II#13		Deletion		A
II#13		Deletion		TGCAAC
II#13		Deletion		A
II#13		Deletion		C
II#13		Deletion		TTA
II#13		Deletion	Deletion	CCA
II#13		Deletion	Frame Shift	C
II#13		Deletion (tandem repeat)	Frame Shift	T
II#13, II#40, II#48		Deletion	Deletion	CTCCGA
II#13, II#41, II#48		Deletion		TGAT
II#13, II#48		Deletion		TTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGA
II#13, II#48		Deletion		GATGATG
II#13, II#48		Deletion	Extension	TCAGTCCT-GCTCCTCGGCCACGAAGTGCACGCAGTTGCCGGCCGGGTCGCGCAGGGCGAACTCCCGCCCCCACG GCTGCTCGCCGATCT-CGGTCATGGCCGGCCCGGAGGCGTCCCGGAAGTTCGTGGACACGAC
II#13, II#48		Deletion	Deletion	CTCGGCGTACAGCTC
II#13, II#48		Deletion	Deletion	GTC
II#14	TTA	Insertion		---
II#14	T	Insertion (tandem repeat)	Frame Shift	-
II#14	A	Insertion	Frame Shift	-
II#14		Deletion (tandem repeat)		A
II#19	T	Insertion		-
II#19	C	SNP (transition)	Substitution	T
II#19	AAGAC	Insertion		-----
II#19	A	Insertion (tandem repeat)		-
II#19	A	SNP (transversion)	Substitution	C
II#19		Deletion		C
II#19		Deletion	Deletion	CAGGCC
II#21	T	SNP (transversion)		G
II#21	T	Insertion		-
II#21	G	Insertion		-
II#21	CGGGGA	Insertion	Insertion	------
II#21		Deletion	Frame Shift	T
II#22	G	Insertion	Frame Shift	-
II#22	G	SNP (transition)		A
II#22	C	SNP (transversion)		A
II#22	C	SNP (transversion)		A
II#22	ACC	Insertion	Insertion	---

II#22	ACC	Insertion	Insertion	---
II#22	A	SNP (transversion)		C
II#22		Deletion	Frame Shift	ATCT
II#23	T	SNP (transition)	Substitution	C
II#23	C	Insertion	Frame Shift	-
II#23	AAT	Insertion	Insertion	---
II#23	AAT	Insertion	Insertion	---
II#23	A	Insertion	Frame Shift	-
II#23		Deletion	Frame Shift	GTCGTCCCGGACCACACCGGCGAAGT
II#23		Deletion	Frame Shift	C
II#23		Deletion	Frame Shift	GT
II#23		Deletion	Frame Shift	GT
II#23		Deletion	Deletion	CGC
II#23		Deletion	Deletion	CGC
II#23		Deletion	Deletion	GAG
II#23		Deletion	Deletion	GAG
II#23		Deletion	Deletion	ATC
II#23		Deletion	Deletion	ATC
II#23		Deletion	Deletion	CAC
II#23		Deletion	Deletion	CAC
II#23		Deletion	Deletion	ATG
II#23		Deletion	Deletion	ATG
II#23		Deletion	Deletion	CAG
II#23		Deletion	Deletion	CAG
II#23		Deletion	Deletion	GTC
II#23		Deletion	Deletion	GTC
II#23		Deletion	Deletion	CTC
II#23		Deletion	Deletion	CTC
II#23		Deletion		AAAA
II#23		Deletion		GAAGA
II#23		Deletion		CATGAGCG
II#23		Deletion		CC
II#23		Deletion		ATAGC
II#23		Deletion		TGT
II#23, II#38, II#48		Deletion	Deletion	GGTCAC
II#23, II#38, II#48, II#53		Deletion	Deletion	CACCTGGTCCTGGACCGCGCTGATGAACAG
II#23, II#40		Deletion	Deletion	ATA
II#23, II#40		Deletion	Deletion	ATA
II#23, II#40		Deletion	Deletion	CAA
II#23, II#40		Deletion	Deletion	CAA
II#23, II#40		Deletion	Deletion	GTT
II#23, II#40		Deletion	Deletion	GTT
II#23, II#40		Deletion	Deletion	CAT
II#23, II#40		Deletion	Deletion	CAT
II#23, II#40		Deletion	Deletion	GAA
II#23, II#40		Deletion	Deletion	GAA

II#23, II#40		Deletion	Deletion	TGG
II#23, II#40		Deletion	Deletion	TGG
II#23, II#40		Deletion	Deletion	GTG
II#23, II#40		Deletion	Deletion	GTG
II#23, II#40		Deletion	Deletion	TGC
II#23, II#40		Deletion	Deletion	TGC
II#23, II#40		Deletion		CTGGTATTGAAA
II#23, II#40		Deletion		TTAGAAAGAGA
II#23, II#48		Deletion		ACTA
II#23, II#53		Deletion		GTCAGA
II#23, II#53		Deletion		TC
II#29	T	Insertion		-
II#29	T	Insertion		-
II#29	T	Insertion		-
II#29	C	Insertion		-
II#29	C	Insertion		-
II#29	C	Insertion		-
II#29	A	Insertion		-
II#29	A	Insertion		-
II#29		Deletion		A
II#29		Deletion		GTCT
II#29, II#59	AT	Insertion		--
II#3	TGAA	Insertion		----
II#3	T	Insertion		-
II#3	A	SNP (transversion)		T
II#3		Deletion		A
II#3		Deletion		CAC
II#3		Deletion	Start Codon Loss	GAACGGCACTGGTCAACTTGGCCAT
II#3		Deletion	Deletion	A-CAAGTTTTAAGGGTTGC
II#3		Deletion	Deletion	GCC
II#3		Deletion	Deletion	GCC
II#3		Deletion	Deletion	G---GC
II#3		Deletion	Deletion	G---GC
II#3		Deletion	Deletion	ATT
II#3		Deletion	Deletion	ATT
II#3		Deletion	Deletion	TGT
II#3		Deletion	Deletion	TGT
II#3		Deletion	Deletion	AAA
II#3		Deletion	Deletion	AAA
II#3		Deletion	Deletion	GTA
II#3		Deletion	Deletion	GTA
II#3		Deletion	Frame Shift	T---G
II#3		Deletion	Frame Shift	T---G
II#3, II#48		Deletion	Extension	CTACATC-TTCACAAGAAC
II#3, II#48		Deletion	Deletion	AAG
II#3, II#48		Deletion	Deletion	AGG

II#3, II#48		Deletion	Deletion	AGG
II#3, II#48		Deletion	Deletion	AGA
II#3, II#48		Deletion	Deletion	AGA
II#35	TCC	Insertion	Insertion	---
II#35	T	SNP (transition)	None	C
II#35	G	Insertion	Frame Shift	-
II#35	A	Insertion (tandem repeat)		-
II#35	A	Deletion		AC
II#35		Deletion		G
II#35		Deletion		C
II#35		Deletion		A
II#35		Deletion		TTT
II#35		Deletion		G
II#35, II#41		Deletion (tandem repeat)		A
II#38	TAA	Insertion		---
II#38	C	Insertion		-
II#38	A	SNP (transition)	Substitution	G
II#38	A	Insertion	Frame Shift	-
II#38	A	Insertion	Frame Shift	-
II#38		Deletion		CAGCA
II#38		Deletion	Frame Shift	AGGGTGTTGTCCGGCAC
II#38		Deletion		A
II#40	T	Insertion	Truncation	-
II#40	G	SNP (transversion)		C
II#40		Deletion		A
II#40		Deletion	Frame Shift	CCCACGGCTGCTCGCCGATCT-CGGTCATGGCCGGCCCGGAGGCGTCCCGGAAGTTCGTGGACACGAC
II#40		Deletion	Frame Shift	TC
II#40		Deletion	Frame Shift	TC
II#41	T	SNP (transversion)	None	G
II#41	T	SNP (transition)	Substitution	C
II#41	G	SNP (transversion)	Substitution	T
II#41	CGG	Insertion		---
II#41	C	Insertion		-
II#41	A	SNP (transversion)	Substitution	C
II#41		Deletion	Frame Shift	A
II#48	T	Insertion		-
II#48	T	Insertion	Frame Shift	-
II#48	CCGC	Insertion		----
II#48	C	SNP (transversion)		A
II#48	C	SNP (transversion)		G
II#48	AT	Insertion		--
II#48	A	SNP (transversion)		T
II#48		Deletion	Deletion	C-AGGCC
II#48		Deletion	Deletion	GCGCACCCACACCCAGGCCAGGGTGTTGTCCGGCAC
II#48		Deletion	Deletion	GTCGTCCCGGACCACACCGGCGAAGTCGTC
II#48		Deletion	Deletion	CTCCAC

II#48		Deletion	Deletion	GAAGTCCCG
II#48		Deletion	Deletion	GGAGAACCCGAGCCGGTCGGTCCA
II#48		Deletion	Start Codon Loss	GAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAGCACCGGAACGGCACTGGTCAACTTGGCCAT
II#48		Deletion	Frame Shift	A
II#48		Deletion		A
II#48		Deletion	Frame Shift	TT
II#48		Deletion	Frame Shift	CTGCAC-A
II#48		Deletion		CT
II#48, II#59		Deletion		GG
II#53	T	Insertion		-
II#53	G	SNP (transversion)	Substitution	C
II#53	CCCACG	Insertion	Insertion	------
II#53	C	Insertion		-
II#53		Deletion	Frame Shift	TTGTCCGGCAC
II#53		Deletion		A
II#59	T	Insertion (tandem repeat)		-
II#59	G	Insertion		-
II#59	G	Insertion		-
II#59	C	SNP (transition)		T
II#59	C	Insertion		-
II#59	C	Insertion		-
II#59	C	Insertion		-
II#59	C	Insertion		-
II#59	C	SNP (transversion)	Substitution	G
II#59	AA	Substitution	Substitution	TC
II#59	A	Insertion		-
II#59		Deletion		A
II#59		Deletion		AA
II#7	C	Insertion		-
II#7	C	Insertion		-
II#7	C	Deletion		AGGCAAA
II#7	C	SNP (transversion)		G
II#7	C	SNP (transversion)	Substitution	A
II#7	AC	Substitution	Substitution	CA
II#7		Deletion		G
II#7		Deletion	Deletion	CCG

Supplemntary Table 2 : Variant nucleotides happened from experiment III

Variant events	Polymorphism type	Variant genotyping	Protein effect	Nucleotide genotyping
III#10	T	Insertion		-
III#10	T	Insertion		-
III#10	C	Insertion		-
III#10		Deletion		TT
III#10		Deletion	Frame Shift	GCCG
III#10		Deletion	Deletion	TTGTCCGGC
III#10, III#32	C	SNP	None	-------C
III#10, III#32	A	SNP	None	-----A
III#14	TTAGGTA	Insertion	Frame Shift	-------
III#14	C	Insertion	Frame Shift	-
III#14	A	Deletion	Frame Shift	CGCGGTGG
III#14		Deletion		ACTATT
III#14		Deletion		A
III#14		Deletion	Frame Shift	CAGGCCAGGGTGTTGTCCGGCACCACCTGGTCCTGGACC GCGCT
III#14		Deletion	Frame Shift	A
III#14, III#17		Deletion	Start Codon Loss	CACCGGAACGGCACTGGTCAACTTGGCCAT
III#14, III#17, III#21, III#23, III#24, III#27, III#32, III#45		Deletion		C
III#14, III#17, III#24, III#27, III#32, III#45	C	Insertion (tandem repeat)		-
III#14, III#17, III#43		Deletion	Extension	CTACATCTTCACAAGAAC
III#14, III#23, III#27, III#53, III#6		Deletion	Frame Shift	C
III#14, III#43		Deletion	Extension	TCAGTCCTGCTCCTC
III#14, III#43		Deletion	Deletion	GCGCAGGGCGAACTCCCGCCCCCACG-GCTGCTCGCCGATCTCGGTCATGGCCGGCCCGGAGGCGT-CCCGGAAGTTCGTGGACACGACCTCCGACCACTCGGCGT ACAGCTCGTCCAGGCCGCGCACCCA
III#14, III#43		Deletion	Deletion	GATGAACAGGGTCACGTCGTCCCGGACCACACCGG-CGAAGTCGTCCTCCACGAAGTCCCGGGA
III#14, III#43		Deletion	Deletion	GAACCCGAGCCGGTCGGTCC-----A
III#14, III#43		Deletion	Deletion	GAACTCGAC
III#14, III#43		Deletion	Deletion	CGCTCC
III#14, III#43		Deletion	Deletion	GGCGACGTCGCG
III#14, III#43, III#8		Deletion		ATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATG ATGATG
III#14, III#43, III#8		Deletion	Deletion	CAC

III#14, III#43, III#8		Deletion	Deletion	GCA
III#14, III#43, III#8		Deletion	Deletion	GTT
III#14, III#43, III#8		Deletion	Deletion	GCCGGCCGGGTC
III#14, III#8		Deletion	Deletion	GGCCACGAAGT-G
III#17	G	Insertion		-
III#17	C	Insertion		-
III#17	C	Insertion		-
III#17	AGCCAG	Insertion		------
III#17		Deletion		ATT
III#17		Deletion	Frame Shift	GGCGACGTCGC
III#17		Deletion	Frame Shift	ACAAGTTTTAAGGGTTG
III#17		Deletion	Frame Shift	A
III#17, III#32	C	Insertion		-
III#17, III#43		Deletion	Deletion	CGCGGTGAG
III#21	T	Insertion		-
III#21	CG	Substitution	Substitution	GC
III#21	C	Insertion		-
III#21	ACAAT	Insertion	Frame Shift	-----
III#21		Deletion		T
III#21		Deletion		G
III#21, III#23	C	Insertion (tandem repeat)		-
III#21, III#43		Deletion		CTCCATA
III#23	T	Insertion		-
III#23	C	Insertion	Frame Shift	-
III#23	AA	Insertion		--
III#23	A	Insertion	Truncation	-
III#23		Deletion		CTTTTTGT
III#23		Deletion	Frame Shift	A
III#23		Deletion	Frame Shift	A
III#24	TGGTACTA	Insertion	Truncation	--------
III#24	T	Insertion	Frame Shift	-
III#24	G	SNP (transversion)	Substitution	T
III#24	AC	Substitution	Substitution	TT
III#24		Deletion	Frame Shift	A
III#24, III#27, III#36, III#53, III#6, III#61		Deletion	Frame Shift	G
III#24, III#27, III#53, III#6	G	Insertion	Frame Shift	-
III#24, III#8		Deletion		AC
III#27	CAATTC	Insertion		------

III#27	C	Insertion		-
III#27	AT	Insertion	Frame Shift	T-
III#27		Deletion	Frame Shift	CCGA
III#27		Deletion		C
III#27, III#53	C	Insertion	Frame Shift	-
III#32	TAA	Substitution	Substitution	CC
III#32	T	Insertion	Frame Shift	-
III#32	CTCG	Insertion	Frame Shift	----
III#32	AC	Deletion	Frame Shift	GA
III#32	A	Insertion	Frame Shift	-
III#32		Deletion		A
III#32		Deletion	Deletion	GCACCA
III#32, III#8		Deletion		C
III#36	T	Insertion		-
III#36	GGGTTC	Insertion		------
III#36	G	Insertion	Frame Shift	-
III#36	A	Insertion		-
III#36		Deletion	Frame Shift	C
III#36		Deletion		GAAC
III#43	G	Insertion		-
III#43	CGTAAGGTC	Insertion		---------
III#43	C	Insertion		-
III#43	A	Deletion	Truncation	GGCCACGAGT-G
III#43	A	Deletion	Frame Shift	CAGGCCGGGTGTTGTCCGGCACCACCTGGTCCTGGACCG CGCT
III#43	A	SNP (transversion)		T
III#43		Deletion		A
III#43		Deletion	Frame Shift	CA
III#43		Deletion	Start Codon Loss	ACCGGAACGGCACTGGTCAACTTGGCCAT
III#43		Deletion	Frame Shift	AC
III#45	TTGGAGCTT	Insertion	Insertion	---------
III#45	TCA	Substitution		CTC
III#45	T	Insertion	Frame Shift	-
III#45	A	Insertion (tandem repeat)		-
III#45		Deletion		T
III#45		Deletion (tandem repeat)		A
III#45		Deletion		G
III#53	TGGGGTT	Insertion		-------
III#53	T	Insertion		-
III#53	C	Insertion		-

III#53	A	Insertion		-
III#53		Deletion		TAAATT
III#53		Deletion	Frame Shift	G
III#53		Deletion	Frame Shift	CTGC-ACA
III#6	C	Insertion	Frame Shift	-
III#6	C	SNP (transversion)	Substitution	A
III#6	AGCTC	Insertion		-----
III#6		Deletion	Deletion	CTC
III#6		Deletion		AAA
III#6		Deletion (tandem repeat)		A
III#61	T	Insertion	Frame Shift	-
III#61	G	Insertion (tandem repeat)		-
III#61	G	Insertion	Frame Shift	-
III#61	CGCTTTAG	Insertion		--------
III#61	A	Insertion (tandem repeat)		-
III#61		Deletion		A
III#61		Deletion	Frame Shift	GTTC
III#61		Deletion		A
III#8	T	SNP (transversion)		A
III#8	C	Insertion	Frame Shift	-
III#8	C	Insertion		-
III#8	AT	Insertion	Frame Shift	--
III#8	AG	Substitution		GA
III#8		Deletion		AG
III#8		Deletion		TT
III#8		Deletion	Extension	TCAGTCCTGCTCCT
III#8		Deletion	Frame Shift	GCGC
III#8		Deletion	Frame Shift	C
III#8		Deletion	Frame Shift	TC
III#8		Deletion	Deletion	ATACAAGTT
III#8		Deletion	Deletion	CATGAATGGGTGTGC
III#8		Deletion		CTGG
III#8		Deletion		GT

Supplemntary Table 2 : Variant nucleotides happened from experiment IV

Variant events	Polymorphism type	Variant genotyping	Protein effect	Nucleotide genotyping
IV#13	TT	Insertion		--
IV#13	T	Insertion (tandem repeat)		-
IV#13	T	SNP (transition)	Substitution	C
IV#13	C	SNP (transition)		T
IV#13	C	SNP (transversion)	Substitution	A
IV#13	C	SNP (transversion)	Substitution	G
IV#13	C	SNP (transition)		T
IV#13	A	Insertion		-
IV#13		Deletion	Frame Shift	G
IV#13		Deletion	Frame Shift	GC
IV#13, IV#80		Deletion	Frame Shift	TG
IV#17	T	SNP (transversion)		A
IV#17	GC	Insertion		--
IV#17	C	Insertion		-
IV#17	C	SNP (transversion)		G
IV#17		Deletion		A
IV#17		Deletion		AGGC
IV#17, IV#9	A	Insertion (tandem repeat)		-
IV#19	T	SNP (transversion)		G
IV#19	G	Insertion		-
IV#19	AA	Insertion	Frame Shift	--
IV#19	A	Insertion (tandem repeat)		-
IV#19		Deletion (tandem repeat)	Frame Shift	C
IV#19		Deletion		GAG
IV#27	G	Insertion		-
IV#27	G	Insertion (tandem repeat)		-
IV#27	CC	Insertion		--
IV#27	C	Insertion	Frame Shift	-
IV#27	AG	Insertion		--
IV#27	A	SNP (transition)	None	G
IV#27		Deletion	Frame Shift	T
IV#32	G	Insertion		-
IV#32	G	Insertion	Frame Shift	-
IV#32	C	SNP (transition)		T
IV#32	C	Insertion		-
IV#32	A	Insertion		-

IV#32		Deletion	Frame Shift	TCCCGGGAGAACCCGAGCC--GGTCGGTCCAGAACTCGACCGCTCCGGCGACGTCGCGCGCGGTGAG
IV#32		Deletion	Frame Shift	C
IV#32		Deletion	Frame Shift	C
IV#32		Deletion		T
IV#32		Deletion		ACA
IV#32		Deletion		CAT
IV#32		Deletion (tandem repeat)		T
IV#32		Deletion		TTT
IV#32		Deletion		AACAT
IV#32		Deletion		ATT
IV#32, IV#39		Deletion		G
IV#32, IV#80		Deletion		G
IV#39	T	Insertion		-
IV#39	G	SNP (transversion)		T
IV#39	G	Insertion		-
IV#39	G	Deletion	Frame Shift	CG
IV#39	C	Insertion		-
IV#39	A	Insertion		-
IV#45	T	Insertion	Frame Shift	-
IV#45	G	SNP (transversion)		T
IV#45	AA	Insertion		--
IV#45	A	Insertion		-
IV#45		Deletion		A
IV#46	T	SNP (transversion)	Substitution	A
IV#46	G	Insertion		-
IV#46	C	Insertion	Frame Shift	-
IV#46	C	Insertion	Frame Shift	-
IV#46	A	Insertion		-
IV#46		Deletion	Frame Shift	G
IV#46		Deletion		CC
IV#46, IV#71	T	Insertion (tandem repeat)		-
IV#54	T	Insertion		-
IV#54	G	Insertion (tandem repeat)		-
IV#54	G	SNP (transversion)		C
IV#54	G	Insertion		-

IV#54	C	SNP (transversion)		G
IV#54	C	Insertion		-
IV#54	C	SNP (transition)		T
IV#54		Deletion		G
IV#54		Deletion (tandem repeat)		T
IV#54, IV#80	A	SNP (transition)		G
IV#60	T	SNP (transversion)		A
IV#60	T	SNP (transversion)		A
IV#60	GA	Insertion	Frame Shift	--
IV#60	C	Insertion	Frame Shift	-
IV#60	A	Insertion		-
IV#60		Deletion		T
IV#60, IV#83		Deletion		GA
IV#60, IV#87		Deletion (tandem repeat)		T
IV#68	CA	Insertion		--
IV#68	CA	Insertion		--
IV#68	C	Insertion		-
IV#71	TG	Insertion	Frame Shift	--
IV#71	T	SNP (transition)	None	C
IV#71	GC	Substitution	Substitution	AA
IV#71	GA	Deletion	Deletion	ACAAG
IV#71	C	SNP (transition)		T
IV#71	C	SNP (transversion)		A
IV#71	A	SNP (transversion)	Substitution	C
IV#71	A	Insertion	Frame Shift	-
IV#71		Deletion (tandem repeat)		C
IV#71		Deletion		TTATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATGATGATGATGATGATG
IV#71		Deletion	Extension	TCAGTCCT-GC--TCCTCGGCCACGAAGT--GCACGCAGTTGCC
IV#71		Deletion	Frame Shift	GGCCGGGTCG-CGCAGGGCGAACTCCCGCCCCCACGGCTGCTCGCCGA
IV#71		Deletion	Frame Shift	CGGTCATGGC
IV#71		Deletion	Deletion	CGGCCC
IV#71		Deletion	Deletion	GGAGGCGTC
IV#71		Deletion	Deletion	CCGGAAGTTCGTGGA

IV#71		Deletion	Deletion	CACGACCTCCGACCACTCGGCGTA
IV#71		Deletion	Deletion	CAGCTCGTC
IV#71		Deletion	Deletion	CAGGCCGC-G
IV#71		Deletion	Deletion	CACCCACACCCAGGCC-AG
IV#71		Deletion	Deletion	GGTGTTGTC
IV#71		Deletion	Deletion	CG-GCACCA-CCTGGTCCTGGACCGC
IV#71		Deletion	Deletion	GCTGAT
IV#71		Deletion	Deletion	GAACAGGGTCACGTCGTCCCGGACCAC ACCGGCGAAGTCGTCCTCCACGAAGTC CCGGGAGAACCCGAGCC-- GGTCGGTCCAGAACTCGACCGCTCCGG CGACGTCGCGCGCGGTGAG
IV#71		Deletion	Deletion	CACCGGAACGGC
IV#71		Deletion	Frame Shift	ACTGGTC
IV#71		Deletion	Start Codon Loss	GGCCAT
IV#71		Deletion	Extension	CTACATCTTCAC
IV#71		Deletion	Deletion	A---AG
IV#71		Deletion		T
IV#71		Deletion		ACC
IV#71, IV#87		Deletion	Deletion	AAC
IV#75	T	Insertion	Frame Shift	-
IV#75	T	Insertion		-
IV#75	GA	Insertion		--
IV#75	G	SNP (transversion)	Substitution	C
IV#75	A	SNP (transversion)	None	C
IV#75		Deletion		TCAAGA
IV#75		Deletion		T
IV#75		Deletion	Frame Shift	G
IV#76	T	SNP (transversion)		A
IV#76	G	Insertion	Frame Shift	-
IV#76	G	SNP (transversion)		C
IV#76	CA	Insertion	Frame Shift	A-
IV#76	C	SNP (transversion)		A
IV#76	C	SNP (transversion)	Substitution	A
IV#76	A	SNP (transversion)		T
IV#76	A	SNP (transversion)		T
IV#76	A	SNP (transversion)		T

IV#76	A	SNP (transversion)	Substitution	C
IV#76		Deletion		TA
IV#76		Deletion	Frame Shift	A
IV#76		Deletion	Deletion	AAG
IV#76		Deletion	Deletion	AGG
IV#76, IV#87		Deletion		G
IV#79	GA	Insertion	Frame Shift	--
IV#79	G	Insertion		-
IV#79	G	Insertion		-
IV#79	A	SNP (transversion)		T
IV#79		Deletion (tandem repeat)		C
IV#80	G	Insertion (tandem repeat)	Frame Shift	-
IV#80	G	SNP (transversion)		T
IV#80	G	Insertion		-
IV#80	CC	Insertion		--
IV#80	C	SNP (transition)		T
IV#80	C	SNP (transition)		T
IV#80	C	SNP (transition)		T
IV#80	C	Insertion		-
IV#80	C	Insertion	Frame Shift	-
IV#80	C	Insertion		-
IV#80	C	Insertion		-
IV#80		Deletion	Frame Shift	G
IV#80		Deletion	Deletion	TGC
IV#80		Deletion		C
IV#83	G	Insertion		-
IV#83	C	Insertion	Frame Shift	-
IV#83	AG	Insertion		--
IV#83	A	SNP (transversion)	Substitution	C
IV#83		Deletion		C
IV#85	TT	Insertion		--
IV#85	TC	Substitution	Substitution	CT
IV#85	T	Insertion		-
IV#85	G	Insertion (tandem repeat)		-
IV#85	G	SNP (transition)	Substitution	A
IV#85	G	Deletion		GGAA
IV#85		Deletion		GAG

IV#85		Deletion		T
IV#85		Deletion		T
IV#85		Deletion		A
IV#85		Deletion		TGGT
IV#85		Deletion (tandem repeat)		A
IV#85		Deletion (tandem repeat)	Frame Shift	T
IV#87	G	Insertion	Frame Shift	-
IV#87	G	SNP (transition)	None	A
IV#87	CCGAC	Substitution	Substitution	ATCCA
IV#87	AGC	Insertion	Frame Shift	#NAME?
IV#87	AA	Insertion	Frame Shift	--
IV#87	A	SNP (transition)	Substitution	G
IV#87		Deletion		TTGCTAAT
IV#87		Deletion		G
IV#87		Deletion	Frame Shift	AG
IV#87		Deletion	Frame Shift	AC
IV#87		Deletion	Frame Shift	G
IV#87, IV#92		Deletion		A
IV#9	G	Insertion		-
IV#9	C	Insertion		-
IV#9	C	Insertion (tandem repeat)	Frame Shift	-
IV#9		Deletion (tandem repeat)		A
IV#9		Deletion		GC
IV#90	T	Insertion		-
IV#90	G	Insertion		-
IV#90	G	Insertion		-
IV#90	C	SNP (transversion)		G
IV#90	C	SNP (transversion)		G
IV#90	A	SNP (transversion)		T
IV#90	A	Insertion		-
IV#90		Deletion		A
IV#90		Deletion	Frame Shift	T
IV#92	T	SNP (transversion)		G
IV#92	T	Insertion		-
IV#92	G	Insertion (tandem repeat)	Frame Shift	-
IV#92	CCG	Insertion	Insertion	---
IV#92	C	SNP (transversion)		A

IV#92	C	SNP (transition)		T
IV#92	AA	Insertion	Frame Shift	--
IV#92	A	Insertion		-
IV#92	A	Insertion (tandem repeat)		-
IV#92	A	Insertion (tandem repeat)		-
IV#92		Deletion	Frame Shift	A
IV#92		Deletion	Deletion	TAC
IV#92		Deletion		CAGTAAC

Supplemntary Table 2 : Variant nucleotides happened from experiment V

Variant events	Polymorphism type	Variant genotyping	Protein effect	Nucleotide genotyping
V#101	TC	Insertion		--
V#101	A	Insertion	Truncation	-
V#101		Deletion		G
V#18	TCG	Insertion	Insertion	---
V#18	G	Insertion		-
V#18	C	SNP (transition)		T
V#18		Deletion (tandem repeat)		C
V#21	GT	Substitution		AG
V#21	AG	Insertion		--
V#25	TAA	Insertion		---
V#25	C	Insertion		-
V#25		Deletion (tandem repeat)		T
V#29	G	Insertion		-
V#29	G	Insertion		-
V#29	C	Insertion		-
V#29		Deletion		C
V#29, V#33	A	Insertion		-
V#3	TCC	Insertion	Insertion	---
V#3	C	Insertion	Frame Shift	-
V#3		Deletion (tandem repeat)		A
V#32	T	Insertion (tandem repeat)		-
V#32	GAT	Insertion		---
V#32, V#95		Deletion (tandem repeat)		A
V#33	T	SNP (transversion)		A
V#33	GA	Substitution		AG
V#33	C	Insertion		-

V#33	A	Insertion	Frame Shift	-
V#37	TA	Insertion	Frame Shift	--
V#37	G	Insertion		-
V#37		Deletion (tandem repeat)		T
V#39	G	Insertion		-
V#39	AAC	Insertion		---
V#39		Deletion		A
V#48	GCA	Insertion	Insertion	---
V#48	G	Insertion		-
V#48		Deletion	Frame Shift	G
V#53	GGT	Insertion		---
V#53	G	Insertion		-
V#53		Deletion	Frame Shift	T
V#59	T	Insertion		-
V#59	CGT	Insertion		---
V#59		Deletion		G
V#64	TG	Insertion	Frame Shift	--
V#64	G	Insertion	Frame Shift	-
V#64		Deletion	Frame Shift	C
V#67	TT	Insertion	Frame Shift	--
V#67	A	Insertion (tandem repeat)		-
V#67		Deletion		A
V#73	G	Insertion		-
V#73		Deletion		A
V#75	GT	Insertion		--
V#75	A	Insertion	Frame Shift	-
V#75		Deletion (tandem repeat)	Frame Shift	T

V#79	CA	Insertion		--
V#79	A	Insertion	Frame Shift	-
V#79		Deletion	Frame Shift	G
V#80	T	Insertion (tandem repeat)		-
V#80	T	SNP (transition)	Substitution	C
V#80	GGG	Substitution	Substitution	ACA
V#80	G	SNP (transversion)	Substitution	C
V#80	CTTCAA	Insertion		------
V#80	CC	Insertion	Frame Shift	--
V#80	C	SNP (transition)	Start Codon Loss	T
V#80		Deletion		A
V#80		Deletion		G
V#80		Deletion	Extension	TCA
V#80		Deletion	Deletion	GGCCGGGTCGCG
V#80		Deletion	Frame Shift	CA
V#80		Deletion	Extension	CTAC
V#80		Deletion (tandem repeat)	Frame Shift	T
V#80, V#97		Deletion		AACT
V#82	T	SNP (transition)	None	C
V#82	CAT	Insertion		---
V#82		Deletion		A
V#82		Deletion (tandem repeat)		AA
V#82		Deletion	Frame Shift	G
V#82		Deletion	Frame Shift	G
V#85	T	Insertion	Frame Shift	-
V#85	CC	Insertion		--

V#85		Deletion	Frame Shift	A
V#86	T	SNP (transversion)	Substitution	A
V#86	C	Insertion		-
V#86	C	SNP (transversion)		A
V#86	ACC	Substitution		TGG
V#86	A	Insertion	Frame Shift	-
V#86		Deletion (tandem repeat)		A
V#86		Deletion	Deletion	GCC
V#86		Deletion	Frame Shift	G
V#86		Deletion		A
V#88	AG	Insertion		--
V#88	A	Insertion		-
V#88		Deletion		A
V#89	T	Insertion	Frame Shift	-
V#89	G	Insertion (tandem repeat)		-
V#89	G	Insertion		-
V#89		Deletion	Frame Shift	G
V#89		Deletion	Frame Shift	A
V#89, V#9, V#91	A	Insertion (tandem repeat)		-
V#9	T	SNP (transversion)		A
V#9	ATA	Insertion	Insertion	---
V#9		Deletion		A
V#91	TC	Insertion		--
V#91	T	Insertion		-
V#91	T	SNP (transversion)		A
V#91		Deletion		A
V#92	GC	Insertion		--

V#92	G	Insertion		-
V#92		Deletion	Frame Shift	G
V#94	CA	Insertion		--
V#94	A	Insertion		-
V#94		Deletion		T
V#95	TTT	Substitution		AAA
V#95	C	Insertion	Frame Shift	-
V#95	AA	Insertion	Frame Shift	--
V#95		Deletion	Frame Shift	T
V#95		Deletion	Frame Shift	C
V#97	T	Insertion (tandem repeat)		-
V#97	CG	Insertion	Frame Shift	--
V#97	CA	Substitution	Substitution	AT
V#97	C	SNP (transversion)		A
V#97	C	SNP (transversion)	Substitution	G
V#97	C	SNP (transversion)		A
V#97	C	Insertion	Frame Shift	-
V#97		Deletion	Frame Shift	A
V#97		Deletion		T
V#98	T	Insertion	Frame Shift	-
V#98	GGA	Insertion	Insertion	---

Product name	Primers	Oligos	Sequence with the extension (5' to 3')	Tm
DDT	Os2-R	-	CCTGCAGGAAGGAATCTTTAAACATACGAACAGATC	58.4
	Os2-F	-	CCATGGAAAAAAGCACCGACTCGGTGC	62.3
	Os1-R	-	GGATCCAAAAAAGCACCGACTCGGTG	59.3
	Os1-F	-	AAGCTTAAGGAATCTTTAAACATACGAACAG	55.9
	BleoR-overlap3-R	-	TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTATG	53.4
	BleoR-overlap3-F	-	CTTGCAACCCTTAAAACTTG	53.2
	BleoR-overlap2-R	-	TTTTTTTTTTTTTTTTTTATGATGATGA	52.5
	BleoR-overlap2-F	-	CCCTTAAAACTTGTGTTCTTGTGAAGA	60.4
	BleoR-overlap1-R	-	ATGATGATGATGTCAGTCCTGC	58.3
	BleoR-overlap1-F	-	CTTGTGAAGATGTAGATGGCCAAGT	61.1
	BleoR - 2,276 R	-	TCAGTCCTGCTCCTCGGC	61.1
	BleoR - 1,902 F	-	ATGGCCAAGTTGACCAGTGC	61.2
	5' Ho-R-2	-	CTACATCTTCACAAGAACACAAGTTTTAAGGGTTGCAAGAGGAGAGCCGGCATTTGTAA	59.4
	5' Ho-R-1	-	AGGAGAGCCGGCATTTGTAA	59.4
	5' Ho-F-2	-	GGATCCGCACCCGAGGAGGTGGGTTACTGATTTTCATTCTGTGGTTC	56.9
	5' Ho-F-1	-	GTTACTGATTTTCATTCTGTGGTTC	56.9
	3' Ho-R-2	-	CCATGGGCACCCGAGGAGGTGGTTTTGTGAATTGCTAATGGTTTGAA	56.9
	3' Ho-R-1	-	TTTTGTGAATTGCTAATGGTTTGAA	56.9
	3' Ho-F-2	-	TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTAAGTCTAATTTTCCCATTCACATC	55.4
	3' Ho-F-1	-	TAAGTCTAATTTTCCCATTCACATC	55.4
	-	Special gRNA oligo2-R	AAACCCACCTCCTCGGGTGC	
	-	Special gRNA oligo2-F	GGCAGCACCCGAGGAGGTGG	
	-	Special gRNA oligo1-R	AAACCCACCTCCTCGGGTGC	
	-	Special gRNA oligo1-F	GGCAGCACCCGAGGAGGTGG	
pgRNA	-	MKK2 Oligo-F	GGCACTTGCAACCCTTAAAACTTGTGG	
	-	MKK2 Oligo-R	AAACCCACAAGTTTTAAGGGTTGCAAG	
pgCtIP	Cam-F	-	CCTGCAGGTGAGACTTTTCAACAAAGGGTAATA	56.6
	Cam-R	-	CTCGAGTGTTCTCTCCAAATGAAATGAACTTC	58.3
	Cas-F	-	AAGCTTGACAAGAAGTACAGCATCGGC	59.3
	Cas-F2	-	CATATGGACAAGAAGTACAGCATCGGC	59.3
	Cas-R	-	GGATCCGTCGCCTCCCAGCTGAGA	61.1
	CtIP-F	-	GGATCCATGAAGGGCGACCTGGAG	58.7
	CtIP-R	-	AGGCCTAGGCCTTCACATTTCAGATTCAAATCCAATA	55.3
	Flag-F	-	CTCGAGATGGACTATAAGGACCACGAC	56.6
	Flag-R	-	AAGCTTCTTATCGTCATCGTCTTTGTAATCA	57.3
	Flag-R2	-	GCGGCCGCCTTATCGTCATCGTCTTTGTAATCA	57.3
	MRE-F	-	GCGGCCGCATGGAGAAGGATGAGGTACG	56.1
	MRE-R	-	CATATGTCAGCAATTCTTCAAACAAGGATC	58
	PolyA-F	-	AGGCCTTATGGGCACCAAAGAACCTG	57.8
	PolyA-R	-	GTTTAAACCTACCTCGAGTTTTTTTTTTTT	51.8
pgMR	Cam-F	-	CCTGCAGGTGAGACTTTTCAACAAAGGGTAATA	56.6
	Cam-R	-	CTCGAGTGTTCTCTCCAAATGAAATGAACTTC	58.3
	Cas-F	-	CATATGGACAAGAAGTACAGCATCGGC	59.3
	Cas-R	-	GGATCCGTCGCCTCCCAGCTGAGA	61.1
	Flag-F	-	GGATCCATGAAGGGCGACCTGGAG	56.6
	Flag-R2	-	AGGCCTTCACATTTCAGATTCAAATCCAATA	57.3
	MRE-F	-	CTCGAGATGGACTATAAGGACCACGAC	56.1
	MRE-R	-	GCGGCCGCCTTATCGTCATCGTCTTTGTAATCA	58
	PolyA-R	-	GCGGCCGCATGGAGAAGGATGAGGTACG	51.8
	PolyA2-F	-	CATATGTCAGCAATTCTTCAAACAAGGATC	57.8
pgCtMR	Cam-F	-	CCTGCAGGTGAGACTTTTCAACAAAGGGTAATA	56.6
	Cam-R	-	CTCGAGTGTTCTCTCCAAATGAAATGAACTTC	58.3
	Cas-F2	-	CATATGGACAAGAAGTACAGCATCGGC	59.3
	Cas-R	-	GGATCCGTCGCCTCCCAGCTGAGA	61.1
	CtIP-F	-	GGATCCATGAAGGGCGACCTGGAG	58.7
	CtIP-R	-	AGGCCTTCACATTTCAGATTCAAATCCAATA	55.3
	Flag-F	-	CTCGAGATGGACTATAAGGACCACGAC	56.6
	Flag-R2	-	GCGGCCGCCTTATCGTCATCGTCTTTGTAATCA	57.3
	MRE-F	-	GCGGCCGCATGGAGAAGGATGAGGTACG	56.1
	MRE-R	-	CATATGTCAGCAATTCTTCAAACAAGGATC	58
	PolyA-F	-	AGGCCTTATGGGCACCAAAGAACCTG	57.8
	PolyA-R	-	GTTTAAACCTACCTCGAGTTTTTTTTTTTT	51.8
XXRC4-cassette	XR-Cass1-F	-	AAGGAATCTTTAAACATACGAACAG	55.9
	XR-Cass1-R	-	AAAAAAGCACCGACTCGGTG	59.3
	XR-Cass2-F	-	AAGGAATCTTTAAACATACGAACAG	55.9
	XR-Cass2-R	-	AAAAAAGCACCGACTCGGTG	59.3
	-	XRCC4-Oligo1	TTCAATCTCTCCATCACCGACGG	
	-	XRCC4-Oligo2	CCGTCGGTGATGGAGAGATTGAA	
pggCtMR	Cam-F	-	CCTGCAGGTTTTTTAAAAAATGATCATGAGACTTTTCAACAAAGGGTAATA	56.6
	Cam-R	-	CTCGAGTGTTCTCTCCAAATGAAATGAACTTC	58.3
	Cas-F2	-	CATATGGACAAGAAGTACAGCATCGGC	59.3
	Cas-R	-	GGATCCGTCGCCTCCCAGCTGAGA	61.1
	CtIP-F	-	GGATCCATGAAGGGCGACCTGGAG	58.7
	CtIP-R	-	AGGCCTTCACATTTCAGATTCAAATCCAATA	55.3
	Flag-F	-	CTCGAGATGGACTATAAGGACCACGAC	56.6
	Flag-R2	-	GCGGCCGCCTTATCGTCATCGTCTTTGTAATCA	57.3
	MRE-F	-	GCGGCCGCATGGAGAAGGATGAGGTACG	56.1
	MRE-R	-	CATATGTCAGCAATTCTTCAAACAAGGATC	58
	PolyA-F	-	AGGCCTTATGGGCACCAAAGAACCTG	57.8
	PolyA-R	-	GTTTAAACCTACCTCGAGTTTTTTTTTTTT	51.8
TaqMan real-time PCR	FAM1-F	-	GCACACCCATTCATGAACTTGTAT	59.8
	FAM1-R	-	GGTGAGCACCGGAACGGC	63.7
	FAM2-F	-	CCGGCCGGCAACTGCGTG	67.3
	FAM2-R	-	AAAAAACATTTGACCAAATGATTTCA	56
	VIC F	-	ATTTCCCGTTCAGCAGTGGT	59.9
	VIC R	-	ACGCCATCCTTCGTTTGGAT	60
HDR efficiency	BleoR - 52 F	-	GGAGCGGTCGAGTTCTGG	59.8
	BleoR - 151 R	-	TGATGAACAGGGTCACGTCG	60
Protein expression	2,817 F-MKK2	-	TCTGCTAGAGATCCACCATCCA	60.1
	2,968 R-MKK2	-	ATTGAAGAGCCTGCACGCAA	60.9
	3,260 F-XRCC4	-	GGGATCCCAACCAAGTTCGT	60
	3,438 R-XRCC4	-	TGCGACCTGGGACTCATTTC	60
	7 F-BleoR	-	AAGTTGACCAGTGCCGTTCC	60.8
	7,831 F-MRE11	-	AGCCGTTCATCCCGAATGTT	60
	8,025 R-MRE11	-	ATGGCACTTGAGGGTTCTGG	60
	11,007 F-Lig4	-	GCTCCTCAATCGTCAACCCA	60
	194 R-BleoR	-	CAGGCCAGGGTGTTGTCC	60.3
	242 F-Rad50	-	CTTACTCTCATCGTCGGCCC	60
	244 F-BRCA1	-	GGTCAGGCACCAGGTACTTC	60
	410 R-Rad50	-	ACCTAGCATTCGGAGGCAAC	60.1
	422 R-BRCA1	-	CTCGCCGCATAGGACATGAA	60.2
	557 F-Rad51	-	GTGGTGGCCTAGGAGGAAAG	59.7
	643 F-CtIP	-	GGGCGTGGAAAGAGAAGGAA	60
	723 R-Rad51	-	TTTCTTGAGCACGCTCTCCC	60.3
	828 R-CtIP	-	TCACAACCTCCTGTTCCAGC	59.9
	9860 R-Lig4	-	GCAATTTCTCTCTCGTTGCTGC	60.7
Sequencing	MKK2-S-7F	-	GCATTTGCAACACCAGACAA	57.8
	MKK2-S-1,139 R	-	TGACTGAGAACTCAATCTGCACT	59.7

Supplementary Table 3: Oligos and primers used in this study.