

# SUPPLEMENTARY DATA

Accompanying:

## **Evolution of hominin detoxification: Neanderthal and modern human AHR respond similarly to TCDD**

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# Supplementary Data SD1

## *SD1\_SeqRetrieval.docx*

### **Retrieval of modern human and ancient hominin AHR mRNA sequences**

The modern human aryl hydrocarbon receptor (AHR) reference gene transcript AHR-002 (ENST00000242057.8) was downloaded from the following Ensembl website, version GRCh38:

[http://www.ensembl.org/Homo\\_sapiens/Transcript/Sequence\\_cDNA?db=core:g=ENSG00000106546;r=7:17298622-17346152;t=ENST00000242057<sup>1\)</sup>](http://www.ensembl.org/Homo_sapiens/Transcript/Sequence_cDNA?db=core:g=ENSG00000106546;r=7:17298622-17346152;t=ENST00000242057<sup>1)</sup>)

The Altai- (Prüfer *et al.*, 2014) and Vindija- (Prüfer *et al.*, 2017) Neanderthal, and Denisovan (Meyer *et al.*, 2012) AHR mRNA sequence were retrieved from the respective chromosome 7 VCF file available online:

Altai: [http://cdna.eva.mpg.de/neandertal/altai/AltaiNeandertal/VCF<sup>1\)</sup>](http://cdna.eva.mpg.de/neandertal/altai/AltaiNeandertal/VCF<sup>1)</sup>);

Vindija: [http://cdna.eva.mpg.de/neandertal/Vindija/VCF/Vindija33.19<sup>1\)</sup>](http://cdna.eva.mpg.de/neandertal/Vindija/VCF/Vindija33.19<sup>1)</sup>);

Denisovan: [https://bioinf.eva.mpg.de/jbrowse/data/ancient<sup>1\)</sup>](https://bioinf.eva.mpg.de/jbrowse/data/ancient<sup>1)</sup>).

Using the Ensemble Data Slicer web tool ([http://grch37.ensembl.org/Homo\\_sapiens/Tools/DataSlicer<sup>1\)</sup>](http://grch37.ensembl.org/Homo_sapiens/Tools/DataSlicer<sup>1)</sup>)) the data subset for the AHR genomic region was extracted from these VCF files and loaded into Excel. Using the filtering functions of Excel the positions where the ancient hominin AHR genes differs from the human reference genome, assembly GRCh37/hg19, were filtered out (Table SD1). Supplementary Data SD6 shows an alignment of all sequences studied here and by Hubbard *et al.* (2016).

1) All websites referred to were accessed October 16, 2018.

**Table SD1.** Differences observed between ancient hominin and modern human reference AHR mRNA sequences

| GRCh38/hg38<br>Chromosome 7<br>Coordinate | GRCh37/hg19<br>Chromosome 7<br>Coordinate | dbSNP<br>ID <sup>1)</sup> | Modern human<br>Reference<br>(GRCh38/hg38) | Neanderthal |         | Denisovan | Functional<br>Region        | Evolutionary details <sup>2)</sup>  |
|---|---|---------------------------|--|-------------|---------|-----------|-----------------------------|---|
|   |   |                           |  | Altai       | Vindija |           |                             |   |
| 17298806                                  | 17338430                                  | rs7796976                 | A  | G           | G       | G         | 5'-UTR                      | A = derived; unique to modern humans<br>G = ancestral; conserved in all other sequenced primates<br>and far beyond  |
| 17335768                                  | 17375392                                  | -                         | T  | C           | C       | C         | Coding variant<br>Val381Ala | T = derived (= Val) and fixed in modern humans<br>C = ancestral (= Ala); highly conserved, including all<br>sequenced primates  |
| 17339486                                  | 17379110                                  | rs2066853                 | G  | A           | A       | A         | Coding variant<br>Arg554Lys | G = derived (= Arg); unique to modern humans<br>A = ancestral (= Lys); conserved in all other sequenced<br>primates   |
| 17343303                                  | 17382927                                  | -                         | G  | A           | A       | A         | 3'-UTR                      | G = derived; unique to modern humans<br>A = ancestral; conserved in all other sequenced primates  |
| 17345312                                  | 17384936                                  | rs770112913<br>rs75433362 | CA   | C-/CA       | C-/CA   | CA        | 3'-UTR                      | CA = ancestral? (gorilla = NA); in modern humans;<br>C- = derived?; in chimpanzee;<br>Altai-Neanderthal = C-/CA heterozygote<br>Vindija-Neanderthal = C-/CA heterozygote<br>Denisovan = CA but possibly C-/CA heterozygote<br>since also 7 [C-] reads out of 41 |

1) Based on dbSNP, build 151 (see: <https://www.ncbi.nlm.nih.gov/SNP/index.html>).

2) Data from the "Multiz Alignment of 100 Vertebrate Species" in the human UCSC Genome browser, assembly GRCh38/hg38.

## **REFERENCES**

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- Meyer, M., Kircher, M., Gansauge, M. T., Li, H., Racimo, F., Mallick, S., Schraiber, J. G., Jay, F., Prüfer, K., de Filippo, C., *et al.* (2012). A high-coverage genome sequence from an archaic Denisovan individual. *Science* **338**(6104), 222-6.
- Prüfer, K., de Filippo, C., Grote, S., Mafessoni, F., Korlević, P., Hajdinjak, M., Vernot, B., Skov, L., Hsieh, P., Peyrégne, S., *et al.* (2017). A high-coverage Neandertal genome from Vindija Cave in Croatia. *Science* doi: 10.1126/science.aao1887.
- Prüfer, K., Racimo, F., Patterson, N., Jay, F., Sankararaman, S., Sawyer, S., Heinze, A., Renaud, G., Sudmant, P. H., de Filippo, C., *et al.* (2014). The complete genome sequence of a Neanderthal from the Altai Mountains. *Nature* **505**(7481), 43-49.

## Supplementary Data SD2

### *SD2\_AHR\_ModernHuman.fas*

#### Synthetic modern human AHR mRNA sequence studied (FASTA format)

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>AHR_ModernHumanRef.seq
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## Supplementary Data SD3

### *SD3\_AHR\_AltaiNeanderthal.fas*

#### Synthetic Altai-Neanderthal AHR mRNA sequence studied (FASTA format)

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aatgtatataaaaaatggcttcggacaaaaatctctgagttctgtgtattttcagtcaaaactttaaacctgtagaatca  
atthaagtgttgaaaaaatttgtctgaaacatttcataatttgtttccagcatgaggtatctaaggatttagaccagag  
gtctagattaatactctatttttacatttaaaccttttattataagtcttacataaaccatttttgttactctctccac  
atgttactggataaattgttttagtggaataataggctttttaatcatgaatatgatgacaatcagttatacagttataaaa  
ttaaaagtttgaaaagcaatattgtatattttatctatataaaaataactaaaatgtatctaagaataataaaatcacgt  
taaaccaaaatacacgtttgtctgtattgtaagtgcacaaacaaaggatacttagtgactgctacattgtgggatttatt  
tctagatgatgtgcacatctaaggatatggatgtgtctaatttagtcttttctgtaccagggtttttcttacaatacctg  
aagacttaccagtattctagtgtattatgaagctttcaacattactatgcacaaactagtgtttttcgatgttactaaat  
tttaggtaaagtctttcatggcttttttcttcaaaatgttactgcttacatataatcatgcatagatttttgcttaaagta  
tgatttataatatcctcattatcaaagttgtatacaataatataataaaaatacaaatatgaataatACTCGAGTtat  
cctGGTACCcctgaaGCGGCCGC

# Supplementary Data SD4

## SD4\_Primer List.xlsx

Table SD4. List of primers used in this study

| Purpose   | Primer Name              | Primer Sequence 5' > 3'         | Length (nt) | Annealing temperature <sup>1)</sup> (°C) |
|---|--------------------------|---------------------------------|-------------|--|
| <b>Generate pSC119159 segment with modern human 185A variant of AHR 5'-UTR</b><br>Upstream primer   | pCMV6-XL4_918-937        | AGCAGAGCTCGTTTAGTGAA            | 20          | 61                                       |
|   | AHR_ENST643-630_XhoI     | AAAAAACTCGAGGGTGCCCGCCGAC       | 26          |  |
| <b>Generate upper pSC119159 segment with partial AHR 5'-UTR carrying Neanderthal 185G variant</b><br>Upstream primer  | pCMV6-XL4_918-937        | AGCAGAGCTCGTTTAGTGAA            | 20          | 58                                       |
|   | AHR_ENST200-170_185G_rev | GCTCCCGGACTTCCCAAATCCAGGGTGCTT  | 31          |  |
| <b>Generate lower pSC119159 segment with partial AHR 5'-UTR carrying Neanderthal 185G variant</b><br>Upstream primer  | AHR_ENST173-203_185G_fwd | CACCCTGGATTTGGGAAGTCCCGGGAGCAGC | 31          | 65                                       |
|   | AHR_ENST643-630_XhoI     | AAAAAACTCGAGGGTGCCCGCCGAC       | 26          |  |
| <b>Overlap extension PCR with purified upper and lower pSC119159 segment carrying Neanderthal 185G AHR 5'-UTR variant</b><br>Upstream primer  | pCMV6-XL4_918-937        | AGCAGAGCTCGTTTAGTGAA            | 20          | 55                                       |
|   | AHR_ENST643-630_XhoI     | AAAAAACTCGAGGGTGCCCGCCGAC       | 26          |  |
| <b>Sequence control of the 185A/G variant in the AHR 5'-UTR-EGFP reporter gene fusion construct in pcDNA3-EGFP</b><br>EGFP coding region reverse primer   | EGFP_cDNA141-123         | GAACCTCAGGGTCAGCTTG             | 19          | 50                                       |
|   |                          |                                 |             |  |
| <b>Identity control of the pcDNA3.1/Zeo(+) expression constructs carrying the AHR gene synthesis product</b><br>Sequencing around Val381Ala variation (position 1785 in Ensembl AHR reference transcript ENST00000242057.8) | AHR_Mut2Ctr1630-1654     | TATGCTTATTGTGCCGAGTCC           | 22          | 50                                       |
|   | AHR_Mut2Ctr1914-1891     | ATTATGGCAGGAAAAGGGTTGGTT        | 24          | 50                                       |
| <b>Quantitative reverse transcription PCR</b>   |                          |                                 |             |  |
| Cytochrome P450 1A1 (CYP1A1) <sup>2)</sup>  | CYP1A1_Hum_F             | TCCTGGAGCCTCATGTATTGGTG         | 24          | 60                                       |
|   | CYP1A1_Hum_R             | TGGTGAAGGGGACGAAGGAAGAGT        | 24          | 60                                       |
| Zeoicin (ZEO) <sup>3)</sup>   | Zeoicin1_F               | TGGGCGCTCTCCGCTTCCTC            | 21          | 60                                       |
|   | Zeoicin1_R               | AACGCGCCTTTTACGGTTCCTG          | 24          | 60                                       |
| β-Actin (ACTB) <sup>4)</sup>  | ACTB-F_Hum_Lin_F         | TCATGAAGTGTGACGTGGACATC         | 23          | 60                                       |
|   | ACTB-R_Hum_Lin_R         | CAGGAGGAGCAATGATCTTGATCT        | 24          | 60                                       |
| Aryl hydrocarbon receptor (AHR) <sup>4)</sup>   | AHR-F_Hum_Lin_F          | ACATCACCTACGCCAGTCGC            | 20          | 60                                       |
|   | AHR-R_Hum_Lin_R          | TCTATGCCGCTTGGAAAGGAT           | 20          | 60                                       |
| Aryl hydrocarbon receptor nuclear translocator (ARNT) <sup>4)</sup>   | ARNT-F_Hum_Lin_F         | GCTGCTGCCTACCCTAGTCTCA          | 22          | 60                                       |
|   | ARNT-R_Hum_Lin_R         | GCTGCTCGTCTGGAATTGT             | 21          | 60                                       |

1) Optimal annealing temperature as determined using the PrimerSelect module of the DNASTAR LaserGene Core Suite, version 10.

All sequencing reactions were outsourced to Macrogen Europe (Amsterdam, The Netherlands) and therefore their standard annealing temperature of 50 °C is listed.

2) qPCR primers spanned an intron, and were verified by gel electrophoresis and Sanger sequencing to amplify only the correct cDNA-derived and not the genomic DNA-derived product.

3) qPCR primers were verified by gel electrophoresis and Sanger sequencing to amplify only the correct product.

4) Derived from Lin et al. (2003); one of the primers in each pair was placed at the junction between two exons to avoid amplification of genomic DNA.

### Literature reference

Lin, P., Hu, S.-W., and Chang, T.-H. (2003). Correlation between Gene Expression of Aryl Hydrocarbon Receptor (Ahr), Hydrocarbon Receptor Nuclear Translocator (Arnt), Cytochromes P4501A1 (CYP1A1) and 1B1 (CYP1B1), and Inducibility of CYP1A1 and CYP1B1 in Human Lymphocytes. *Toxicological Sciences* 71(1), 20-26.

# Supplementary Data SD5

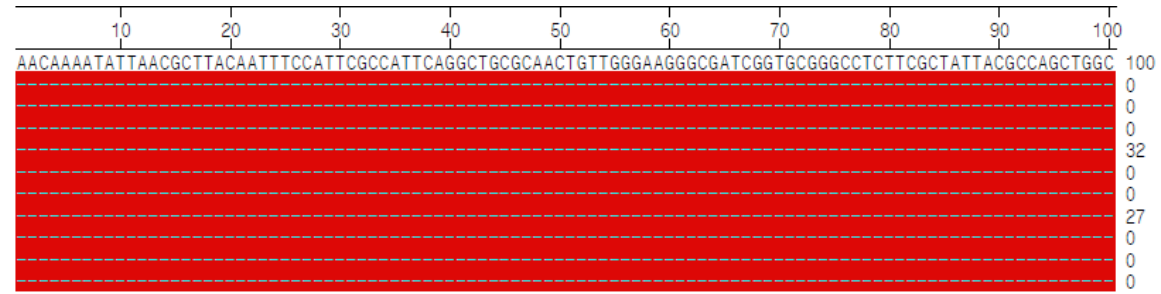
## *SD5\_AHR 5'UTR Mutagenesis.docx*

### **Isolation and mutation of the 5'-UTR sequence from AHR cDNA clone SC119159.**

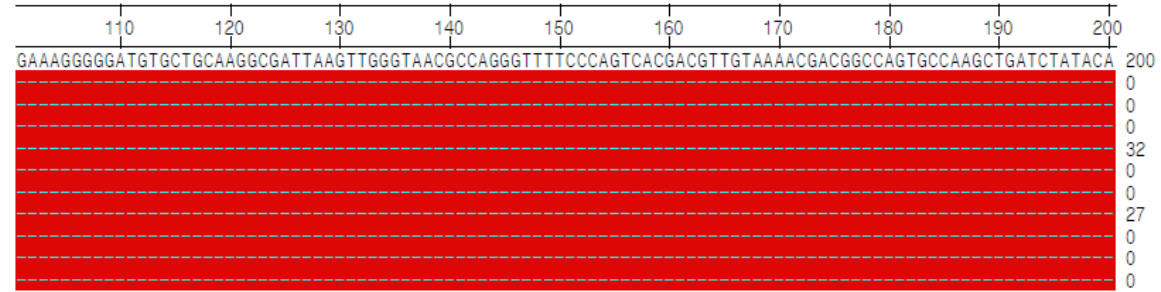
Alignment of the template sequence, modern human AHR mRNA reference sequence, primers, overlapping intermediate PCR segments, final mutated PCR product, and insert generated to create the Neanderthal 185G variant of the AHR 5'-untranslated region (UTR) by overlap PCR to be inserted into EGFP reporter vector pCMV3-EGFP. The ruler above the alignments shows the position in the Origene construct carrying AHR cDNA clone SC119195 in vector pCMV6-XL4; numbers at the right of each alignment block refer to position within the specific sequence shown on that specific line. Nucleotide positions deviating from the deduced sequence of SC119159 in pCMV6-XL4 are highlighted in red.

|                                   |   |
|-----------------------------------|---|
| pCMV6-XL4_SC119159_Deduced:       | Relevant portion of the nucleotide sequence of AHR cDNA clone SC119159 in pCMV6-XL4 as deduced from the sequence information provided by Origene in combination with newly generated sequence information.                            |
| AHR_002_Hum_ENST00000242057.8:    | Modern human AHR mRNA reference sequence retrieved from the Ensembl database.   |
| Primer_Up_pCMV6-XL4_918-937:      | Upper primer for generation of the upstream overlap PCR segment.  |
| Upper_overlap_SC119159_918-1169:  | Upstream overlap PCR segment.   |
| Primer_AHR_ENST200-170_185G_rev:  | Reverse mutagenesis primer to incorporate the G variant at position 185 of the AHR 5'-UTR sequence (position numbering of AHR_002_Hum_ENST00000242057.8). Note that the reversed complement of this primer is shown in the alignment. |
| Primer_AHR_ENST173-203_185G_fwd:  | Forward mutagenesis primer to incorporate the G variant at position 185 of the AHR 5'-UTR sequence (position numbering of AHR_002_Hum_ENST00000242057.8).   |
| Lower_overlap_SC119159_1142-1612: | Downstream overlap PCR segment.   |
| Primer_Down_AHR_ENST643-630_Xhol: | Lower primer for generation of the downstream overlap PCR segment. Note that the reversed complement of this primer is shown in the alignment.  |
| pCMV6-XL4_SC119159_918-1612_Xhol: | Complete SC119159 segment amplified and mutated by overlap PCR.   |
| EcoRI-XhoI_SC119159_979-1612:     | EcoRI – XhoI restriction subfragment inserted into EGFP reporter vector pCMV3-EGFP.   |
| 5'-UTR_SC119159_993-1612:         | Complete AHR 5'-UTR sequence comprised by the inserted EcoRI – XhoI restriction fragment.   |

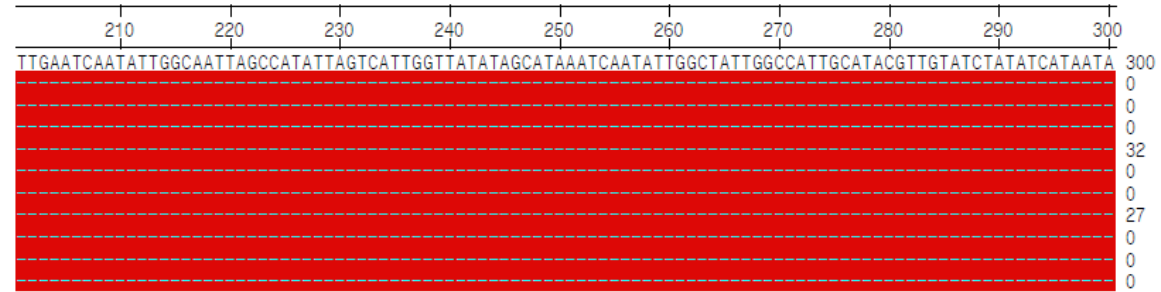
pCMV6-XL4\_SC119159\_Deduced  
 AHR\_002\_Hum\_ENST00000242057.8  
 Primer\_Up\_pCMV6-XL4\_918-937  
 Upper\_overlap\_SC119159\_918-1169  
 Primer\_AHR\_ENST200-170\_185G\_rev  
 Primer\_AHR\_ENST173-203\_185G\_fwd  
 Lower\_overlap\_SC119159\_1142-1612  
 Primer\_Down\_AHR\_ENST643-630\_XhoI  
 pCMV6-XL4\_SC119159\_918-1612\_XhoI  
 EcoRI-XhoI\_SC119159\_979-1612  
 5'-UTR\_SC119159\_993-1612



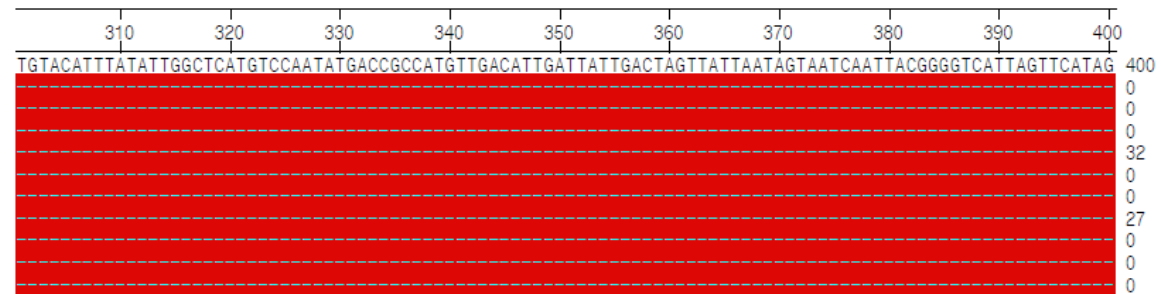
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 AHR\_002\_Hum\_ENST00000242057.8  
 Primer\_Up\_pCMV6-XL4\_918-937  
 Upper\_overlap\_SC119159\_918-1169  
 Primer\_AHR\_ENST200-170\_185G\_rev  
 Primer\_AHR\_ENST173-203\_185G\_fwd  
 Lower\_overlap\_SC119159\_1142-1612  
 Primer\_Down\_AHR\_ENST643-630\_XhoI  
 pCMV6-XL4\_SC119159\_918-1612\_XhoI  
 EcoRI-XhoI\_SC119159\_979-1612  
 5'-UTR\_SC119159\_993-1612

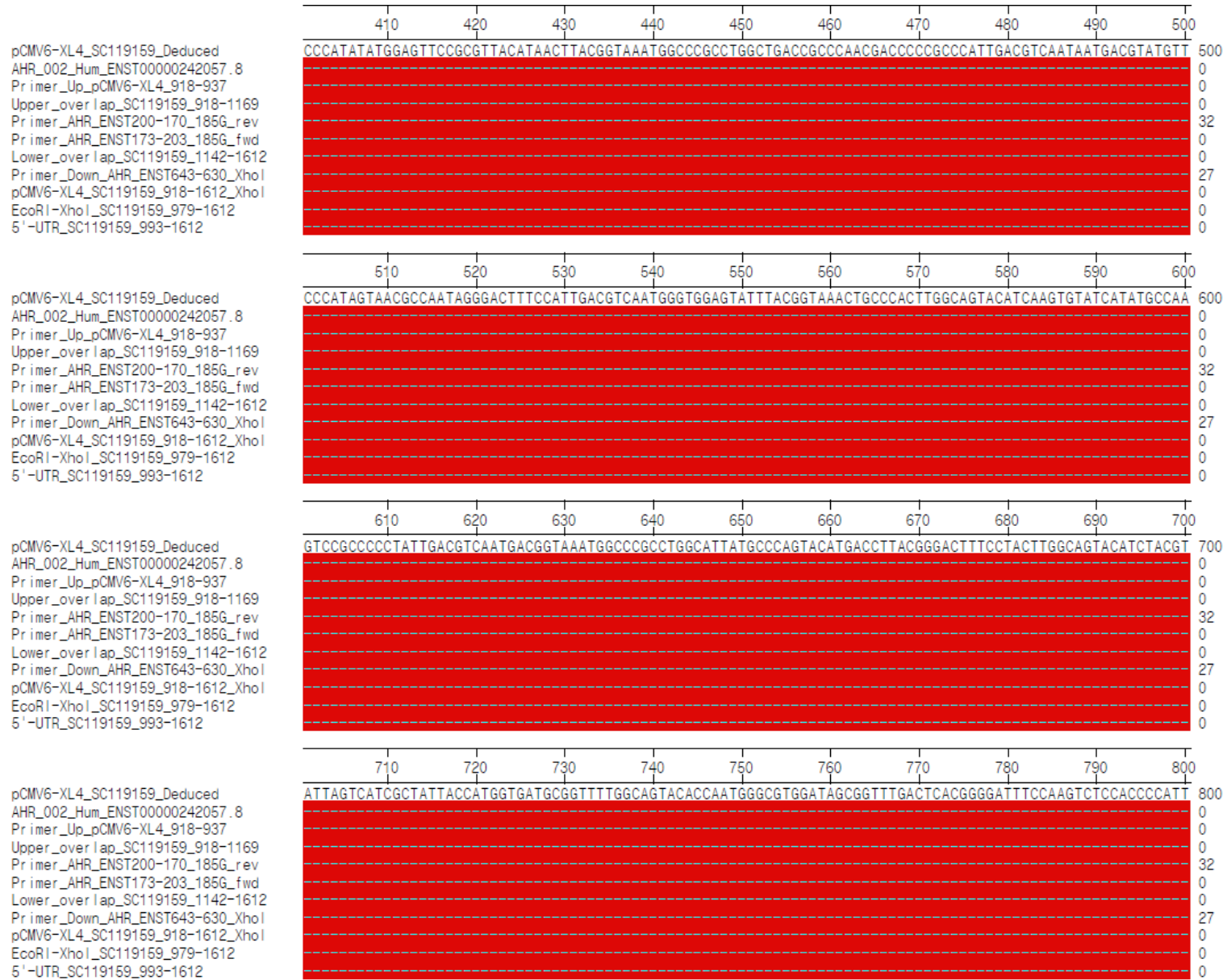


pCMV6-XL4\_SC119159\_Deduced  
 AHR\_002\_Hum\_ENST00000242057.8  
 Primer\_Up\_pCMV6-XL4\_918-937  
 Upper\_overlap\_SC119159\_918-1169  
 Primer\_AHR\_ENST200-170\_185G\_rev  
 Primer\_AHR\_ENST173-203\_185G\_fwd  
 Lower\_overlap\_SC119159\_1142-1612  
 Primer\_Down\_AHR\_ENST643-630\_XhoI  
 pCMV6-XL4\_SC119159\_918-1612\_XhoI  
 EcoRI-XhoI\_SC119159\_979-1612  
 5'-UTR\_SC119159\_993-1612



pCMV6-XL4\_SC119159\_Deduced  
 AHR\_002\_Hum\_ENST00000242057.8  
 Primer\_Up\_pCMV6-XL4\_918-937  
 Upper\_overlap\_SC119159\_918-1169  
 Primer\_AHR\_ENST200-170\_185G\_rev  
 Primer\_AHR\_ENST173-203\_185G\_fwd  
 Lower\_overlap\_SC119159\_1142-1612  
 Primer\_Down\_AHR\_ENST643-630\_XhoI  
 pCMV6-XL4\_SC119159\_918-1612\_XhoI  
 EcoRI-XhoI\_SC119159\_979-1612  
 5'-UTR\_SC119159\_993-1612





|                                  |  |     |     |     |     |     |     |     |     |     |     |
|----------------------------------|--|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|                                  | 810  | 820 | 830 | 840 | 850 | 860 | 870 | 880 | 890 | 900 |     |
| pCMV6-XL4_SC119159_Deduced       | GACGTC AATGGGAGTTTGT TTTGGCACCAAAATCAACGGGACTTTC CAAAATGTCGTAATAACCCCGCCCGTTGACGCAAATGGGCGGTAGGCGTGTAC |     |     |     |     |     |     |     |     |     | 900 |
| AHR_002_Hum_ENST00000242057.8    |  |     |     |     |     |     |     |     |     |     | 0   |
| Primer_Up_pCMV6-XL4_918-937      |  |     |     |     |     |     |     |     |     |     | 0   |
| Upper_overlap_SC119159_918-1169  |  |     |     |     |     |     |     |     |     |     | 0   |
| Primer_AHR_ENST200-170_185G_rev  |  |     |     |     |     |     |     |     |     |     | 32  |
| Primer_AHR_ENST173-203_185G_fwd  |  |     |     |     |     |     |     |     |     |     | 0   |
| Lower_overlap_SC119159_1142-1612 |  |     |     |     |     |     |     |     |     |     | 0   |
| Primer_Down_AHR_ENST643-630_XhoI |  |     |     |     |     |     |     |     |     |     | 27  |
| pCMV6-XL4_SC119159_918-1612_XhoI |  |     |     |     |     |     |     |     |     |     | 0   |
| EcoRI-XhoI_SC119159_979-1612     |  |     |     |     |     |     |     |     |     |     | 0   |
| 5'-UTR_SC119159_993-1612         |  |     |     |     |     |     |     |     |     |     | 0   |

|                                  |   |     |     |     |     |     |     |     |     |      |      |
|----------------------------------|---|-----|-----|-----|-----|-----|-----|-----|-----|------|------|
|                                  | 910   | 920 | 930 | 940 | 950 | 960 | 970 | 980 | 990 | 1000 |      |
| pCMV6-XL4_SC119159_Deduced       | GGTGGGAGGTCTATATAAGCAGAGCTCGTTTAGTGAACCGTCAGAATTTTGTAAACGACTCACTATAGGGCGGCCGCGAATTCGGCACCAGGGGAGGCA |     |     |     |     |     |     |     |     |      | 1000 |
| AHR_002_Hum_ENST00000242057.8    |   |     |     |     |     |     |     |     |     |      | 31   |
| Primer_Up_pCMV6-XL4_918-937      | AGCAGAGCTCGTTTAGTGAA  |     |     |     |     |     |     |     |     |      | 20   |
| Upper_overlap_SC119159_918-1169  | AGCAGAGCTCGTTTAGTGAACCGTCAGAATTTTGTAAACGACTCACTATAGGGCGGCCGCGAATTCGGCACCAGGGGAGGCA                  |     |     |     |     |     |     |     |     |      | 83   |
| Primer_AHR_ENST200-170_185G_rev  |   |     |     |     |     |     |     |     |     |      | 32   |
| Primer_AHR_ENST173-203_185G_fwd  |   |     |     |     |     |     |     |     |     |      | 0    |
| Lower_overlap_SC119159_1142-1612 |   |     |     |     |     |     |     |     |     |      | 0    |
| Primer_Down_AHR_ENST643-630_XhoI |   |     |     |     |     |     |     |     |     |      | 27   |
| pCMV6-XL4_SC119159_918-1612_XhoI | AGCAGAGCTCGTTTAGTGAACCGTCAGAATTTTGTAAACGACTCACTATAGGGCGGCCGCGAATTCGGCACCAGGGGAGGCA                  |     |     |     |     |     |     |     |     |      | 83   |
| EcoRI-XhoI_SC119159_979-1612     | GAATTCGGCACCAGGGGAGGCA  |     |     |     |     |     |     |     |     |      | 22   |
| 5'-UTR_SC119159_993-1612         | GGGAGGCA  |     |     |     |     |     |     |     |     |      | 8    |

|                                  |   |      |      |      |      |      |      |      |      |      |      |
|----------------------------------|---|------|------|------|------|------|------|------|------|------|------|
|                                  | 1010  | 1020 | 1030 | 1040 | 1050 | 1060 | 1070 | 1080 | 1090 | 1100 |      |
| pCMV6-XL4_SC119159_Deduced       | GTGGCTGGGGAGTCCCCTCGACGCTCTGTTCCGAGAGCGTGCCCCGGACCGCCAGCTCAGAACAGGGGCGAGCCGTGTAGCCGAACGGAAGCTGGGAGCAG |      |      |      |      |      |      |      |      |      | 1100 |
| AHR_002_Hum_ENST00000242057.8    | GTGGCTGGGGAGTCCCCTCGACGCTCTGTTCCGAGAGCGTGCCCCGGACCGCCAGCTCAGAACAGGGGCGAGCCGTGTAGCCGAACGGAAGCTGGGAGCAG |      |      |      |      |      |      |      |      |      | 131  |
| Primer_Up_pCMV6-XL4_918-937      |   |      |      |      |      |      |      |      |      |      | 20   |
| Upper_overlap_SC119159_918-1169  | GTGGCTGGGGAGTCCCCTCGACGCTCTGTTCCGAGAGCGTGCCCCGGACCGCCAGCTCAGAACAGGGGCGAGCCGTGTAGCCGAACGGAAGCTGGGAGCAG |      |      |      |      |      |      |      |      |      | 183  |
| Primer_AHR_ENST200-170_185G_rev  |   |      |      |      |      |      |      |      |      |      | 32   |
| Primer_AHR_ENST173-203_185G_fwd  |   |      |      |      |      |      |      |      |      |      | 0    |
| Lower_overlap_SC119159_1142-1612 |   |      |      |      |      |      |      |      |      |      | 0    |
| Primer_Down_AHR_ENST643-630_XhoI |   |      |      |      |      |      |      |      |      |      | 27   |
| pCMV6-XL4_SC119159_918-1612_XhoI | GTGGCTGGGGAGTCCCCTCGACGCTCTGTTCCGAGAGCGTGCCCCGGACCGCCAGCTCAGAACAGGGGCGAGCCGTGTAGCCGAACGGAAGCTGGGAGCAG |      |      |      |      |      |      |      |      |      | 183  |
| EcoRI-XhoI_SC119159_979-1612     | GTGGCTGGGGAGTCCCCTCGACGCTCTGTTCCGAGAGCGTGCCCCGGACCGCCAGCTCAGAACAGGGGCGAGCCGTGTAGCCGAACGGAAGCTGGGAGCAG |      |      |      |      |      |      |      |      |      | 122  |
| 5'-UTR_SC119159_993-1612         | GTGGCTGGGGAGTCCCCTCGACGCTCTGTTCCGAGAGCGTGCCCCGGACCGCCAGCTCAGAACAGGGGCGAGCCGTGTAGCCGAACGGAAGCTGGGAGCAG |      |      |      |      |      |      |      |      |      | 108  |

|                                  |  |      |      |      |      |      |      |      |      |      |      |
|----------------------------------|--|------|------|------|------|------|------|------|------|------|------|
|                                  | 1110   | 1120 | 1130 | 1140 | 1150 | 1160 | 1170 | 1180 | 1190 | 1200 |      |
| pCMV6-XL4_SC119159_Deduced       | CCGGGACTGGTGGCCCGCCGAGCTCCGAGCGGGGAAGCACCCCTGGATTTAGGAAGTCCCGGGAGCAGCGCGGCGGCACCTCCCTCACCAAGGGGC |      |      |      |      |      |      |      |      |      | 1200 |
| AHR_002_Hum_ENST00000242057.8    | CCGGGACTGGTGGCCCGCCGAGCTCCGAGCGGGGAAGCACCCCTGGATTTAGGAAGTCCCGGGAGCAGCGCGGCGGCACCTCCCTCACCAAGGGGC |      |      |      |      |      |      |      |      |      | 231  |
| Primer_Up_pCMV6-XL4_918-937      |  |      |      |      |      |      |      |      |      |      | 20   |
| Upper_overlap_SC119159_918-1169  | CCGGGACTGGTGGCCCGCCGAGCTCCGAGCGGGGAAGCACCCCTGGATTTAGGAAGTCCCGGGAGCAGCGCGGCGGCACCTCCCTCACCAAGGGGC |      |      |      |      |      |      |      |      |      | 252  |
| Primer_AHR_ENST200-170_185G_rev  | AAGCACCCCTGGATTTAGGAAGTCCCGGGAGC   |      |      |      |      |      |      |      |      |      | 1    |
| Primer_AHR_ENST173-203_185G_fwd  | CACCCCTGGATTTAGGAAGTCCCGGGAGCAGC   |      |      |      |      |      |      |      |      |      | 31   |
| Lower_overlap_SC119159_1142-1612 | CACCCCTGGATTTAGGAAGTCCCGGGAGCAGCGCGGCGGCACCTCCCTCACCAAGGGGC                                      |      |      |      |      |      |      |      |      |      | 59   |
| Primer_Down_AHR_ENST643-630_XhoI |  |      |      |      |      |      |      |      |      |      | 27   |
| pCMV6-XL4_SC119159_918-1612_XhoI | CCGGGACTGGTGGCCCGCCGAGCTCCGAGCGGGGAAGCACCCCTGGATTTAGGAAGTCCCGGGAGCAGCGCGGCGGCACCTCCCTCACCAAGGGGC |      |      |      |      |      |      |      |      |      | 283  |
| EcoRI-XhoI_SC119159_979-1612     | CCGGGACTGGTGGCCCGCCGAGCTCCGAGCGGGGAAGCACCCCTGGATTTAGGAAGTCCCGGGAGCAGCGCGGCGGCACCTCCCTCACCAAGGGGC |      |      |      |      |      |      |      |      |      | 222  |
| 5'-UTR_SC119159_993-1612         | CCGGGACTGGTGGCCCGCCGAGCTCCGAGCGGGGAAGCACCCCTGGATTTAGGAAGTCCCGGGAGCAGCGCGGCGGCACCTCCCTCACCAAGGGGC |      |      |      |      |      |      |      |      |      | 208  |

pCMV6-XL4\_SC119159\_Deduced  
 AHR\_002\_Hum\_ENST00000242057.8  
 Primer\_Up\_pCMV6-XL4\_918-937  
 Upper\_over\_lap\_SC119159\_918-1169  
 Primer\_AHR\_ENST200-170\_185G\_rev  
 Primer\_AHR\_ENST173-203\_185G\_fwd  
 Lower\_over\_lap\_SC119159\_1142-1612  
 Primer\_Down\_AHR\_ENST643-630\_Xhol  
 pCMV6-XL4\_SC119159\_918-1612\_Xhol  
 EcoRI-Xhol\_SC119159\_979-1612  
 5'-UTR\_SC119159\_993-1612

|  |  |      |      |      |      |      |      |      |      |      |      |
|--|--|------|------|------|------|------|------|------|------|------|------|
|  | 1210   | 1220 | 1230 | 1240 | 1250 | 1260 | 1270 | 1280 | 1290 | 1300 |      |
|  | CGCGGCACGGTACAGGGGCGCGGCCACCGTGAGCGACCCAGGCCAGGATTCTAAATAGACGGCCAGGCTCCTCCTCCGCCGGGCGCCTCACCTG |      |      |      |      |      |      |      |      |      | 1300 |
|  | CGCGGCACGGTACAGGGGCGCGGCCACCGTGAGCGACCCAGGCCAGGATTCTAAATAGACGGCCAGGCTCCTCCTCCGCCGGGCGCCTCACCTG |      |      |      |      |      |      |      |      |      | 331  |
|  |  |      |      |      |      |      |      |      |      |      | 20   |
|  |  |      |      |      |      |      |      |      |      |      | 252  |
|  |  |      |      |      |      |      |      |      |      |      | 1    |
|  |  |      |      |      |      |      |      |      |      |      | 31   |
|  | CGCGGCACGGTACAGGGGCGCGGCCACCGTGAGCGACCCAGGCCAGGATTCTAAATAGACGGCCAGGCTCCTCCTCCGCCGGGCGCCTCACCTG |      |      |      |      |      |      |      |      |      | 159  |
|  | -----  |      |      |      |      |      |      |      |      |      | 27   |
|  | CGCGGCACGGTACAGGGGCGCGGCCACCGTGAGCGACCCAGGCCAGGATTCTAAATAGACGGCCAGGCTCCTCCTCCGCCGGGCGCCTCACCTG |      |      |      |      |      |      |      |      |      | 383  |
|  | CGCGGCACGGTACAGGGGCGCGGCCACCGTGAGCGACCCAGGCCAGGATTCTAAATAGACGGCCAGGCTCCTCCTCCGCCGGGCGCCTCACCTG |      |      |      |      |      |      |      |      |      | 322  |
|  | CGCGGCACGGTACAGGGGCGCGGCCACCGTGAGCGACCCAGGCCAGGATTCTAAATAGACGGCCAGGCTCCTCCTCCGCCGGGCGCCTCACCTG |      |      |      |      |      |      |      |      |      | 308  |

pCMV6-XL4\_SC119159\_Deduced  
 AHR\_002\_Hum\_ENST00000242057.8  
 Primer\_Up\_pCMV6-XL4\_918-937  
 Upper\_over\_lap\_SC119159\_918-1169  
 Primer\_AHR\_ENST200-170\_185G\_rev  
 Primer\_AHR\_ENST173-203\_185G\_fwd  
 Lower\_over\_lap\_SC119159\_1142-1612  
 Primer\_Down\_AHR\_ENST643-630\_Xhol  
 pCMV6-XL4\_SC119159\_918-1612\_Xhol  
 EcoRI-Xhol\_SC119159\_979-1612  
 5'-UTR\_SC119159\_993-1612

|  |   |      |      |      |      |      |      |      |      |      |      |
|--|---|------|------|------|------|------|------|------|------|------|------|
|  | 1310  | 1320 | 1330 | 1340 | 1350 | 1360 | 1370 | 1380 | 1390 | 1400 |      |
|  | CGGGCATTGCCGCGCGCCTCCGCCGGTGTAGACGGCACCTGCGCCGCCTTGTCTCGCGGGTCTCCGCCCTCGCCACCCTCACTGCGCCAGGCCAGGC |      |      |      |      |      |      |      |      |      | 1400 |
|  | CGGGCATTGCCGCGCGCCTCCGCCGGTGTAGACGGCACCTGCGCCGCCTTGTCTCGCGGGTCTCCGCCCTCGCCACCCTCACTGCGCCAGGCCAGGC |      |      |      |      |      |      |      |      |      | 431  |
|  |   |      |      |      |      |      |      |      |      |      | 20   |
|  |   |      |      |      |      |      |      |      |      |      | 252  |
|  |   |      |      |      |      |      |      |      |      |      | 1    |
|  |   |      |      |      |      |      |      |      |      |      | 31   |
|  | CGGGCATTGCCGCGCGCCTCCGCCGGTGTAGACGGCACCTGCGCCGCCTTGTCTCGCGGGTCTCCGCCCTCGCCACCCTCACTGCGCCAGGCCAGGC |      |      |      |      |      |      |      |      |      | 259  |
|  | -----   |      |      |      |      |      |      |      |      |      | 27   |
|  | CGGGCATTGCCGCGCGCCTCCGCCGGTGTAGACGGCACCTGCGCCGCCTTGTCTCGCGGGTCTCCGCCCTCGCCACCCTCACTGCGCCAGGCCAGGC |      |      |      |      |      |      |      |      |      | 483  |
|  | CGGGCATTGCCGCGCGCCTCCGCCGGTGTAGACGGCACCTGCGCCGCCTTGTCTCGCGGGTCTCCGCCCTCGCCACCCTCACTGCGCCAGGCCAGGC |      |      |      |      |      |      |      |      |      | 422  |
|  | CGGGCATTGCCGCGCGCCTCCGCCGGTGTAGACGGCACCTGCGCCGCCTTGTCTCGCGGGTCTCCGCCCTCGCCACCCTCACTGCGCCAGGCCAGGC |      |      |      |      |      |      |      |      |      | 408  |

pCMV6-XL4\_SC119159\_Deduced  
 AHR\_002\_Hum\_ENST00000242057.8  
 Primer\_Up\_pCMV6-XL4\_918-937  
 Upper\_over\_lap\_SC119159\_918-1169  
 Primer\_AHR\_ENST200-170\_185G\_rev  
 Primer\_AHR\_ENST173-203\_185G\_fwd  
 Lower\_over\_lap\_SC119159\_1142-1612  
 Primer\_Down\_AHR\_ENST643-630\_Xhol  
 pCMV6-XL4\_SC119159\_918-1612\_Xhol  
 EcoRI-Xhol\_SC119159\_979-1612  
 5'-UTR\_SC119159\_993-1612

|  |  |      |      |      |      |      |      |      |      |      |      |
|--|--|------|------|------|------|------|------|------|------|------|------|
|  | 1410   | 1420 | 1430 | 1440 | 1450 | 1460 | 1470 | 1480 | 1490 | 1500 |      |
|  | AGCTCACCTGTACTGGCGGGCTGCGGAAGCCTGCGTGAGCCGAGGCGTTGAGGCGCGGCCACGCCACTGTCCCAGAGGACGCAGGTGGAGCGGG |      |      |      |      |      |      |      |      |      | 1500 |
|  | AGCTCACCTGTACTGGCGGGCTGCGGAAGCCTGCGTGAGCCGAGGCGTTGAGGCGCGGCCACGCCACTGTCCCAGAGGACGCAGGTGGAGCGGG |      |      |      |      |      |      |      |      |      | 531  |
|  |  |      |      |      |      |      |      |      |      |      | 20   |
|  |  |      |      |      |      |      |      |      |      |      | 252  |
|  |  |      |      |      |      |      |      |      |      |      | 1    |
|  |  |      |      |      |      |      |      |      |      |      | 31   |
|  | AGCTCACCTGTACTGGCGGGCTGCGGAAGCCTGCGTGAGCCGAGGCGTTGAGGCGCGGCCACGCCACTGTCCCAGAGGACGCAGGTGGAGCGGG |      |      |      |      |      |      |      |      |      | 359  |
|  | -----  |      |      |      |      |      |      |      |      |      | 27   |
|  | AGCTCACCTGTACTGGCGGGCTGCGGAAGCCTGCGTGAGCCGAGGCGTTGAGGCGCGGCCACGCCACTGTCCCAGAGGACGCAGGTGGAGCGGG |      |      |      |      |      |      |      |      |      | 583  |
|  | AGCTCACCTGTACTGGCGGGCTGCGGAAGCCTGCGTGAGCCGAGGCGTTGAGGCGCGGCCACGCCACTGTCCCAGAGGACGCAGGTGGAGCGGG |      |      |      |      |      |      |      |      |      | 522  |
|  | AGCTCACCTGTACTGGCGGGCTGCGGAAGCCTGCGTGAGCCGAGGCGTTGAGGCGCGGCCACGCCACTGTCCCAGAGGACGCAGGTGGAGCGGG |      |      |      |      |      |      |      |      |      | 508  |

pCMV6-XL4\_SC119159\_Deduced  
 AHR\_002\_Hum\_ENST00000242057.8  
 Primer\_Up\_pCMV6-XL4\_918-937  
 Upper\_over\_lap\_SC119159\_918-1169  
 Primer\_AHR\_ENST200-170\_185G\_rev  
 Primer\_AHR\_ENST173-203\_185G\_fwd  
 Lower\_over\_lap\_SC119159\_1142-1612  
 Primer\_Down\_AHR\_ENST643-630\_Xhol  
 pCMV6-XL4\_SC119159\_918-1612\_Xhol  
 EcoRI-Xhol\_SC119159\_979-1612  
 5'-UTR\_SC119159\_993-1612

|  |   |      |      |      |      |      |      |      |      |      |      |
|--|---|------|------|------|------|------|------|------|------|------|------|
|  | 1510  | 1520 | 1530 | 1540 | 1550 | 1560 | 1570 | 1580 | 1590 | 1600 |      |
|  | CGCGGCTTCGCGGAACCCGGCGCCGGCCGCGCAGTGGTCCCAGCCTACACCGGGTTCGCGGGACCCGGCCGCAAGTCCCAGGGAGTAGCCGCGCCGT |      |      |      |      |      |      |      |      |      | 1600 |
|  | CGCGGCTTCGCGGAACCCGGCGCCGGCCGCGCAGTGGTCCCAGCCTACACCGGGTTCGCGGGACCCGGCCGCAAGTCCCAGGGAGTAGCCGCGCCGT |      |      |      |      |      |      |      |      |      | 631  |
|  |   |      |      |      |      |      |      |      |      |      | 20   |
|  |   |      |      |      |      |      |      |      |      |      | 252  |
|  |   |      |      |      |      |      |      |      |      |      | 1    |
|  |   |      |      |      |      |      |      |      |      |      | 31   |
|  | CGCGGCTTCGCGGAACCCGGCGCCGGCCGCGCAGTGGTCCCAGCCTACACCGGGTTCGCGGGACCCGGCCGCAAGTCCCAGGGAGTAGCCGCGCCGT |      |      |      |      |      |      |      |      |      | 459  |
|  | -----   |      |      |      |      |      |      |      |      |      | 25   |
|  | CGCGGCTTCGCGGAACCCGGCGCCGGCCGCGCAGTGGTCCCAGCCTACACCGGGTTCGCGGGACCCGGCCGCAAGTCCCAGGGAGTAGCCGCGCCGT |      |      |      |      |      |      |      |      |      | 683  |
|  | CGCGGCTTCGCGGAACCCGGCGCCGGCCGCGCAGTGGTCCCAGCCTACACCGGGTTCGCGGGACCCGGCCGCAAGTCCCAGGGAGTAGCCGCGCCGT |      |      |      |      |      |      |      |      |      | 622  |
|  | CGCGGCTTCGCGGAACCCGGCGCCGGCCGCGCAGTGGTCCCAGCCTACACCGGGTTCGCGGGACCCGGCCGCAAGTCCCAGGGAGTAGCCGCGCCGT |      |      |      |      |      |      |      |      |      | 608  |

|                                  | 1610  | 1620       | 1630 | 1640 | 1650 | 1660 | 1670 | 1680 | 1690 | 1700 |      |     |
|----------------------------------|---|------------|------|------|------|------|------|------|------|------|------|-----|
| pCMV6-XL4_SC119159_Deduced       | CGGCTGGGCACCATGAACAGCAGCAGCGCCAACATCACCTACGCCAGTCGCAAGCGGCGGAAGCCGGTGCAGAAAAACAGTAAAGCCAATCCCAGCTGAAG |            |      |      |      |      |      |      |      |      | 1700 |     |
| AHR_002_Hum_ENST00000242057.8    | CGGCTGGGCACCATGAACAGCAGCAGCGCCAACATCACCTACGCCAGTCGCAAGCGGCGGAAGCCGGTGCAGAAAAACAGTAAAGCCAATCCCAGCTGAAG |            |      |      |      |      |      |      |      |      | 731  |     |
| Primer_Up_pCMV6-XL4_918-937      |   |            |      |      |      |      |      |      |      |      | 20   |     |
| Upper_overlap_SC119159_918-1169  |   |            |      |      |      |      |      |      |      |      | 252  |     |
| Primer_AHR_ENST200-170_185G_rev  |   |            |      |      |      |      |      |      |      |      | 1    |     |
| Primer_AHR_ENST173-203_185G_fwd  |   |            |      |      |      |      |      |      |      |      | 31   |     |
| Lower_overlap_SC119159_1142-1612 | CGGCTGGGCACCC   | CGAGTTTTTT |      |      |      |      |      |      |      |      |      | 483 |
| Primer_Down_AHR_ENST643-630_XhoI | CGGCTGGGCACCC   | CGAGTTTTTT |      |      |      |      |      |      |      |      |      | 1   |
| pCMV6-XL4_SC119159_918-1612_XhoI | CGGCTGGGCACCC   | CGAGTTTTTT |      |      |      |      |      |      |      |      |      | 707 |
| EcoRI-XhoI_SC119159_979-1612     | CGGCTGGGCACCC   | CGAGTTTTTT |      |      |      |      |      |      |      |      |      | 646 |
| 5'-UTR_SC119159_993-1612         | CGGCTGGGCACC  |            |      |      |      |      |      |      |      |      | 620  |     |



## **Supplementary Data SD6**

*SD6\_AHR cDNA Alignment.pptx*

**Alignment of AHR mRNA sequence variants studied**

**Alignment of cDNA copies of the AHR mRNA sequence variants studied using the MegAlign module of the DNASTAR LaserGene 10 Core Suite.** Sequence differences with the present-day human Ensembl reference AHR transcript sequence (upper line; "gold" standard transcript AHR-201; Ensembl code ENST00000242057.8) are highlighted in red. The synthesized complete modern human AHR cDNA sequence derived from ENST00000242057.8 is aligned below (AHR\_Modern.seq), and on the third line the complete Altai-Neanderthal cDNA sequence (AHR\_Neanderthal.seq) synthesized according to Prüfer et al., Nature, Vol. 505 (2014), p. 43-49. The extra 3'-terminal T of these synthesis products was added based on the RefSeq AHR transcript NM\_001621.4, which is also manually curated. The respective sequence files of the modern human and Neanderthal AHR cDNA synthesized are available in FASTA format (Supplementary Data, SD2 and SD3, respectively) . To show the difference with the AHR mRNA coding region sequence investigated by Hubbard et al. [Mol. Biol. Evol. 33(10):2648–2658], the next three lines show the alignment of the coding region of the reference AHR mRNA (AHR\_002\_Hum\_ENST00000245057.8\_CDS.seq), and the codon-optimized modern human AHR cDNA synthesized as the parent sequence (AHR\_Modern\_Hubbard.seq) for the generation of their Neanderthal AHR cDNA (AHR\_Neanderthal\_Hubbard.seq) by mutagenesis (two positions indicated by a green arrow).

|                                       |   |     |     |     |     |     |
|---------------------------------------|---|-----|-----|-----|-----|-----|
|                                       | 10  | 20  | 30  | 40  | 50  |     |
| AHR_002_Hum_ENST00000242057.8.seq     | ATTCAGCCGGTGCGCGCGGCGGCGGGAGGCAAGTGGCTGGGGAGTCCCCTC   |     |     |     |     | 50  |
| AHR_Modern.seq                        | ATTCAGCCGGTGCGCGCGGCGGCGGGAGGCAAGTGGCTGGGGAGTCCCCTC   |     |     |     |     | 50  |
| AHR_Neanderthal.seq                   | ATTCAGCCGGTGCGCGCGGCGGCGGGAGGCAAGTGGCTGGGGAGTCCCCTC   |     |     |     |     | 50  |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | .....   |     |     |     |     | 0   |
| AHR_Modern_Hubbard.seq                | .....   |     |     |     |     | 0   |
| AHR_Neanderthal_Hubbard.seq           | .....   |     |     |     |     | 0   |
|                                       |   |     |     |     |     |     |
|                                       | 60  | 70  | 80  | 90  | 100 |     |
| AHR_002_Hum_ENST00000242057.8.seq     | GACGCTCTGTTC CGAGAGCGT GCCCGGACC GCCAGCT CAGAACAGGGGC |     |     |     |     | 100 |
| AHR_Modern.seq                        | GACGCTCTGTTC CGAGAGCGT GCCCGGACC GCCAGCT CAGAACAGGGGC |     |     |     |     | 100 |
| AHR_Neanderthal.seq                   | GACGCTCTGTTC CGAGAGCGT GCCCGGACC GCCAGCT CAGAACAGGGGC |     |     |     |     | 100 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | .....   |     |     |     |     | 0   |
| AHR_Modern_Hubbard.seq                | .....   |     |     |     |     | 0   |
| AHR_Neanderthal_Hubbard.seq           | .....   |     |     |     |     | 0   |
|                                       |   |     |     |     |     |     |
|                                       | 110   | 120 | 130 | 140 | 150 |     |
| AHR_002_Hum_ENST00000242057.8.seq     | AGCCGTGTAGCCGAACGGAAGCTGGGAGCAGCCGGGACTGGTGGCCCGCG    |     |     |     |     | 150 |
| AHR_Modern.seq                        | AGCCGTGTAGCCGAACGGAAGCTGGGAGCAGCCGGGACTGGTGGCCCGCG    |     |     |     |     | 150 |
| AHR_Neanderthal.seq                   | AGCCGTGTAGCCGAACGGAAGCTGGGAGCAGCCGGGACTGGTGGCCCGCG    |     |     |     |     | 150 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | .....   |     |     |     |     | 0   |
| AHR_Modern_Hubbard.seq                | .....   |     |     |     |     | 0   |
| AHR_Neanderthal_Hubbard.seq           | .....   |     |     |     |     | 0   |
|                                       |   |     |     |     |     |     |
|                                       | 160   | 170 | 180 | 190 | 200 |     |
| AHR_002_Hum_ENST00000242057.8.seq     | CCCGAGCTCCGCAGGCGGGAAGCACCTGGATTTAGGAAGTCCCGGGAGC     |     |     |     |     | 200 |
| AHR_Modern.seq                        | CCCGAGCTCCGCAGGCGGGAAGCACCTGGATTTAGGAAGTCCCGGGAGC     |     |     |     |     | 200 |
| AHR_Neanderthal.seq                   | CCCGAGCTCCGCAGGCGGGAAGCACCTGGATTTAGGAAGTCCCGGGAGC     |     |     |     |     | 200 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | .....   |     |     |     |     | 0   |
| AHR_Modern_Hubbard.seq                | .....   |     |     |     |     | 0   |
| AHR_Neanderthal_Hubbard.seq           | .....   |     |     |     |     | 0   |
|                                       |   |     |     |     |     |     |
|                                       | 210   | 220 | 230 | 240 | 250 |     |
| AHR_002_Hum_ENST00000242057.8.seq     | AGCGCGGCGGCACCTCCCTCACCCAAGGGGCGCGGCGACGGTCACGGGG     |     |     |     |     | 250 |
| AHR_Modern.seq                        | AGCGCGGCGGCACCTCCCTCACCCAAGGGGCGCGGCGACGGTCACGGGG     |     |     |     |     | 250 |
| AHR_Neanderthal.seq                   | AGCGCGGCGGCACCTCCCTCACCCAAGGGGCGCGGCGACGGTCACGGGG     |     |     |     |     | 250 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | .....   |     |     |     |     | 0   |
| AHR_Modern_Hubbard.seq                | .....   |     |     |     |     | 0   |
| AHR_Neanderthal_Hubbard.seq           | .....   |     |     |     |     | 0   |
|                                       |   |     |     |     |     |     |
|                                       | 260   | 270 | 280 | 290 | 300 |     |
| AHR_002_Hum_ENST00000242057.8.seq     | CGCGGCGCCACCCTGAGCGACCCAGGCCAGGATTCTAAATAGACGGCCCA    |     |     |     |     | 300 |
| AHR_Modern.seq                        | CGCGGCGCCACCCTGAGCGACCCAGGCCAGGATTCTAAATAGACGGCCCA    |     |     |     |     | 300 |
| AHR_Neanderthal.seq                   | CGCGGCGCCACCCTGAGCGACCCAGGCCAGGATTCTAAATAGACGGCCCA    |     |     |     |     | 300 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | .....   |     |     |     |     | 0   |
| AHR_Modern_Hubbard.seq                | .....   |     |     |     |     | 0   |
| AHR_Neanderthal_Hubbard.seq           | .....   |     |     |     |     | 0   |

|                                       |   |     |     |     |     |
|---------------------------------------|---|-----|-----|-----|-----|
|                                       | 310   | 320 | 330 | 340 | 350 |
| AHR_002_Hum_ENST00000242057.8.seq     | GGCT CCT CCT CCGCCCGGGCCGCCT CA CCT GCGGGCATT GCCGC GCGCC       |     |     |     |     |
| AHR_Modern.seq                        | GGCT CCT CCT CCGCCCGGGCCGCCT CA CCT GCGGGCATT GCCGC GCGCC       |     |     |     |     |
| AHR_Neanderthal.seq                   | GGCT CCT CCT CCGCCCGGGCCGCCT CA CCT GCGGGCATT GCCGC GCGCC       |     |     |     |     |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | -----   |     |     |     |     |
| AHR_Modern_Hubbard.seq                | -----   |     |     |     |     |
| AHR_Neanderthal_Hubbard.seq           | -----   |     |     |     |     |
|                                       | 360   | 370 | 380 | 390 | 400 |
| AHR_002_Hum_ENST00000242057.8.seq     | TCCGCCGGT GTA GACGGCA CCT GCGCCGCCT T GCT C GCGGGT CT CCGCCC    |     |     |     |     |
| AHR_Modern.seq                        | TCCGCCGGT GTA GACGGCA CCT GCGCCGCCT T GCT C GCGGGT CT CCGCCC    |     |     |     |     |
| AHR_Neanderthal.seq                   | TCCGCCGGT GTA GACGGCA CCT GCGCCGCCT T GCT C GCGGGT CT CCGCCC    |     |     |     |     |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | -----   |     |     |     |     |
| AHR_Modern_Hubbard.seq                | -----   |     |     |     |     |
| AHR_Neanderthal_Hubbard.seq           | -----   |     |     |     |     |
|                                       | 410   | 420 | 430 | 440 | 450 |
| AHR_002_Hum_ENST00000242057.8.seq     | CT CGCCCA CCT CA CT GCGCCAGGCCAGGCAGCT CACCT GT ACT GGC GC      |     |     |     |     |
| AHR_Modern.seq                        | CT CGCCCA CCT CA CT GCGCCAGGCCAGGCAGCT CACCT GT ACT GGC GC      |     |     |     |     |
| AHR_Neanderthal.seq                   | CT CGCCCA CCT CA CT GCGCCAGGCCAGGCAGCT CACCT GT ACT GGC GC      |     |     |     |     |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | -----   |     |     |     |     |
| AHR_Modern_Hubbard.seq                | -----   |     |     |     |     |
| AHR_Neanderthal_Hubbard.seq           | -----   |     |     |     |     |
|                                       | 460   | 470 | 480 | 490 | 500 |
| AHR_002_Hum_ENST00000242057.8.seq     | GGGCT GCGGA AGCC T GC GT GA GCCGAGGC GT T GA GGC GCGGC GCCAC GC |     |     |     |     |
| AHR_Modern.seq                        | GGGCT GCGGA AGCC T GC GT GA GCCGAGGC GT T GA GGC GCGGC GCCAC GC |     |     |     |     |
| AHR_Neanderthal.seq                   | GGGCT GCGGA AGCC T GC GT GA GCCGAGGC GT T GA GGC GCGGC GCCAC GC |     |     |     |     |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | -----   |     |     |     |     |
| AHR_Modern_Hubbard.seq                | -----   |     |     |     |     |
| AHR_Neanderthal_Hubbard.seq           | -----   |     |     |     |     |
|                                       | 510   | 520 | 530 | 540 | 550 |
| AHR_002_Hum_ENST00000242057.8.seq     | CA CT GT CCCGAGAGGAC GCAGGT GGAGCGGGCGCGGCT T C GCGGAA CCG      |     |     |     |     |
| AHR_Modern.seq                        | CA CT GT CCCGAGAGGAC GCAGGT GGAGCGGGCGCGGCT T C GCGGAA CCG      |     |     |     |     |
| AHR_Neanderthal.seq                   | CA CT GT CCCGAGAGGAC GCAGGT GGAGCGGGCGCGGCT T C GCGGAA CCG      |     |     |     |     |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | -----   |     |     |     |     |
| AHR_Modern_Hubbard.seq                | -----   |     |     |     |     |
| AHR_Neanderthal_Hubbard.seq           | -----   |     |     |     |     |
|                                       | 560   | 570 | 580 | 590 | 600 |
| AHR_002_Hum_ENST00000242057.8.seq     | GCGCCGGCCGCGCCGAGT GGTCCCAGCCTACA CCGGGTT CCGGGGACCCGG          |     |     |     |     |
| AHR_Modern.seq                        | GCGCCGGCCGCGCCGAGT GGTCCCAGCCTACA CCGGGTT CCGGGGACCCGG          |     |     |     |     |
| AHR_Neanderthal.seq                   | GCGCCGGCCGCGCCGAGT GGTCCCAGCCTACA CCGGGTT CCGGGGACCCGG          |     |     |     |     |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | -----   |     |     |     |     |
| AHR_Modern_Hubbard.seq                | -----   |     |     |     |     |
| AHR_Neanderthal_Hubbard.seq           | -----   |     |     |     |     |
|                                       | 610   | 620 | 630 | 640 | 650 |
| AHR_002_Hum_ENST00000242057.8.seq     | CCGCCA GT GCCCGGGGA GT AGCCGCCGCCGT CGGCT GGGCACCA T GAA CA     |     |     |     |     |
| AHR_Modern.seq                        | CCGCCA GT GCCCGGGGA GT AGCCGCCGCCGT CGGCT GGGCACCA T GAA CA     |     |     |     |     |
| AHR_Neanderthal.seq                   | CCGCCA GT GCCCGGGGA GT AGCCGCCGCCGT CGGCT GGGCACCA T GAA CA     |     |     |     |     |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | -----   |     |     |     |     |
| AHR_Modern_Hubbard.seq                | -----   |     |     |     |     |
| AHR_Neanderthal_Hubbard.seq           | -----   |     |     |     |     |
|                                       | 660   | 670 | 680 | 690 | 700 |
| AHR_002_Hum_ENST00000242057.8.seq     | GCAGCA GCGCCAACATCACCTACGCCA GT CGCAA GC GCGCGGAAGCCGGT G       |     |     |     |     |
| AHR_Modern.seq                        | GCAGCA GCGCCAACATCACCTACGCCA GT CGCAA GC GCGCGGAAGCCGGT G       |     |     |     |     |
| AHR_Neanderthal.seq                   | GCAGCA GCGCCAACATCACCTACGCCA GT CGCAA GC GCGCGGAAGCCGGT G       |     |     |     |     |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | -----   |     |     |     |     |
| AHR_Modern_Hubbard.seq                | -----   |     |     |     |     |
| AHR_Neanderthal_Hubbard.seq           | -----   |     |     |     |     |
|                                       | 710   | 720 | 730 | 740 | 750 |
| AHR_002_Hum_ENST00000242057.8.seq     | CAGAAAACAGTAAA GCCAA TCCAGCT GAAGGAA TCAA GT CAA T CCT TC       |     |     |     |     |
| AHR_Modern.seq                        | CAGAAAACAGTAAA GCCAA TCCAGCT GAAGGAA TCAA GT CAA T CCT TC       |     |     |     |     |
| AHR_Neanderthal.seq                   | CAGAAAACAGTAAA GCCAA TCCAGCT GAAGGAA TCAA GT CAA T CCT TC       |     |     |     |     |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | -----   |     |     |     |     |
| AHR_Modern_Hubbard.seq                | -----   |     |     |     |     |
| AHR_Neanderthal_Hubbard.seq           | -----   |     |     |     |     |

|                                       |  |      |
|---------------------------------------|--|------|
|                                       | 760                      770                      780                      790                      800      |      |
| AHR_002_Hum_ENST00000242057.8.seq     | CAAGCGGCATAGAGACCGACTTAATACAGAGTTGGACCGTTGGCTAGCC  | 800  |
| AHR_Modern.seq                        | CAAGCGGCATAGAGACCGACTTAATACAGAGTTGGACCGTTGGCTAGCC  | 800  |
| AHR_Neanderthal.seq                   | CAAGCGGCATAGAGACCGACTTAATACAGAGTTGGACCGTTGGCTAGCC  | 800  |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | CAAGCGGCATAGAGACCGACTTAATACAGAGTTGGACCGTTGGCTAGCC  | 157  |
| AHR_Modern_Hubbard.seq                | CAAACGGCAACCGGACCGGCTAAACACGAGATCTGGAACCGCTGGCTAGCC  | 157  |
| AHR_Neanderthal_Hubbard.seq           | CAAACGGCAACCGGACCGGCTAAACACGAGATCTGGAACCGCTGGCTAGCC  | 157  |
|                                       |  |      |
|                                       | 810                      820                      830                      840                      850      |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TGCTGCCTTTCCCAAAAGATGTTATTAATAAGTTGGACAAACTTTCAGTT   | 850  |
| AHR_Modern.seq                        | TGCTGCCTTTCCCAAAAGATGTTATTAATAAGTTGGACAAACTTTCAGTT   | 850  |
| AHR_Neanderthal.seq                   | TGCTGCCTTTCCCAAAAGATGTTATTAATAAGTTGGACAAACTTTCAGTT   | 850  |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | TGCTGCCTTTCCCAAAAGATGTTATTAATAAGTTGGACAAACTTTCAGTT   | 207  |
| AHR_Modern_Hubbard.seq                | TGCTCCCTTTCCCACAGATGATGATGAAAGGCTGGAIAAACTGACGCTG  | 207  |
| AHR_Neanderthal_Hubbard.seq           | TGCTCCCTTTCCCACAGATGATGATGAAAGGCTGGAIAAACTGACGCTG  | 207  |
|                                       |  |      |
|                                       | 860                      870                      880                      890                      900      |      |
| AHR_002_Hum_ENST00000242057.8.seq     | CTTAGGCTCAGCGTCAGTTACCTGAGAGCCAAAGAGCTTCTTTGATGTTGC  | 900  |
| AHR_Modern.seq                        | CTTAGGCTCAGCGTCAGTTACCTGAGAGCCAAAGAGCTTCTTTGATGTTGC  | 900  |
| AHR_Neanderthal.seq                   | CTTAGGCTCAGCGTCAGTTACCTGAGAGCCAAAGAGCTTCTTTGATGTTGC  | 900  |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | CTTAGGCTCAGCGTCAGTTACCTGAGAGCCAAAGAGCTTCTTTGATGTTGC  | 257  |
| AHR_Modern_Hubbard.seq                | CTCGGGCTCAGCGTCAGTTACCTGGGGCCAAAGAGCTTCTTTGATGTTGC   | 257  |
| AHR_Neanderthal_Hubbard.seq           | CTCGGGCTCAGCGTCAGTTACCTGGGGCCAAAGAGCTTCTTTGATGTTGC   | 257  |
|                                       |  |      |
|                                       | 910                      920                      930                      940                      950      |      |
| AHR_002_Hum_ENST00000242057.8.seq     | ATTAAAATCCTCCCCTACTGAAAGAAACGGAGGCCAGGATAACTGTAGAG   | 950  |
| AHR_Modern.seq                        | ATTAAAATCCTCCCCTACTGAAAGAAACGGAGGCCAGGATAACTGTAGAG   | 950  |
| AHR_Neanderthal.seq                   | ATTAAAATCCTCCCCTACTGAAAGAAACGGAGGCCAGGATAACTGTAGAG   | 950  |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | ATTAAAATCCTCCCCTACTGAAAGAAACGGAGGCCAGGATAACTGTAGAG   | 307  |
| AHR_Modern_Hubbard.seq                | TTTAAAACGACCCCAACGAAAGGAAACGGAGGCCAGGATAACTGGGCGG  | 307  |
| AHR_Neanderthal_Hubbard.seq           | TTTAAAACGACCCCAACGAAAGGAAACGGAGGCCAGGATAACTGGGCGG  | 307  |
|                                       |  |      |
|                                       | 960                      970                      980                      990                      1000     |      |
| AHR_002_Hum_ENST00000242057.8.seq     | CAGCAAATTTCAAGAAAGGCTGAACTTACAAGAAGGAGAATTCCTATTA  | 1000 |
| AHR_Modern.seq                        | CAGCAAATTTCAAGAAAGGCTGAACTTACAAGAAGGAGAATTCCTATTA  | 1000 |
| AHR_Neanderthal.seq                   | CAGCAAATTTCAAGAAAGGCTGAACTTACAAGAAGGAGAATTCCTATTA  | 1000 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | CAGCAAATTTCAAGAAAGGCTGAACTTACAAGAAGGAGAATTCCTATTA  | 357  |
| AHR_Modern_Hubbard.seq                | CTTGCATAATTCGGGAAAGGCTGAACTTACAAGAAGGAGAATTCCTATTA   | 357  |
| AHR_Neanderthal_Hubbard.seq           | CTTGCATAATTCGGGAAAGGCTGAACTTACAAGAAGGAGAATTCCTATTA   | 357  |
|                                       |  |      |
|                                       | 1010                      1020                      1030                      1040                      1050 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | CAGGCTCTGAATGGCTTTGTATTAGTTGTCACTACAGATGCTTTGGTCTT   | 1050 |
| AHR_Modern.seq                        | CAGGCTCTGAATGGCTTTGTATTAGTTGTCACTACAGATGCTTTGGTCTT   | 1050 |
| AHR_Neanderthal.seq                   | CAGGCTCTGAATGGCTTTGTATTAGTTGTCACTACAGATGCTTTGGTCTT   | 1050 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | CAGGCTCTGAATGGCTTTGTATTAGTTGTCACTACAGATGCTTTGGTCTT   | 407  |
| AHR_Modern_Hubbard.seq                | CAGGCTCTGAATGGCTTTGTATTAGTTGTCACTACAGATGCTTTGGTCTT   | 407  |
| AHR_Neanderthal_Hubbard.seq           | CAGGCTCTGAATGGCTTTGTATTAGTTGTCACTACAGATGCTTTGGTCTT   | 407  |
|                                       |  |      |
|                                       | 1060                      1070                      1080                      1090                      1100 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TTATGCTTCTTCTACTATACAAGATTATCTAGGGTTTCAGCAGTCTGATG   | 1100 |
| AHR_Modern.seq                        | TTATGCTTCTTCTACTATACAAGATTATCTAGGGTTTCAGCAGTCTGATG   | 1100 |
| AHR_Neanderthal.seq                   | TTATGCTTCTTCTACTATACAAGATTATCTAGGGTTTCAGCAGTCTGATG   | 1100 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | TTATGCTTCTTCTACTATACAAGATTATCTAGGGTTTCAGCAGTCTGATG   | 457  |
| AHR_Modern_Hubbard.seq                | GTAGCTTACGACCAACATCAAGATTAAGCTGGGTTTCAGCAGTCTGATG  | 457  |
| AHR_Neanderthal_Hubbard.seq           | GTAGCTTACGACCAACATCAAGATTAAGCTGGGTTTCAGCAGTCTGATG  | 457  |
|                                       |  |      |
|                                       | 1110                      1120                      1130                      1140                      1150 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TCATACATCAGAGTGTATATGAACTTATCCAATACCGAAGACCGAGCTGAA  | 1150 |
| AHR_Modern.seq                        | TCATACATCAGAGTGTATATGAACTTATCCAATACCGAAGACCGAGCTGAA  | 1150 |
| AHR_Neanderthal.seq                   | TCATACATCAGAGTGTATATGAACTTATCCAATACCGAAGACCGAGCTGAA  | 1150 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | TCATACATCAGAGTGTATATGAACTTATCCAATACCGAAGACCGAGCTGAA  | 507  |
| AHR_Modern_Hubbard.seq                | TSATCAACAGAGGTATAGAACTGATCCAACCGAAGATTCGGCTGAA   | 507  |
| AHR_Neanderthal_Hubbard.seq           | TSATCAACAGAGGTATAGAACTGATCCAACCGAAGATTCGGCTGAA   | 507  |
|                                       |  |      |
|                                       | 1160                      1170                      1180                      1190                      1200 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TTTCAGCGTCAGCTACACTGGGCATTAATCCTTCTCAGTGTACAGAGTC  | 1200 |
| AHR_Modern.seq                        | TTTCAGCGTCAGCTACACTGGGCATTAATCCTTCTCAGTGTACAGAGTC  | 1200 |
| AHR_Neanderthal.seq                   | TTTCAGCGTCAGCTACACTGGGCATTAATCCTTCTCAGTGTACAGAGTC  | 1200 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | TTTCAGCGTCAGCTACACTGGGCATTAATCCTTCTCAGTGTACAGAGTC  | 557  |
| AHR_Modern_Hubbard.seq                | TTTCAGCGTCAGCTCACTGGGCTTGTAAACCGACAGTGTACGAAAC   | 557  |
| AHR_Neanderthal_Hubbard.seq           | TTTCAGCGTCAGCTCACTGGGCTTGTAAACCGACAGTGTACGAAAC   | 557  |

|                                       |  |      |
|---------------------------------------|--|------|
|                                       | 1210                    1220                    1230                    1240                    1250 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TGGA CAAGGAAT TGAAGAA GCCACT GGTCT CCCCCA GACAGT AGTCT GTT   | 1250 |
| AHR_Modern.seq                        | TGGA CAAGGAAT TGAAGAA GCCACT GGTCT CCCCCA GACAGT AGTCT GTT   | 1250 |
| AHR_Neanderthal.seq                   | TGGA CAAGGAAT TGAAGAA GCCACT GGTCT CCCCCA GACAGT AGTCT GTT   | 1250 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | TGGA CAAGGAAT TGAAGAA GCCACT GGTCT CCCCCA GACAGT AGTCT GTT   | 607  |
| AHR_Modern_Hubbard.seq                | GGG CA GGG AT T GAAGAA GC T AC GGG CT CCCCCA GAC GT GT T GT  | 607  |
| AHR_Neanderthal_Hubbard.seq           | GGG CA GGG AT T GAAGAA GC T AC GGG CT CCCCCA GAC GT GT T GT  | 607  |
|                                       | 1260                    1270                    1280                    1290                    1300 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | ATAA CCCA GACCAGATT CCTCCA GAAAAC TCTCCTT TAAT GGAGAGGT GC   | 1300 |
| AHR_Modern.seq                        | ATAA CCCA GACCAGATT CCTCCA GAAAAC TCTCCTT TAAT GGAGAGGT GC   | 1300 |
| AHR_Neanderthal.seq                   | ATAA CCCA GACCAGATT CCTCCA GAAAAC TCTCCTT TAAT GGAGAGGT GC   | 1300 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | ATAA CCCA GACCAGATT CCTCCA GAAAAC TCTCCTT TAAT GGAGAGGT GC   | 657  |
| AHR_Modern_Hubbard.seq                | A GAA CCC GAT T CAGAT T CC C C GAAAAC A C C C C T T AT GGA A C GGT GC                                | 657  |
| AHR_Neanderthal_Hubbard.seq           | A GAA CCC GAT T CAGAT T CC C C GAAAAC A C C C C T T AT GGA A C GGT GC                                | 657  |
|                                       | 1310                    1320                    1330                    1340                    1350 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TT CAT ATGTCGT CT AAGGT GT CT GCTGGA TAATT CATCTGGT TTTCTGGC   | 1350 |
| AHR_Modern.seq                        | TT CAT ATGTCGT CT AAGGT GT CT GCTGGA TAATT CATCTGGT TTTCTGGC   | 1350 |
| AHR_Neanderthal.seq                   | TT CAT ATGTCGT CT AAGGT GT CT GCTGGA TAATT CATCTGGT TTTCTGGC   | 1350 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | TT CAT ATGTCGT CT AAGGT GT CT GCTGGA TAATT CATCTGGT TTTCTGGC   | 707  |
| AHR_Modern_Hubbard.seq                | TT CAT T T G C G C T C C G G T G C T G C T G A T A A C A G A A C C G G T T T C T G G C               | 707  |
| AHR_Neanderthal_Hubbard.seq           | TT CAT T T G C G C T C C G G T G C T G C T G A T A A C A G A A C C G G T T T C T G G C               | 707  |
|                                       | 1360                    1370                    1380                    1390                    1400 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | AATGAA TTTCCAAGGGAAGTTAAAGTATCTT CATGGACAGAAAAAGAAAG   | 1400 |
| AHR_Modern.seq                        | AATGAA TTTCCAAGGGAAGTTAAAGTATCTT CATGGACAGAAAAAGAAAG   | 1400 |
| AHR_Neanderthal.seq                   | AATGAA TTTCCAAGGGAAGTTAAAGTATCTT CATGGACAGAAAAAGAAAG   | 1400 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | AATGAA TTTCCAAGGGAAGTTAAAGTATCTT CATGGACAGAAAAAGAAAG   | 757  |
| AHR_Modern_Hubbard.seq                | CATGAA TTTCCA GGG AAG T T AAGTA CT CA GGG CAGAAAAAGAAAG  | 757  |
| AHR_Neanderthal_Hubbard.seq           | CATGAA TTTCCA GGG AAG T T AAGTA CT CA GGG CAGAAAAAGAAAG  | 757  |
|                                       | 1410                    1420                    1430                    1440                    1450 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | GGAAAGAT GGATCAATACTTCCACCTCAGTTGGCTTTGTTTGCGATAGCT  | 1450 |
| AHR_Modern.seq                        | GGAAAGAT GGATCAATACTTCCACCTCAGTTGGCTTTGTTTGCGATAGCT  | 1450 |
| AHR_Neanderthal.seq                   | GGAAAGAT GGATCAATACTTCCACCTCAGTTGGCTTTGTTTGCGATAGCT  | 1450 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | GGAAAGAT GGATCAATACTTCCACCTCAGTTGGCTTTGTTTGCGATAGCT  | 807  |
| AHR_Modern_Hubbard.seq                | G G A A A G A T G G C A G A T C T C C C C C C C A G T G G C T T G T T G C G A T A G C T              | 807  |
| AHR_Neanderthal_Hubbard.seq           | G G A A A G A T G G C A G A T C T C C C C C C C A G T G G C T T G T T G C G A T A G C T              | 807  |
|                                       | 1460                    1470                    1480                    1490                    1500 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | ACTCCA CTTCAGCCACCATCCATACTTGAATCCGGACCAAAAAATTTTAT  | 1500 |
| AHR_Modern.seq                        | ACTCCA CTTCAGCCACCATCCATACTTGAATCCGGACCAAAAAATTTTAT  | 1500 |
| AHR_Neanderthal.seq                   | ACTCCA CTTCAGCCACCATCCATACTTGAATCCGGACCAAAAAATTTTAT  | 1500 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | ACTCCA CTTCAGCCACCATCCATACTTGAATCCGGACCAAAAAATTTTAT  | 857  |
| AHR_Modern_Hubbard.seq                | A C C C C C T C C A G C C C C C A G C A T C T C G A A A T C C G G A C C A A A A A T T T T A T        | 857  |
| AHR_Neanderthal_Hubbard.seq           | A C C C C C T C C A G C C C C C A G C A T C T C G A A A T C C G G A C C A A A A A T T T T A T        | 857  |
|                                       | 1510                    1520                    1530                    1540                    1550 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | C T T T A G A A C C A A A C A C A A A C T A G A C T T C A C A C C T A T T G G T T G T G A T G C C A  | 1550 |
| AHR_Modern.seq                        | C T T T A G A A C C A A A C A C A A A C T A G A C T T C A C A C C T A T T G G T T G T G A T G C C A  | 1550 |
| AHR_Neanderthal.seq                   | C T T T A G A A C C A A A C A C A A A C T A G A C T T C A C A C C T A T T G G T T G T G A T G C C A  | 1550 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | C T T T A G A A C C A A A C A C A A A C T A G A C T T C A C A C C T A T T G G T T G T G A T G C C A  | 907  |
| AHR_Modern_Hubbard.seq                | C T T G G A C C A A A C A C A A A C T G A C T T C A C C C A T G G G T G G A T G C T A                | 907  |
| AHR_Neanderthal_Hubbard.seq           | C T T G G A C C A A A C A C A A A C T G A C T T C A C C C A T G G G T G G A T G C T A                | 907  |
|                                       | 1560                    1570                    1580                    1590                    1600 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | AA GGAA GAAT TGT T T T A GGAT AT ACTGAA GCAGA GCTGTGCA CGAGAGGC                                      | 1600 |
| AHR_Modern.seq                        | AA GGAA GAAT TGT T T T A GGAT AT ACTGAA GCAGA GCTGTGCA CGAGAGGC                                      | 1600 |
| AHR_Neanderthal.seq                   | AA GGAA GAAT TGT T T T A GGAT AT ACTGAA GCAGA GCTGTGCA CGAGAGGC                                      | 1600 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | AA GGAA GAAT TGT T T T A GGAT AT ACTGAA GCAGA GCTGTGCA CGAGAGGC                                      | 957  |
| AHR_Modern_Hubbard.seq                | A A G G G G A T G T T T T A G G A T A T A C T G A A G C A G A G C T G T G C A C G A G A G G C        | 957  |
| AHR_Neanderthal_Hubbard.seq           | A A G G G G A T G T T T T A G G A T A T A C T G A A G C A G A G C T G T G C A C G A G A G G C        | 957  |
|                                       | 1610                    1620                    1630                    1640                    1650 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TCAGGT TATCAGTTTATTCATGCAGCTGATATGCTTTATTGTGCCGAGTC  | 1650 |
| AHR_Modern.seq                        | TCAGGT TATCAGTTTATTCATGCAGCTGATATGCTTTATTGTGCCGAGTC  | 1650 |
| AHR_Neanderthal.seq                   | TCAGGT TATCAGTTTATTCATGCAGCTGATATGCTTTATTGTGCCGAGTC  | 1650 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | TCAGGT TATCAGTTTATTCATGCAGCTGATATGCTTTATTGTGCCGAGTC  | 1007 |
| AHR_Modern_Hubbard.seq                | A C C G G T A C A G T T A T C A C G C T G C T G A T A T G C T T A T T G T G C C G A G A G C          | 1007 |
| AHR_Neanderthal_Hubbard.seq           | A C C G G T A C A G T T A T C A C G C T G C T G A T A T G C T T A T T G T G C C G A G A G C          | 1007 |

1660 1670 1680 1690 1700  
AHR\_002\_Hum\_ENST00000242057.8.seq CCATATCCGAATGATTAAGACTGGA GAAA GT GGCATGATAGTTTCCGGC 1700  
AHR\_Modern.seq CCATATCCGAATGATTAAGACTGGA GAAA GT GGCATGATAGTTTCCGGC 1700  
AHR\_Neanderthal.seq CCATATCCGAATGATTAAGACTGGA GAAA GT GGCATGATAGTTTCCGGC 1700  
AHR\_002\_Hum\_ENST00000242057.8\_CDS.seq CCGATCCGAATGATTAAGACTGGA GAAA GT GGCATGATAGTTTCCGGC 1057  
AHR\_Modern\_Hubbard.seq CCAATCCGATGATTAAGACTGGG GAAA GT GGCATGATAGTTTCCGGC 1057  
AHR\_Neanderthal\_Hubbard.seq CCAATCCGATGATTAAGACTGGG GAAA GT GGCATGATAGTTTCCGGC 1057

1710 1720 1730 1740 1750  
AHR\_002\_Hum\_ENST00000242057.8.seq TTCTTACAAAAAACACCGATGGACTTGGGTCCA GTCTAATGCACGCCTG 1750  
AHR\_Modern.seq TTCTTACAAAAAACACCGATGGACTTGGGTCCA GTCTAATGCACGCCTG 1750  
AHR\_Neanderthal.seq TTCTTACAAAAAACACCGATGGACTTGGGTCCA GTCTAATGCACGCCTG 1750  
AHR\_002\_Hum\_ENST00000242057.8\_CDS.seq TTCTTACAAAAAACACCGATGGACTTGGGTCCA GTCTAATGCACGCCTG 1107  
AHR\_Modern\_Hubbard.seq TCTTACAAAAAACACCGATGGACTTGGGTCCA GTCTAATGCACGCCTG 1107  
AHR\_Neanderthal\_Hubbard.seq TCTTACAAAAAACACCGATGGACTTGGGTCCA GTCTAATGCACGCCTG 1107

1760 1770 1780 1790 1800  
AHR\_002\_Hum\_ENST00000242057.8.seq CTTTATAAAAATGGAAGACCA GATTATATCATTGTA ACTCAGAGACCACT 1800  
AHR\_Modern.seq CTTTATAAAAATGGAAGACCA GATTATATCATTGTA ACTCAGAGACCACT 1800  
AHR\_Neanderthal.seq CTTTATAAAAATGGAAGACCA GATTATATCATTGTA ACTCAGAGACCACT 1800  
AHR\_002\_Hum\_ENST00000242057.8\_CDS.seq CTTTATAAAAATGGAAGACCA GATTATATCATTGTA ACTCAGAGACCACT 1157  
AHR\_Modern\_Hubbard.seq CTCTATAAAAATGGAAGACCA GATTATATCATTGTA ACTCAGAGACCACT 1157  
AHR\_Neanderthal\_Hubbard.seq CTCTATAAAAATGGAAGACCA GATTATATCATTGTA ACTCAGAGACCACT 1157

1810 1820 1830 1840 1850  
AHR\_002\_Hum\_ENST00000242057.8.seq AACAGATGAGGAAGGAA CA GGCATTTACGAAAACGAAATACGAAGTTGC 1850  
AHR\_Modern.seq AACAGATGAGGAAGGAA CA GGCATTTACGAAAACGAAATACGAAGTTGC 1850  
AHR\_Neanderthal.seq AACAGATGAGGAAGGAA CA GGCATTTACGAAAACGAAATACGAAGTTGC 1850  
AHR\_002\_Hum\_ENST00000242057.8\_CDS.seq AACAGATGAGGAAGGAA CA GGCATTTACGAAAACGAAATACGAAGTTGC 1207  
AHR\_Modern\_Hubbard.seq GACGATGAGGAAGGAA CA GGCATTTACGAAAACGAAATACGAAGTTGC 1207  
AHR\_Neanderthal\_Hubbard.seq GACGATGAGGAAGGAA CA GGCATTTACGAAAACGAAATACGAAGTTGC 1207

1860 1870 1880 1890 1900  
AHR\_002\_Hum\_ENST00000242057.8.seq CTTTTATGTTTACCCTGGAGAA GCTGTGTTGATGAGGCAACCAACCT 1900  
AHR\_Modern.seq CTTTTATGTTTACCCTGGAGAA GCTGTGTTGATGAGGCAACCAACCT 1900  
AHR\_Neanderthal.seq CTTTTATGTTTACCCTGGAGAA GCTGTGTTGATGAGGCAACCAACCT 1900  
AHR\_002\_Hum\_ENST00000242057.8\_CDS.seq CTTTTATGTTTACCCTGGAGAA GCTGTGTTGATGAGGCAACCAACCT 1257  
AHR\_Modern\_Hubbard.seq CTTTATGTTTACCCTGGAGAA GCTGTGTTGATGAGGCAACCAACCT 1257  
AHR\_Neanderthal\_Hubbard.seq CTTTATGTTTACCCTGGAGAA GCTGTGTTGATGAGGCAACCAACCT 1257

1910 1920 1930 1940 1950  
AHR\_002\_Hum\_ENST00000242057.8.seq TTTCCCTGCCATAATGGATCCCCTTACCACTAAGGACTAAAAATGGCACTAG 1950  
AHR\_Modern.seq TTTCCCTGCCATAATGGATCCCCTTACCACTAAGGACTAAAAATGGCACTAG 1950  
AHR\_Neanderthal.seq TTTCCCTGCCATAATGGATCCCCTTACCACTAAGGACTAAAAATGGCACTAG 1950  
AHR\_002\_Hum\_ENST00000242057.8\_CDS.seq TTTCCCTGCCATAATGGATCCCCTTACCACTAAGGACTAAAAATGGCACTAG 1307  
AHR\_Modern\_Hubbard.seq TTTCCCTGCCATAATGGATCCCCTTACCACTAAGGACTAAAAATGGCACTAG 1307  
AHR\_Neanderthal\_Hubbard.seq TTTCCCTGCCATAATGGATCCCCTTACCACTAAGGACTAAAAATGGCACTAG 1307

1960 1970 1980 1990 2000  
AHR\_002\_Hum\_ENST00000242057.8.seq TGGAAAAGACTCTGCTACCACATCCACTCTAAGCAA GGACTCTCTCAATC 2000  
AHR\_Modern.seq TGGAAAAGACTCTGCTACCACATCCACTCTAAGCAA GGACTCTCTCAATC 2000  
AHR\_Neanderthal.seq TGGAAAAGACTCTGCTACCACATCCACTCTAAGCAA GGACTCTCTCAATC 2000  
AHR\_002\_Hum\_ENST00000242057.8\_CDS.seq TGGAAAAGACTCTGCTACCACATCCACTCTAAGCAA GGACTCTCTCAATC 1357  
AHR\_Modern\_Hubbard.seq GGGAAAAGACTCTGCTACCACATCCACTCTAAGCAA GGACTCTCTCAATC 1357  
AHR\_Neanderthal\_Hubbard.seq GGGAAAAGACTCTGCTACCACATCCACTCTAAGCAA GGACTCTCTCAATC 1357

2010 2020 2030 2040 2050  
AHR\_002\_Hum\_ENST00000242057.8.seq CTAGTTCCTCCTGGCTGCCATGATGCAA CAAGATGAGTCTATTATCTC 2050  
AHR\_Modern.seq CTAGTTCCTCCTGGCTGCCATGATGCAA CAAGATGAGTCTATTATCTC 2050  
AHR\_Neanderthal.seq CTAGTTCCTCCTGGCTGCCATGATGCAA CAAGATGAGTCTATTATCTC 2050  
AHR\_002\_Hum\_ENST00000242057.8\_CDS.seq CTAGTTCCTCCTGGCTGCCATGATGCAA CAAGATGAGTCTATTATCTC 1407  
AHR\_Modern\_Hubbard.seq CAGCAACCTCCTGGCTGCCATGATGCAA CAAGATGAGTCTATTATCTC 1407  
AHR\_Neanderthal\_Hubbard.seq CAGCAACCTCCTGGCTGCCATGATGCAA CAAGATGAGTCTATTATCTC 1407

2060 2070 2080 2090 2100  
AHR\_002\_Hum\_ENST00000242057.8.seq TATCCTGCTTCAAGTACTTCAAGTACTGCACCTTTT GAAAACAACCTTTT 2100  
AHR\_Modern.seq TATCCTGCTTCAAGTACTTCAAGTACTGCACCTTTT GAAAACAACCTTTT 2100  
AHR\_Neanderthal.seq TATCCTGCTTCAAGTACTTCAAGTACTGCACCTTTT GAAAACAACCTTTT 2100  
AHR\_002\_Hum\_ENST00000242057.8\_CDS.seq TATCCTGCTTCAAGTACTTCAAGTACTGCACCTTTT GAAAACAACCTTTT 1457  
AHR\_Modern\_Hubbard.seq TATCCTGCTTCAAGTACTTCAAGTACTGCACCTTTT GAAAACAACCTTTT 1457  
AHR\_Neanderthal\_Hubbard.seq TATCCTGCTTCAAGTACTTCAAGTACTGCACCTTTT GAAAACAACCTTTT 1457

|                                       |  |      |      |      |      |      |
|---------------------------------------|--|------|------|------|------|------|
|                                       | 210  | 2120 | 2130 | 2140 | 2150 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | CAACGAATCTATGAATGAATGCAGAAATTTGGCAAATAACTGCAACCGA  |      |      |      |      | 2150 |
| AHR_Modern.seq                        | CAACGAATCTATGAATGAATGCAGAAATTTGGCAAATAACTGCAACCGA  |      |      |      |      | 2150 |
| AHR_Neanderthal.seq                   | CAACGAATCTATGAATGAATGCAGAAATTTGGCAAATAACTGCAACCGA  |      |      |      |      | 2150 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | CAACGAATCTATGAATGAATGCAGAAATTTGGCAAATAACTGCAACCGA  |      |      |      |      | 1507 |
| AHR_Modern_Hubbard.seq                | CAACGAAAGGATGAAAGAAATGCGGAACTGGCAAGATAAACGCCTCA    |      |      |      |      | 1507 |
| AHR_Neanderthal_Hubbard.seq           | CAACGAAAGGATGAAAGAAATGCGGAACTGGCAAGATAAACGCCTCA    |      |      |      |      | 1507 |
|                                       |  |      |      |      |      |      |
|                                       | 2160   | 2170 | 2180 | 2190 | 2200 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TGGGAAATGATACTATCCTGAAACATGAGCAAATTGACCAGCCTCAGGAT |      |      |      |      | 2200 |
| AHR_Modern.seq                        | TGGGAAATGATACTATCCTGAAACATGAGCAAATTGACCAGCCTCAGGAT |      |      |      |      | 2200 |
| AHR_Neanderthal.seq                   | TGGGAAATGATACTATCCTGAAACATGAGCAAATTGACCAGCCTCAGGAT |      |      |      |      | 2200 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | TGGGAAATGATACTATCCTGAAACATGAGCAAATTGACCAGCCTCAGGAT |      |      |      |      | 1557 |
| AHR_Modern_Hubbard.seq                | TGGGAAAGATACATCCTGAAACAAGAGCAGATGACCAGCCCAAGGAT    |      |      |      |      | 1557 |
| AHR_Neanderthal_Hubbard.seq           | TGGGAAAGATACATCCTGAAACAAGAGCAGATGACCAGCCCAAGGAT    |      |      |      |      | 1557 |
|                                       |  |      |      |      |      |      |
|                                       | 2210   | 2220 | 2230 | 2240 | 2250 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | GTGAACATCATTTGCTGGAGGTCACCAGGGCTCTTTCAAGATAGTAAAAA |      |      |      |      | 2250 |
| AHR_Modern.seq                        | GTGAACATCATTTGCTGGAGGTCACCAGGGCTCTTTCAAGATAGTAAAAA |      |      |      |      | 2250 |
| AHR_Neanderthal.seq                   | GTGAACATCATTTGCTGGAGGTCACCAGGGCTCTTTCAAGATAGTAAAAA |      |      |      |      | 2250 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | GTGAACATCATTTGCTGGAGGTCACCAGGGCTCTTTCAAGATAGTAAAAA |      |      |      |      | 1607 |
| AHR_Modern_Hubbard.seq                | GTGAACATCATTTGCTGGAGGTCACCAGGGCTCTTTCAAGATAGTAAAAA |      |      |      |      | 1607 |
| AHR_Neanderthal_Hubbard.seq           | GTGAACATCATTTGCTGGAGGTCACCAGGGCTCTTTCAAGATAGTAAAAA |      |      |      |      | 1607 |
|                                       |  |      |      |      |      |      |
|                                       | 2260   | 2270 | 2280 | 2290 | 2300 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | CAGTGACTTGTAACGATAAATAAAAACTTAGGCATTGATTTTGAAAGACA |      |      |      |      | 2300 |
| AHR_Modern.seq                        | CAGTGACTTGTAACGATAAATAAAAACTTAGGCATTGATTTTGAAAGACA |      |      |      |      | 2300 |
| AHR_Neanderthal.seq                   | CAGTGACTTGTAACGATAAATAAAAACTTAGGCATTGATTTTGAAAGACA |      |      |      |      | 2300 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | CAGTGACTTGTAACGATAAATAAAAACTTAGGCATTGATTTTGAAAGACA |      |      |      |      | 1657 |
| AHR_Modern_Hubbard.seq                | CAGGACCTTGTAACGATGATGAAAACTTAGGCATTGATTTTGAAAGACA  |      |      |      |      | 1657 |
| AHR_Neanderthal_Hubbard.seq           | CAGGACCTTGTAACGATGATGAAAACTTAGGCATTGATTTTGAAAGACA  |      |      |      |      | 1657 |
|                                       |  |      |      |      |      |      |
|                                       | 2310   | 2320 | 2330 | 2340 | 2350 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TCAGACACATGCAGAAAGAAAAATTTTCAGAAATGATTTTCTGGTGAG   |      |      |      |      | 2350 |
| AHR_Modern.seq                        | TCAGACACATGCAGAAAGAAAAATTTTCAGAAATGATTTTCTGGTGAG   |      |      |      |      | 2350 |
| AHR_Neanderthal.seq                   | TCAGACACATGCAGAAAGAAAAATTTTCAGAAATGATTTTCTGGTGAG   |      |      |      |      | 2350 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | TCAGACACATGCAGAAAGAAAAATTTTCAGAAATGATTTTCTGGTGAG   |      |      |      |      | 1707 |
| AHR_Modern_Hubbard.seq                | TCAGACACATGCAGAAAGAAAAATTTTCAGAAATGATTTTCTGGTGAG   |      |      |      |      | 1707 |
| AHR_Neanderthal_Hubbard.seq           | TCAGACACATGCAGAAAGAAAAATTTTCAGAAATGATTTTCTGGTGAG   |      |      |      |      | 1707 |
|                                       |  |      |      |      |      |      |
|                                       | 2360   | 2370 | 2380 | 2390 | 2400 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | GTTGACTTCAGAGACATGACTTAAACGGATGAAATCCTGACGATGTCCTA |      |      |      |      | 2400 |
| AHR_Modern.seq                        | GTTGACTTCAGAGACATGACTTAAACGGATGAAATCCTGACGATGTCCTA |      |      |      |      | 2400 |
| AHR_Neanderthal.seq                   | GTTGACTTCAGAGACATGACTTAAACGGATGAAATCCTGACGATGTCCTA |      |      |      |      | 2400 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | GTTGACTTCAGAGACATGACTTAAACGGATGAAATCCTGACGATGTCCTA |      |      |      |      | 1757 |
| AHR_Modern_Hubbard.seq                | GTTGACTTCAGAGACATGACTTAAACGGATGAAATCCTGACGATGTCCTA |      |      |      |      | 1757 |
| AHR_Neanderthal_Hubbard.seq           | GTTGACTTCAGAGACATGACTTAAACGGATGAAATCCTGACGATGTCCTA |      |      |      |      | 1757 |
|                                       |  |      |      |      |      |      |
|                                       | 2410   | 2420 | 2430 | 2440 | 2450 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | AGATTCTTTAAGTAAGTCTCCCTTCATACCTTCAGATTATCAACAGCAAC |      |      |      |      | 2450 |
| AHR_Modern.seq                        | AGATTCTTTAAGTAAGTCTCCCTTCATACCTTCAGATTATCAACAGCAAC |      |      |      |      | 2450 |
| AHR_Neanderthal.seq                   | AGATTCTTTAAGTAAGTCTCCCTTCATACCTTCAGATTATCAACAGCAAC |      |      |      |      | 2450 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | AGATTCTTTAAGTAAGTCTCCCTTCATACCTTCAGATTATCAACAGCAAC |      |      |      |      | 1807 |
| AHR_Modern_Hubbard.seq                | GGATAGCCTTGAAGAAAGCCCTTCATCCAGAGGATTAACAACAGCAAC   |      |      |      |      | 1807 |
| AHR_Neanderthal_Hubbard.seq           | GGATAGCCTTGAAGAAAGCCCTTCATCCAGAGGATTAACAACAGCAAC   |      |      |      |      | 1807 |
|                                       |  |      |      |      |      |      |
|                                       | 2460   | 2470 | 2480 | 2490 | 2500 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | AGTCCTTGGCTCTGAACTCAAAGCTGATGGTACAGGAAACCTACATCTA  |      |      |      |      | 2500 |
| AHR_Modern.seq                        | AGTCCTTGGCTCTGAACTCAAAGCTGATGGTACAGGAAACCTACATCTA  |      |      |      |      | 2500 |
| AHR_Neanderthal.seq                   | AGTCCTTGGCTCTGAACTCAAAGCTGATGGTACAGGAAACCTACATCTA  |      |      |      |      | 2500 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | AGTCCTTGGCTCTGAACTCAAAGCTGATGGTACAGGAAACCTACATCTA  |      |      |      |      | 1857 |
| AHR_Modern_Hubbard.seq                | AGATSCCTGGCTCTGAACAAGAGCTGATGGTACAGGAAACCTACATCTE  |      |      |      |      | 1857 |
| AHR_Neanderthal_Hubbard.seq           | AGATSCCTGGCTCTGAACAAGAGCTGATGGTACAGGAAACCTACATCTE  |      |      |      |      | 1857 |
|                                       |  |      |      |      |      |      |
|                                       | 2510   | 2520 | 2530 | 2540 | 2550 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | GAACAGCAACAGCAACATCACAAAAGCAAGTAGTAGTGGAGCCACAGCA  |      |      |      |      | 2550 |
| AHR_Modern.seq                        | GAACAGCAACAGCAACATCACAAAAGCAAGTAGTAGTGGAGCCACAGCA  |      |      |      |      | 2550 |
| AHR_Neanderthal.seq                   | GAACAGCAACAGCAACATCACAAAAGCAAGTAGTAGTGGAGCCACAGCA  |      |      |      |      | 2550 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq | GAACAGCAACAGCAACATCACAAAAGCAAGTAGTAGTGGAGCCACAGCA  |      |      |      |      | 1907 |
| AHR_Modern_Hubbard.seq                | GAACAGCAACAGCAACATCACCAAGCAAGTAGTAGTGGAGCCACAGCA   |      |      |      |      | 1907 |
| AHR_Neanderthal_Hubbard.seq           | GAACAGCAACAGCAACATCACCAAGCAAGTAGTAGTGGAGCCACAGCA   |      |      |      |      | 1907 |

|   |   |
|---|---|
| <p>AHR_002_Hum_ENST00000242057.8.seq<br/> AHR_Modern.seq<br/> AHR_Neanderthal.seq<br/> AHR_002_Hum_ENST00000242057.8_CDS.seq<br/> AHR_Modern_Hubbard.seq<br/> AHR_Neanderthal_Hubbard.seq</p> | <pre> 2560      2570      2580      2590      2600 ACAGCTGTGTCA GAAGATGAA GCACATGCAA GTTAA TGGCATGTTT GAAA 2600 ACAGCTGTGTCA GAAGATGAA GCACATGCAA GTTAA TGGCATGTTT GAAA 2600 ACAGCTGTGTCA GAAGATGAA GCACATGCAA GTTAA TGGCATGTTT GAAA 2600 ACAGCTGTGTCA GAAGATGAA GCACATGCAA GTTAA TGGCATGTTT GAAA 1957 G CAGCTGTG G CA GAAGATGAA GCACATGCA GT GAA GGCATGTT GAAA 1957 G CAGCTGTG G CA GAAGATGAA GCACATGCA GT GAA GGCATGTT GAAA 1957 </pre>   |
| <p>AHR_002_Hum_ENST00000242057.8.seq<br/> AHR_Modern.seq<br/> AHR_Neanderthal.seq<br/> AHR_002_Hum_ENST00000242057.8_CDS.seq<br/> AHR_Modern_Hubbard.seq<br/> AHR_Neanderthal_Hubbard.seq</p> | <pre> 2610      2620      2630      2640      2650 ATTGGA ACTCTA ACCAATT CGTGCCTT TCAA TTGTCCA CAGCAA GACCCA 2650 ATTGGA ACTCTA ACCAATT CGTGCCTT TCAA TTGTCCA CAGCAA GACCCA 2650 ATTGGA ACTCTA ACCAATT CGTGCCTT TCAA TTGTCCA CAGCAA GACCCA 2650 ATTGGA ACTCTA ACCAATT CGTGCCTT TCAA TTGTCCA CAGCAA GACCCA 2007 A TTGGAAC A GCAACCA ATT CGTGCCT TCAA GTGCC CAGCA GACCC 2007 A TTGGAAC A GCAACCA ATT CGTGCCT TCAA GTGCC CAGCA GACCC 2007 </pre>   |
| <p>AHR_002_Hum_ENST00000242057.8.seq<br/> AHR_Modern.seq<br/> AHR_Neanderthal.seq<br/> AHR_002_Hum_ENST00000242057.8_CDS.seq<br/> AHR_Modern_Hubbard.seq<br/> AHR_Neanderthal_Hubbard.seq</p> | <pre> 2660      2670      2680      2690      2700 CAACAA TATAAT GTCTT TACA GACTTACA TGGGATCAGTCAA GAGT TCCC 2700 CAACAA TATAAT GTCTT TACA GACTTACA TGGGATCAGTCAA GAGT TCCC 2700 CAACAA TATAAT GTCTT TACA GACTTACA TGGGATCAGTCAA GAGT TCCC 2700 CAACAA TATAAT GTCTT TACA GACTTACA TGGGATCAGTCAA GAGT TCCC 2057 CA GCACTA GAA GTT T CAC GA T T CCA GGCATCAG CAGAGT TCCC 2057 CA GCACTA GAA GTT T CAC GA T T CCA GGCATCAG CAGAGT TCCC 2057 </pre>   |
| <p>AHR_002_Hum_ENST00000242057.8.seq<br/> AHR_Modern.seq<br/> AHR_Neanderthal.seq<br/> AHR_002_Hum_ENST00000242057.8_CDS.seq<br/> AHR_Modern_Hubbard.seq<br/> AHR_Neanderthal_Hubbard.seq</p> | <pre> 2710      2720      2730      2740      2750 CTACAA ATCTGAA ATGGAT TCTATG CCTTATAC ACA GAAC TTTATTT CCT 2750 CTACAA ATCTGAA ATGGAT TCTATG CCTTATAC ACA GAAC TTTATTT CCT 2750 CTACAA ATCTGAA ATGGAT TCTATG CCTTATAC ACA GAAC TTTATTT CCT 2750 CTACAA ATCTGAA ATGGAT TCTATG CCTTATAC ACA GAAC TTTATTT CCT 2107 CTACAAA A G GAA ATGGAT A GATGCC TAA ACC CAGAACTT AT G A GCT 2107 CTACAAA A G GAA ATGGAT A GATGCC TAA ACC CAGAACTT AT G A GCT 2107 </pre>                                     |
| <p>AHR_002_Hum_ENST00000242057.8.seq<br/> AHR_Modern.seq<br/> AHR_Neanderthal.seq<br/> AHR_002_Hum_ENST00000242057.8_CDS.seq<br/> AHR_Modern_Hubbard.seq<br/> AHR_Neanderthal_Hubbard.seq</p> | <pre> 2760      2770      2780      2790      2800 GTAATCAG CCTGTA TTA CCACAA CATTCCA AATGTACA GAGCTGGACTAC 2800 GTAATCAG CCTGTA TTA CCACAA CATTCCA AATGTACA GAGCTGGACTAC 2800 GTAATCAG CCTGTA TTA CCACAA CATTCCA AATGTACA GAGCTGGACTAC 2800 GTAATCAG CCTGTA TTA CCACAA CATTCCA AATGTACA GAGCTGGACTAC 2157 G AA CAGCC CGT G T C C C CA CA CA GCAAATG C A C GAGCTGGA T TAC 2157 G AA CAGCC CGT G T C C C CA CA CA GCAAATG C A C GAGCTGGA T TAC 2157 </pre>                                       |
| <p>AHR_002_Hum_ENST00000242057.8.seq<br/> AHR_Modern.seq<br/> AHR_Neanderthal.seq<br/> AHR_002_Hum_ENST00000242057.8_CDS.seq<br/> AHR_Modern_Hubbard.seq<br/> AHR_Neanderthal_Hubbard.seq</p> | <pre> 2810      2820      2830      2840      2850 CCTATG GGGAGT TTTG AACCA TCCCA TACCCCA CTACTTCTAG TT TAGA 2850 CCTATG GGGAGT TTTG AACCA TCCCA TACCCCA CTACTTCTAG TT TAGA 2850 CCTATG GGGAGT TTTG AACCA TCCCA TACCCCA CTACTTCTAG TT TAGA 2850 CCTATG GGGAGT TTTG AACCA TCCCA TACCCCA CTACTTCTAG TT TAGA 2207 CCATG GCGAG GTT GAACC A G C C C C T A C C C C A C A C A G A G T T G A 2207 CCATG GCGAG GTT GAACC A G C C C C T A C C C C A C A C A G A G T T G A 2207 </pre>                     |
| <p>AHR_002_Hum_ENST00000242057.8.seq<br/> AHR_Modern.seq<br/> AHR_Neanderthal.seq<br/> AHR_002_Hum_ENST00000242057.8_CDS.seq<br/> AHR_Modern_Hubbard.seq<br/> AHR_Neanderthal_Hubbard.seq</p> | <pre> 2860      2870      2880      2890      2900 AGATTTT GTCACTT GTTTACA ACTTCTG AAAACCAA AAGCATGGATTAA 2900 AGATTTT GTCACTT GTTTACA ACTTCTG AAAACCAA AAGCATGGATTAA 2900 AGATTTT GTCACTT GTTTACA ACTTCTG AAAACCAA AAGCATGGATTAA 2900 AGATTTT GTCACTT GTTTACA ACTTCTG AAAACCAA AAGCATGGATTAA 2257 AGATTT TGTCACTT GTTTACA ACTTCTG AAAACCAA AAGCATGGATTAA 2257 AGATTT TGTCACTT GTTTACA ACTTCTG AAAACCAA AAGCATGGATTAA 2257 </pre>   |
| <p>AHR_002_Hum_ENST00000242057.8.seq<br/> AHR_Modern.seq<br/> AHR_Neanderthal.seq<br/> AHR_002_Hum_ENST00000242057.8_CDS.seq<br/> AHR_Modern_Hubbard.seq<br/> AHR_Neanderthal_Hubbard.seq</p> | <pre> 2910      2920      2930      2940      2950 ATCCACAG TCAGCCATAATA AACTCCTCAGACATGTTATGCTGGGGCCGTG 2950 ATCCACAG TCAGCCATAATA AACTCCTCAGACATGTTATGCTGGGGCCGTG 2950 ATCCACAG TCAGCCATAATA AACTCCTCAGACATGTTATGCTGGGGCCGTG 2950 ATCCACAG TCAGCCATAATA AACTCCTCAGACATGTTATGCTGGGGCCGTG 2307 A C C C A G A G C G C T A T A T A C C C C A G A C T G T A G C T G G G C T G T G 2307 A C C C A G A G C G C T A T A T A C C C C A G A C T G T A G C T G G G C T G T G 2307 </pre>                 |
| <p>AHR_002_Hum_ENST00000242057.8.seq<br/> AHR_Modern.seq<br/> AHR_Neanderthal.seq<br/> AHR_002_Hum_ENST00000242057.8_CDS.seq<br/> AHR_Modern_Hubbard.seq<br/> AHR_Neanderthal_Hubbard.seq</p> | <pre> 2960      2970      2980      2990      3000 TCGATG TATCAGTGCCA GCCA GAACCTCAGCACA CCA CGTGGGTCAGAT 3000 TCGATG TATCAGTGCCA GCCA GAACCTCAGCACA CCA CGTGGGTCAGAT 3000 TCGATG TATCAGTGCCA GCCA GAACCTCAGCACA CCA CGTGGGTCAGAT 3000 TCGATG TATCAGTGCCA GCCA GAACCTCAGCACA CCA CGTGGGTCAGAT 2357 A C C A T G T A C A G T G C C G C C G A A C C C A G C A C C C A C G T G G G C A G A T 2357 A C C A T G T A C A G T G C C G C C G A A C C C A G C A C C C A C G T G G G C A G A T 2357 </pre> |



3010 3020 3030 3040 3050

AHR\_002\_Hum\_ENST00000242057.8.seq GCAGTACAATCCAGTACTGCCAGGCCAACAGGCATTTTAAACAAGTTTC 3050  
 AHR\_Modern.seq GCAGTACAATCCAGTACTGCCAGGCCAACAGGCATTTTAAACAAGTTTC 3050  
 AHR\_Neanderthal.seq GCAGTACAATCCAGTACTGCCAGGCCAACAGGCATTTTAAACAAGTTTC 3050  
 AHR\_002\_Hum\_ENST00000242057.8\_CDS.seq GCAGTACAATCCAGTACTGCCAGGCCAACAGGCATTTTAAACAAGTTTC 2407  
 AHR\_Modern\_Hubbard.seq GCAGTACAACCCGTCTGCCGGCCAACAGGCATTCTTAAACAAGTTTC 2407  
 AHR\_Neanderthal\_Hubbard.seq GCAGTACAACCCGTCTGCCGGCCAACAGGCATTCTTAAACAAGTTTC 2407

3060 3070 3080 3090 3100

AHR\_002\_Hum\_ENST00000242057.8.seq AGAATGGAGTTTTAAATGAAACATATCCAAGCTGAATTAATAACATAAAT 3100  
 AHR\_Modern.seq AGAATGGAGTTTTAAATGAAACATATCCAAGCTGAATTAATAACATAAAT 3100  
 AHR\_Neanderthal.seq AGAATGGAGTTTTAAATGAAACATATCCAAGCTGAATTAATAACATAAAT 3100  
 AHR\_002\_Hum\_ENST00000242057.8\_CDS.seq AGAATGGAGTTTTAAATGAAACATATCCAAGCTGAATTAATAACATAAAT 2457  
 AHR\_Modern\_Hubbard.seq AGAAGGCGTCTTAAAGAAACATATCCAAGCTGAATTAATAACATAAAT 2457  
 AHR\_Neanderthal\_Hubbard.seq AGAAGGCGTCTTAAAGAAACATATCCAAGCTGAATTAATAACATAAAT 2457

3110 3120 3130 3140 3150

AHR\_002\_Hum\_ENST00000242057.8.seq AACACTCAGACTACCACACATCTTCAGCCACTTCATCATCCGTCAGAAAC 3150  
 AHR\_Modern.seq AACACTCAGACTACCACACATCTTCAGCCACTTCATCATCCGTCAGAAAC 3150  
 AHR\_Neanderthal.seq AACACTCAGACTACCACACATCTTCAGCCACTTCATCATCCGTCAGAAAC 3150  
 AHR\_002\_Hum\_ENST00000242057.8\_CDS.seq AACACTCAGACTACCACACATCTTCAGCCACTTCATCATCCGTCAGAAAC 2507  
 AHR\_Modern\_Hubbard.seq AACACTCAGACTACCACACATCTTCAGCCACTTCATCATCCGTCAGAAAC 2507  
 AHR\_Neanderthal\_Hubbard.seq AACACTCAGACTACCACACATCTTCAGCCACTTCATCATCCGTCAGAAAC 2507

3160 3170 3180 3190 3200

AHR\_002\_Hum\_ENST00000242057.8.seq CAGACCTTTTCTGATTTGACATCCAGTGGATTCTGTAAATCCAAAGCCC 3200  
 AHR\_Modern.seq CAGACCTTTTCTGATTTGACATCCAGTGGATTCTGTAAATCCAAAGCCC 3200  
 AHR\_Neanderthal.seq CAGACCTTTTCTGATTTGACATCCAGTGGATTCTGTAAATCCAAAGCCC 3200  
 AHR\_002\_Hum\_ENST00000242057.8\_CDS.seq CAGACCTTTTCTGATTTGACATCCAGTGGATTCTGTAAATCCAAAGCCC 2547  
 AHR\_Modern\_Hubbard.seq TGGCCCTTTCTGATTTGACATCCAGTGGATTCTGTAAATCCAAAGCCC 2547  
 AHR\_Neanderthal\_Hubbard.seq TGGCCCTTTCTGATTTGACATCCAGTGGATTCTGTAAATCCAAAGCCC 2547

3210 3220 3230 3240 3250

AHR\_002\_Hum\_ENST00000242057.8.seq AATTTTGACCTGGTTTTGGATTAATTAAGTTTGTGAAGGATTATGGAA 3250  
 AHR\_Modern.seq AATTTTGACCTGGTTTTGGATTAATTAAGTTTGTGAAGGATTATGGAA 3250  
 AHR\_Neanderthal.seq AATTTTGACCTGGTTTTGGATTAATTAAGTTTGTGAAGGATTATGGAA 3250  
 AHR\_002\_Hum\_ENST00000242057.8\_CDS.seq AATTTTGACCTGGTTTTGGATTAATTAAGTTTGTGAAGGATTATGGAA 2547  
 AHR\_Modern\_Hubbard.seq AATTTTGACCTGGTTTTGGATTAATTAAGTTTGTGAAGGATTATGGAA 2547  
 AHR\_Neanderthal\_Hubbard.seq AATTTTGACCTGGTTTTGGATTAATTAAGTTTGTGAAGGATTATGGAA 2547

3260 3270 3280 3290 3300

AHR\_002\_Hum\_ENST00000242057.8.seq AAATAAAAGTCACTGTTGGACGTCAAGCAAGTTTCAATGGAAGGCAATTGA 3300  
 AHR\_Modern.seq AAATAAAAGTCACTGTTGGACGTCAAGCAAGTTTCAATGGAAGGCAATTGA 3300  
 AHR\_Neanderthal.seq AAATAAAAGTCACTGTTGGACGTCAAGCAAGTTTCAATGGAAGGCAATTGA 3300  
 AHR\_002\_Hum\_ENST00000242057.8\_CDS.seq AAATAAAAGTCACTGTTGGACGTCAAGCAAGTTTCAATGGAAGGCAATTGA 2547  
 AHR\_Modern\_Hubbard.seq AAATAAAAGTCACTGTTGGACGTCAAGCAAGTTTCAATGGAAGGCAATTGA 2547  
 AHR\_Neanderthal\_Hubbard.seq AAATAAAAGTCACTGTTGGACGTCAAGCAAGTTTCAATGGAAGGCAATTGA 2547

3310 3320 3330 3340 3350

AHR\_002\_Hum\_ENST00000242057.8.seq TGCATGCTATTCACAATTAATCCAAACCAAAATTTTAAATTTTTCGTTTTAG 3350  
 AHR\_Modern.seq TGCATGCTATTCACAATTAATCCAAACCAAAATTTTAAATTTTTCGTTTTAG 3350  
 AHR\_Neanderthal.seq TGCATGCTATTCACAATTAATCCAAACCAAAATTTTAAATTTTTCGTTTTAG 3350  
 AHR\_002\_Hum\_ENST00000242057.8\_CDS.seq TGCATGCTATTCACAATTAATCCAAACCAAAATTTTAAATTTTTCGTTTTAG 2547  
 AHR\_Modern\_Hubbard.seq TGCATGCTATTCACAATTAATCCAAACCAAAATTTTAAATTTTTCGTTTTAG 2547  
 AHR\_Neanderthal\_Hubbard.seq TGCATGCTATTCACAATTAATCCAAACCAAAATTTTAAATTTTTCGTTTTAG 2547

3360 3370 3380 3390 3400

AHR\_002\_Hum\_ENST00000242057.8.seq AAAAGGGAGTTAAAAATGGTATCAAAATACATATACTACAGTCAAGAT 3400  
 AHR\_Modern.seq AAAAGGGAGTTAAAAATGGTATCAAAATACATATACTACAGTCAAGAT 3400  
 AHR\_Neanderthal.seq AAAAGGGAGTTAAAAATGGTATCAAAATACATATACTACAGTCAAGAT 3400  
 AHR\_002\_Hum\_ENST00000242057.8\_CDS.seq AAAAGGGAGTTAAAAATGGTATCAAAATACATATACTACAGTCAAGAT 2547  
 AHR\_Modern\_Hubbard.seq AAAAGGGAGTTAAAAATGGTATCAAAATACATATACTACAGTCAAGAT 2547  
 AHR\_Neanderthal\_Hubbard.seq AAAAGGGAGTTAAAAATGGTATCAAAATACATATACTACAGTCAAGAT 2547

3410 3420 3430 3440 3450

AHR\_002\_Hum\_ENST00000242057.8.seq AGAAAGGGTGTGCCACGGAGTGGTGAAGTACCGTCTACATTCACATTA 3450  
 AHR\_Modern.seq AGAAAGGGTGTGCCACGGAGTGGTGAAGTACCGTCTACATTCACATTA 3450  
 AHR\_Neanderthal.seq AGAAAGGGTGTGCCACGGAGTGGTGAAGTACCGTCTACATTCACATTA 3450  
 AHR\_002\_Hum\_ENST00000242057.8\_CDS.seq AGAAAGGGTGTGCCACGGAGTGGTGAAGTACCGTCTACATTCACATTA 2547  
 AHR\_Modern\_Hubbard.seq AGAAAGGGTGTGCCACGGAGTGGTGAAGTACCGTCTACATTCACATTA 2547  
 AHR\_Neanderthal\_Hubbard.seq AGAAAGGGTGTGCCACGGAGTGGTGAAGTACCGTCTACATTCACATTA 2547

|                                       |   |      |      |      |      |      |
|---------------------------------------|---|------|------|------|------|------|
|                                       | 3460  | 3470 | 3480 | 3490 | 3500 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TTCTGGGCACCACAAAAATATACAAAACCTTATCAGGGAAACTAAGATTCT |      |      |      |      | 3500 |
| AHR_Modern.seq                        | TTCTGGGCACCACAAAAATATACAAAACCTTATCAGGGAAACTAAGATTCT |      |      |      |      | 3500 |
| AHR_Neanderthal.seq                   | TTCTGGGCACCACAAAAATATACAAAACCTTATCAGGGAAACTAAGATTCT |      |      |      |      | 3500 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |   |      |      |      |      | 2547 |
| AHR_Modern_Hubbard.seq                |   |      |      |      |      | 2547 |
| AHR_Neanderthal_Hubbard.seq           |   |      |      |      |      | 2547 |

|                                       |  |      |      |      |      |      |
|---------------------------------------|--|------|------|------|------|------|
|                                       | 3510   | 3520 | 3530 | 3540 | 3550 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TTTAAATTAGAAAAATTTCTCTATTTGAATTATTTCTGTCACAGTAAAAA |      |      |      |      | 3550 |
| AHR_Modern.seq                        | TTTAAATTAGAAAAATTTCTCTATTTGAATTATTTCTGTCACAGTAAAAA |      |      |      |      | 3550 |
| AHR_Neanderthal.seq                   | TTTAAATTAGAAAAATTTCTCTATTTGAATTATTTCTGTCACAGTAAAAA |      |      |      |      | 3550 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  |      |      |      |      | 2547 |
| AHR_Modern_Hubbard.seq                |  |      |      |      |      | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  |      |      |      |      | 2547 |

|                                       |   |      |      |      |      |      |
|---------------------------------------|---|------|------|------|------|------|
|                                       | 3560  | 3570 | 3580 | 3590 | 3600 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TAAAATACTTTGAGTTTGGAGCTACTGGATTCTTATTAGTCCCCAAATA |      |      |      |      | 3600 |
| AHR_Modern.seq                        | TAAAATACTTTGAGTTTGGAGCTACTGGATTCTTATTAGTCCCCAAATA |      |      |      |      | 3600 |
| AHR_Neanderthal.seq                   | TAAAATACTTTGAGTTTGGAGCTACTGGATTCTTATTAGTCCCCAAATA |      |      |      |      | 3600 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |   |      |      |      |      | 2547 |
| AHR_Modern_Hubbard.seq                |   |      |      |      |      | 2547 |
| AHR_Neanderthal_Hubbard.seq           |   |      |      |      |      | 2547 |

|                                       |  |      |      |      |      |      |
|---------------------------------------|--|------|------|------|------|------|
|                                       | 3610   | 3620 | 3630 | 3640 | 3650 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | CAAAGTAGAGAACTAACTAGTTTTCTATCATGTTAACCTCTGCTTT |      |      |      |      | 3650 |
| AHR_Modern.seq                        | CAAAGTAGAGAACTAACTAGTTTTCTATCATGTTAACCTCTGCTTT |      |      |      |      | 3650 |
| AHR_Neanderthal.seq                   | CAAAGTAGAGAACTAACTAGTTTTCTATCATGTTAACCTCTGCTTT |      |      |      |      | 3650 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  |      |      |      |      | 2547 |
| AHR_Modern_Hubbard.seq                |  |      |      |      |      | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  |      |      |      |      | 2547 |

|                                       |   |      |      |      |      |      |
|---------------------------------------|---|------|------|------|------|------|
|                                       | 3660  | 3670 | 3680 | 3690 | 3700 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TATCTCAGATGTAAAATAAATGGTTTTGGTGCTTTTTATAAAAAAGATAAT |      |      |      |      | 3700 |
| AHR_Modern.seq                        | TATCTCAGATGTAAAATAAATGGTTTTGGTGCTTTTTATAAAAAAGATAAT |      |      |      |      | 3700 |
| AHR_Neanderthal.seq                   | TATCTCAGATGTAAAATAAATGGTTTTGGTGCTTTTTATAAAAAAGATAAT |      |      |      |      | 3700 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |   |      |      |      |      | 2547 |
| AHR_Modern_Hubbard.seq                |   |      |      |      |      | 2547 |
| AHR_Neanderthal_Hubbard.seq           |   |      |      |      |      | 2547 |

|                                       |  |      |      |      |      |      |
|---------------------------------------|--|------|------|------|------|------|
|                                       | 3710   | 3720 | 3730 | 3740 | 3750 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | CTCAGTGCTTTCCTCCTTCACTGTTTCATCTAAGTGCCTCACATTTTTTT |      |      |      |      | 3750 |
| AHR_Modern.seq                        | CTCAGTGCTTTCCTCCTTCACTGTTTCATCTAAGTGCCTCACATTTTTTT |      |      |      |      | 3750 |
| AHR_Neanderthal.seq                   | CTCAGTGCTTTCCTCCTTCACTGTTTCATCTAAGTGCCTCACATTTTTTT |      |      |      |      | 3750 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  |      |      |      |      | 2547 |
| AHR_Modern_Hubbard.seq                |  |      |      |      |      | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  |      |      |      |      | 2547 |

|                                       |   |      |      |      |      |      |
|---------------------------------------|---|------|------|------|------|------|
|                                       | 3760  | 3770 | 3780 | 3790 | 3800 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | CTACCTATAACACTCTAGGATGTATATTTATATAAAGTATTCTTTTTCT |      |      |      |      | 3800 |
| AHR_Modern.seq                        | CTACCTATAACACTCTAGGATGTATATTTATATAAAGTATTCTTTTTCT |      |      |      |      | 3800 |
| AHR_Neanderthal.seq                   | CTACCTATAACACTCTAGGATGTATATTTATATAAAGTATTCTTTTTCT |      |      |      |      | 3800 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |   |      |      |      |      | 2547 |
| AHR_Modern_Hubbard.seq                |   |      |      |      |      | 2547 |
| AHR_Neanderthal_Hubbard.seq           |   |      |      |      |      | 2547 |

|                                       |   |      |      |      |      |      |
|---------------------------------------|---|------|------|------|------|------|
|                                       | 3810  | 3820 | 3830 | 3840 | 3850 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TTTTTAAATTAATACTTTCTGCACACAAATATTATTTGTGTTTCCTAAA |      |      |      |      | 3850 |
| AHR_Modern.seq                        | TTTTTAAATTAATACTTTCTGCACACAAATATTATTTGTGTTTCCTAAA |      |      |      |      | 3850 |
| AHR_Neanderthal.seq                   | TTTTTAAATTAATACTTTCTGCACACAAATATTATTTGTGTTTCCTAAA |      |      |      |      | 3850 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |   |      |      |      |      | 2547 |
| AHR_Modern_Hubbard.seq                |   |      |      |      |      | 2547 |
| AHR_Neanderthal_Hubbard.seq           |   |      |      |      |      | 2547 |

|                                       |  |      |      |      |      |      |
|---------------------------------------|--|------|------|------|------|------|
|                                       | 3860   | 3870 | 3880 | 3890 | 3900 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TCCAACCATTTTCATTAATTCAGGCATATTTAACTCCTACTGCTTACCTA |      |      |      |      | 3900 |
| AHR_Modern.seq                        | TCCAACCATTTTCATTAATTCAGGCATATTTAACTCCTACTGCTTACCTA |      |      |      |      | 3900 |
| AHR_Neanderthal.seq                   | TCCAACCATTTTCATTAATTCAGGCATATTTAACTCCTACTGCTTACCTA |      |      |      |      | 3900 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  |      |      |      |      | 2547 |
| AHR_Modern_Hubbard.seq                |  |      |      |      |      | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  |      |      |      |      | 2547 |

|                                       |  |      |
|---------------------------------------|--|------|
|                                       | 3910                      3920                      3930                      3940                      3950 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | CTTTCTCAGGTAAGGGCAAATAATGATCGAAAAAATAATTATTTATTA   | 3950 |
| AHR_Modern.seq                        | CTTTCTCAGGTAAGGGCAAATAATGATCGAAAAAATAATTATTTATTA   | 3950 |
| AHR_Neanderthal.seq                   | CTTTCTCAGGTAAGGGCAAATAATGATCGAAAAAATAATTATTTATTA   | 3950 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |

|                                       |  |      |
|---------------------------------------|--|------|
|                                       | 3960                      3970                      3980                      3990                      4000 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | CATAATTTAGTTGTTCTAGACTATAAATGTTGCTATGTGCCTTATGTTG  | 4000 |
| AHR_Modern.seq                        | CATAATTTAGTTGTTCTAGACTATAAATGTTGCTATGTGCCTTATGTTG  | 4000 |
| AHR_Neanderthal.seq                   | CATAATTTAGTTGTTCTAGACTATAAATGTTGCTATGTGCCTTATGTTG  | 4000 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |

|                                       |  |      |
|---------------------------------------|--|------|
|                                       | 4010                      4020                      4030                      4040                      4050 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | AAAAAATTTAAAAGTAAAATGCTTTCCAAATTATTTCTTAATTATTATA  | 4050 |
| AHR_Modern.seq                        | AAAAAATTTAAAAGTAAAATGCTTTCCAAATTATTTCTTAATTATTATA  | 4050 |
| AHR_Neanderthal.seq                   | AAAAAATTTAAAAGTAAAATGCTTTCCAAATTATTTCTTAATTATTATA  | 4050 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |

|                                       |  |      |
|---------------------------------------|--|------|
|                                       | 4060                      4070                      4080                      4090                      4100 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | AAAAATTTAAGACAATAGCACTTAAATTCCTCAACAGTGTTTTCAGAA GA  | 4100 |
| AHR_Modern.seq                        | AAAAATTTAAGACAATAGCACTTAAATTCCTCAACAGTGTTTTCAGAA GA  | 4100 |
| AHR_Neanderthal.seq                   | AAAAATTTAAGACAATAGCACTTAAATTCCTCAACAGTGTTTTCAGAA GA  | 4100 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |

|                                       |  |      |
|---------------------------------------|--|------|
|                                       | 4110                      4120                      4130                      4140                      4150 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | AATAAATATACCACTCTTTACCTTTATGATATCTCCATGATGATAGTTG  | 4150 |
| AHR_Modern.seq                        | AATAAATATACCACTCTTTACCTTTATGATATCTCCATGATGATAGTTG  | 4150 |
| AHR_Neanderthal.seq                   | AATAAATATACCACTCTTTACCTTTATGATATCTCCATGATGATAGTTG  | 4150 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |

|                                       |  |      |
|---------------------------------------|--|------|
|                                       | 4160                      4170                      4180                      4190                      4200 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | AATGTTGCAATGTGAAAAATCTGCTGTTAACTGCAACCTTGTTTATTTAAA  | 4200 |
| AHR_Modern.seq                        | AATGTTGCAATGTGAAAAATCTGCTGTTAACTGCAACCTTGTTTATTTAAA  | 4200 |
| AHR_Neanderthal.seq                   | AATGTTGCAATGTGAAAAATCTGCTGTTAACTGCAACCTTGTTTATTTAAA  | 4200 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |

|                                       |  |      |
|---------------------------------------|--|------|
|                                       | 4210                      4220                      4230                      4240                      4250 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TTGCAAGAAGCTTTATTTCTAGCTTTTTTAATTAAGCAAAGCACCCATTTTC   | 4250 |
| AHR_Modern.seq                        | TTGCAAGAAGCTTTATTTCTAGCTTTTTTAATTAAGCAAAGCACCCATTTTC   | 4250 |
| AHR_Neanderthal.seq                   | TTGCAAGAAGCTTTATTTCTAGCTTTTTTAATTAAGCAAAGCACCCATTTTC   | 4250 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |

|                                       |  |      |
|---------------------------------------|--|------|
|                                       | 4260                      4270                      4280                      4290                      4300 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | AATGTGTATAAATTTGCTTTAAAAACTGTTTAGACCTATAATCCTTGAT  | 4300 |
| AHR_Modern.seq                        | AATGTGTATAAATTTGCTTTAAAAACTGTTTAGACCTATAATCCTTGAT  | 4300 |
| AHR_Neanderthal.seq                   | AATGTGTATAAATTTGCTTTAAAAACTGTTTAGACCTATAATCCTTGAT  | 4300 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |

|                                       |  |      |
|---------------------------------------|--|------|
|                                       | 4310                      4320                      4330                      4340                      4350 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | AATATATTTGTTGACTTTATAAATTTGCTTCTTAGAACAGTGGAACCT   | 4350 |
| AHR_Modern.seq                        | AATATATTTGTTGACTTTATAAATTTGCTTCTTAGAACAGTGGAACCT   | 4350 |
| AHR_Neanderthal.seq                   | AATATATTTGTTGACTTTATAAATTTGCTTCTTAGAACAGTGGAACCT   | 4350 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |

|                                       |  |      |
|---------------------------------------|--|------|
|                                       | 4360            4370            4380            4390            4400 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | ATGTGTTTTCTCATATTTGAGGAGTGTTAAGATTGCAGATAGCAAAGTT                    | 4400 |
| AHR_Modern.seq                        | ATGTGTTTTCTCATATTTGAGGAGTGTTAAGATTGCAGATAGCAAAGTT                    | 4400 |
| AHR_Neanderthal.seq                   | ATGTGTTTTCTCATATTTGAGGAGTGTTAAGATTGCAGATAGCAAAGTT                    | 4400 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |
|                                       |  |      |
|                                       | 4410            4420            4430            4440            4450 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TGGTGCAAAGTATTGTAATGAGTGAATTGAATGGTGCATTGTATAGATAT                   | 4450 |
| AHR_Modern.seq                        | TGGTGCAAAGTATTGTAATGAGTGAATTGAATGGTGCATTGTATAGATAT                   | 4450 |
| AHR_Neanderthal.seq                   | TGGTGCAAAGTATTGTAATGAGTGAATTGAATGGTGCATTGTATAGATAT                   | 4450 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |
|                                       |  |      |
|                                       | 4460            4470            4480            4490            4500 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | AATGAACAAAATATTTGTAAGATATTTGCAGTTTTTCATTTTAAAAAGT                    | 4500 |
| AHR_Modern.seq                        | AATGAACAAAATATTTGTAAGATATTTGCAGTTTTTCATTTTAAAAAGT                    | 4500 |
| AHR_Neanderthal.seq                   | AATGAACAAAATATTTGTAAGATATTTGCAGTTTTTCATTTTAAAAAGT                    | 4500 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |
|                                       |  |      |
|                                       | 4510            4520            4530            4540            4550 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | CCATACCTTATATATGCACCTTAATTTGTTGGGGCTTTACATACTTTATCA                  | 4550 |
| AHR_Modern.seq                        | CCATACCTTATATATGCACCTTAATTTGTTGGGGCTTTACATACTTTATCA                  | 4550 |
| AHR_Neanderthal.seq                   | CCATACCTTATATATGCACCTTAATTTGTTGGGGCTTTACATACTTTATCA                  | 4550 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |
|                                       |  |      |
|                                       | 4560            4570            4580            4590            4600 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | ATGTGCTTTCTAAGAAATCAAGTAATGAATCCAACCTGCTTAAAGTTGGT                   | 4600 |
| AHR_Modern.seq                        | ATGTGCTTTCTAAGAAATCAAGTAATGAATCCAACCTGCTTAAAGTTGGT                   | 4600 |
| AHR_Neanderthal.seq                   | ATGTGCTTTCTAAGAAATCAAGTAATGAATCCAACCTGCTTAAAGTTGGT                   | 4600 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |
|                                       |  |      |
|                                       | 4610            4620            4630            4640            4650 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | ATTAATAAAAAGACAACCCACATAGTTCGTTACCTTCAAACCTTAGGTTT                   | 4650 |
| AHR_Modern.seq                        | ATTAATAAAAAGACAACCCACATAGTTCGTTACCTTCAAACCTTAGGTTT                   | 4650 |
| AHR_Neanderthal.seq                   | ATTAATAAAAAGACAACCCACATAGTTCGTTACCTTCAAACCTTAGGTTT                   | 4650 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |
|                                       |  |      |
|                                       | 4660            4670            4680            4690            4700 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TTTTAATGATATACTGATCTTCATTACCAATAGGCAAATTAATCACCCCTA                  | 4700 |
| AHR_Modern.seq                        | TTTTAATGATATACTGATCTTCATTACCAATAGGCAAATTAATCACCCCTA                  | 4700 |
| AHR_Neanderthal.seq                   | TTTTAATGATATACTGATCTTCATTACCAATAGGCAAATTAATCACCCCTA                  | 4700 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |
|                                       |  |      |
|                                       | 4710            4720            4730            4740            4750 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | CCAACTTACTGTCCTAACATGGTTAAAAGAAAAAATGACACCATCTTT                     | 4750 |
| AHR_Modern.seq                        | CCAACTTACTGTCCTAACATGGTTAAAAGAAAAAATGACACCATCTTT                     | 4750 |
| AHR_Neanderthal.seq                   | CCAACTTACTGTCCTAACATGGTTAAAAGAAAAAATGACACCATCTTT                     | 4750 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |
|                                       |  |      |
|                                       | 4760            4770            4780            4790            4800 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TATTCTTTTTTTTTTTTTTTTTGAAGAGAGTCTTACTCTGCCGCCCAA                     | 4800 |
| AHR_Modern.seq                        | TATTCTTTTTTTTTTTTTTTTTGAAGAGAGTCTTACTCTGCCGCCCAA                     | 4800 |
| AHR_Neanderthal.seq                   | TATTCTTTTTTTTTTTTTTTTTGAAGAGAGTCTTACTCTGCCGCCCAA                     | 4800 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |

|                                       |  |      |
|---------------------------------------|--|------|
|                                       | 4810                      4820                      4830                      4840                      4850 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | ACTGGA GT GCAGTGGCA CAATCT TGGCTCACTGCAACCTCTACCTCCTGG   | 4850 |
| AHR_Modern.seq                        | ACTGGA GT GCAGTGGCA CAATCT TGGCTCACTGCAACCTCTACCTCCTGG   | 4850 |
| AHR_Neanderthal.seq                   | ACTGGA GT GCAGTGGCA CAATCT TGGCTCACTGCAACCTCTACCTCCTGG   | 4850 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |
|                                       |  |      |
|                                       | 4860                      4870                      4880                      4890                      4900 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | GT TCAA GT GATTCT CTTGCCTCAGCCTCCCGAGT TGGTGGGATTACAGGC  | 4900 |
| AHR_Modern.seq                        | GT TCAA GT GATTCT CTTGCCTCAGCCTCCCGAGT TGGTGGGATTACAGGC  | 4900 |
| AHR_Neanderthal.seq                   | GT TCAA GT GATTCT CTTGCCTCAGCCTCCCGAGT TGGTGGGATTACAGGC  | 4900 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |
|                                       |  |      |
|                                       | 4910                      4920                      4930                      4940                      4950 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | ATGTGCCACCATGCCCA GCTAATTTTTGTATTTTTAGTAGAAACGGGTTT  | 4950 |
| AHR_Modern.seq                        | ATGTGCCACCATGCCCA GCTAATTTTTGTATTTTTAGTAGAAACGGGTTT  | 4950 |
| AHR_Neanderthal.seq                   | ATGTGCCACCATGCCCA GCTAATTTTTGTATTTTTAGTAGAAACGGGTTT  | 4950 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |
|                                       |  |      |
|                                       | 4960                      4970                      4980                      4990                      5000 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | CACCATGT TGGCCAGACTGGTCTCAAACCTCCTGACCTCAGGTGAGCCTCC   | 5000 |
| AHR_Modern.seq                        | CACCATGT TGGCCAGACTGGTCTCAAACCTCCTGACCTCAGGTGAGCCTCC   | 5000 |
| AHR_Neanderthal.seq                   | CACCATGT TGGCCAGACTGGTCTCAAACCTCCTGACCTCAGGTGAGCCTCC   | 5000 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |
|                                       |  |      |
|                                       | 5010                      5020                      5030                      5040                      5050 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | CACCTTGGCCTCCCAAAGT GCTGGGATTACA GGCCTGAGCCA CTGCATT C   | 5050 |
| AHR_Modern.seq                        | CACCTTGGCCTCCCAAAGT GCTGGGATTACA GGCCTGAGCCA CTGCATT C   | 5050 |
| AHR_Neanderthal.seq                   | CACCTTGGCCTCCCAAAGT GCTGGGATTACA GGCCTGAGCCA CTGCATT C   | 5050 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |
|                                       |  |      |
|                                       | 5060                      5070                      5080                      5090                      5100 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | AGCTCTCTTTTCTTTAGATATGAGAGCTGAAGA GCTTAGACACATTTTG   | 5100 |
| AHR_Modern.seq                        | AGCTCTCTTTTCTTTAGATATGAGAGCTGAAGA GCTTAGACACATTTTG   | 5100 |
| AHR_Neanderthal.seq                   | AGCTCTCTTTTCTTTAGATATGAGAGCTGAAGA GCTTAGACACATTTTG   | 5100 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |
|                                       |  |      |
|                                       | 5110                      5120                      5130                      5140                      5150 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | CATGTATTATTTGAAAATCTGATGGAA TCCCAA ACTGAGATGTATTA AAAA   | 5150 |
| AHR_Modern.seq                        | CATGTATTATTTGAAAATCTGATGGAA TCCCAA ACTGAGATGTATTA AAAA   | 5150 |
| AHR_Neanderthal.seq                   | CATGTATTATTTGAAAATCTGATGGAA TCCCAA ACTGAGATGTATTA AAAA   | 5150 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |
|                                       |  |      |
|                                       | 5160                      5170                      5180                      5190                      5200 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TACAATTTTGGCCGGTGCA GTGGCTCAGCCTGT AATCCCAGCACTTG  | 5200 |
| AHR_Modern.seq                        | TACAATTTTGGCCGGTGCA GTGGCTCAGCCTGT AATCCCAGCACTTG  | 5200 |
| AHR_Neanderthal.seq                   | TACAATTTTGGCCGGTGCA GTGGCTCAGCCTGT AATCCCAGCACTTG  | 5200 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |
|                                       |  |      |
|                                       | 5210                      5220                      5230                      5240                      5250 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | GGGAGGCGAGGAGGGTGGAT CACGAGGTCAAGA GATGGAGACCATCCTG  | 5250 |
| AHR_Modern.seq                        | GGGAGGCGAGGAGGGTGGAT CACGAGGTCAAGA GATGGAGACCATCCTG  | 5250 |
| AHR_Neanderthal.seq                   | GGGAGGCGAGGAGGGTGGAT CACGAGGTCAAGA GATGGAGACCATCCTG  | 5250 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |

|                                       |  |      |
|---------------------------------------|--|------|
|                                       | 5260            5270            5280            5290            5300 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | ACCAACAT GGTGAAACCT GTCTCTACTAAAAATACAGAAAT TAGCTGGG                 | 5300 |
| AHR_Modern.seq                        | ACCAACAT GGTGAAACCT GTCTCTACTAAAAATACAGAAAT TAGCTGGG                 | 5300 |
| AHR_Neanderthal.seq                   | ACCAACAT GGTGAAACCT GTCTCTACTAAAAATACAGAAAT TAGCTGGG                 | 5300 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |

|                                       |  |      |
|---------------------------------------|--|------|
|                                       | 5310            5320            5330            5340            5350 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | CATGGT GCGGTGAGCCT GTAGTCCTAGCTACTCAGGAGGCTGAGGCAGGA                 | 5350 |
| AHR_Modern.seq                        | CATGGT GCGGTGAGCCT GTAGTCCTAGCTACTCAGGAGGCTGAGGCAGGA                 | 5350 |
| AHR_Neanderthal.seq                   | CATGGT GCGGTGAGCCT GTAGTCCTAGCTACTCAGGAGGCTGAGGCAGGA                 | 5350 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |

|                                       |  |      |
|---------------------------------------|--|------|
|                                       | 5360            5370            5380            5390            5400 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | GAATAGCCTGAACTGGGAATCGGAGGTTGCAGAGCCAAGATCGCCCCAC                    | 5400 |
| AHR_Modern.seq                        | GAATAGCCTGAACTGGGAATCGGAGGTTGCAGAGCCAAGATCGCCCCAC                    | 5400 |
| AHR_Neanderthal.seq                   | GAATAGCCTGAACTGGGAATCGGAGGTTGCAGAGCCAAGATCGCCCCAC                    | 5400 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |

|                                       |  |      |
|---------------------------------------|--|------|
|                                       | 5410            5420            5430            5440            5450 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TGCACTCCAGCCTGGCAATAGACCGAGACTCCGTCTCCAAAAAAAAAAAAA                  | 5450 |
| AHR_Modern.seq                        | TGCACTCCAGCCTGGCAATAGACCGAGACTCCGTCTCCAAAAAAAAAAAAA                  | 5450 |
| AHR_Neanderthal.seq                   | TGCACTCCAGCCTGGCAATAGACCGAGACTCCGTCTCCAAAAAAAAAAAAA                  | 5450 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |

|                                       |  |      |
|---------------------------------------|--|------|
|                                       | 5460            5470            5480            5490            5500 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | AATACAATTTTATTTCTTTTACTTTTTTTAGTAAGTTAATGTATATAAA                    | 5500 |
| AHR_Modern.seq                        | AATACAATTTTATTTCTTTTACTTTTTTTAGTAAGTTAATGTATATAAA                    | 5500 |
| AHR_Neanderthal.seq                   | AATACAATTTTATTTCTTTTACTTTTTTTAGTAAGTTAATGTATATAAA                    | 5500 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |

|                                       |  |      |
|---------------------------------------|--|------|
|                                       | 5510            5520            5530            5540            5550 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | AATGGCTTCGGACAAAATATCTCTGAGTTCGTGTATTTTCAGTCAAAC                     | 5550 |
| AHR_Modern.seq                        | AATGGCTTCGGACAAAATATCTCTGAGTTCGTGTATTTTCAGTCAAAC                     | 5550 |
| AHR_Neanderthal.seq                   | AATGGCTTCGGACAAAATATCTCTGAGTTCGTGTATTTTCAGTCAAAC                     | 5550 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |

|                                       |  |      |
|---------------------------------------|--|------|
|                                       | 5560            5570            5580            5590            5600 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TTTAAACCTGTAGAATCAATTTAAGTGTTGGAAAAATTTGTCTGAAACA                    | 5600 |
| AHR_Modern.seq                        | TTTAAACCTGTAGAATCAATTTAAGTGTTGGAAAAATTTGTCTGAAACA                    | 5600 |
| AHR_Neanderthal.seq                   | TTTAAACCTGTAGAATCAATTTAAGTGTTGGAAAAATTTGTCTGAAACA                    | 5600 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |

|                                       |  |      |
|---------------------------------------|--|------|
|                                       | 5610            5620            5630            5640            5650 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TTTCATAATTTGTTCCAGCATGAGGTATCTAAGGATTTAGACCAGAGGT                    | 5650 |
| AHR_Modern.seq                        | TTTCATAATTTGTTCCAGCATGAGGTATCTAAGGATTTAGACCAGAGGT                    | 5650 |
| AHR_Neanderthal.seq                   | TTTCATAATTTGTTCCAGCATGAGGTATCTAAGGATTTAGACCAGAGGT                    | 5650 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |

|                                       |  |      |
|---------------------------------------|--|------|
|                                       | 5660            5670            5680            5690            5700 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | CTAGATTAATACTCTATTTTTACATTTAAACCTTTTTATATAAGTCTTAC                   | 5700 |
| AHR_Modern.seq                        | CTAGATTAATACTCTATTTTTACATTTAAACCTTTTTATATAAGTCTTAC                   | 5700 |
| AHR_Neanderthal.seq                   | CTAGATTAATACTCTATTTTTACATTTAAACCTTTTTATATAAGTCTTAC                   | 5700 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  | 2547 |
| AHR_Modern_Hubbard.seq                |  | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  | 2547 |

|                                       |  |      |      |      |      |      |
|---------------------------------------|--|------|------|------|------|------|
|                                       | 5710   | 5720 | 5730 | 5740 | 5750 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | ATAAACCATTTTGT TACTCTCTCCACATGTTACTGGATAAATGTTTA |      |      |      |      | 5750 |
| AHR_Modern.seq                        | ATAAACCATTTTGT TACTCTCTCCACATGTTACTGGATAAATGTTTA |      |      |      |      | 5750 |
| AHR_Neanderthal.seq                   | ATAAACCATTTTGT TACTCTCTCCACATGTTACTGGATAAATGTTTA |      |      |      |      | 5750 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  |      |      |      |      | 2547 |
| AHR_Modern_Hubbard.seq                |  |      |      |      |      | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  |      |      |      |      | 2547 |

|                                       |  |      |      |      |      |      |
|---------------------------------------|--|------|------|------|------|------|
|                                       | 5760   | 5770 | 5780 | 5790 | 5800 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | GTGGAAAATAGGCTTTTAAATCATGAATATGATGACAATCAGTTATACAG |      |      |      |      | 5800 |
| AHR_Modern.seq                        | GTGGAAAATAGGCTTTTAAATCATGAATATGATGACAATCAGTTATACAG |      |      |      |      | 5800 |
| AHR_Neanderthal.seq                   | GTGGAAAATAGGCTTTTAAATCATGAATATGATGACAATCAGTTATACAG |      |      |      |      | 5800 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  |      |      |      |      | 2547 |
| AHR_Modern_Hubbard.seq                |  |      |      |      |      | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  |      |      |      |      | 2547 |

|                                       |   |      |      |      |      |      |
|---------------------------------------|---|------|------|------|------|------|
|                                       | 5810  | 5820 | 5830 | 5840 | 5850 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TTATAAAATTTAAAAGTTTGAAAAGCAATATTTGATATTTTTATCTATATA |      |      |      |      | 5850 |
| AHR_Modern.seq                        | TTATAAAATTTAAAAGTTTGAAAAGCAATATTTGATATTTTTATCTATATA |      |      |      |      | 5850 |
| AHR_Neanderthal.seq                   | TTATAAAATTTAAAAGTTTGAAAAGCAATATTTGATATTTTTATCTATATA |      |      |      |      | 5850 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |   |      |      |      |      | 2547 |
| AHR_Modern_Hubbard.seq                |   |      |      |      |      | 2547 |
| AHR_Neanderthal_Hubbard.seq           |   |      |      |      |      | 2547 |

|                                       |   |      |      |      |      |      |
|---------------------------------------|---|------|------|------|------|------|
|                                       | 5860  | 5870 | 5880 | 5890 | 5900 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | AAATAACTAAAAATGTATCTAAGAATAATAAAATCACGTAAAACCAAATAC |      |      |      |      | 5900 |
| AHR_Modern.seq                        | AAATAACTAAAAATGTATCTAAGAATAATAAAATCACGTAAAACCAAATAC |      |      |      |      | 5900 |
| AHR_Neanderthal.seq                   | AAATAACTAAAAATGTATCTAAGAATAATAAAATCACGTAAAACCAAATAC |      |      |      |      | 5900 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |   |      |      |      |      | 2547 |
| AHR_Modern_Hubbard.seq                |   |      |      |      |      | 2547 |
| AHR_Neanderthal_Hubbard.seq           |   |      |      |      |      | 2547 |

|                                       |  |      |      |      |      |      |
|---------------------------------------|--|------|------|------|------|------|
|                                       | 5910   | 5920 | 5930 | 5940 | 5950 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | ACGTTTGTCTGTATTTGTAAGTGCCAAACAAAGGATACTTAGTGCACTGC |      |      |      |      | 5950 |
| AHR_Modern.seq                        | ACGTTTGTCTGTATTTGTAAGTGCCAAACAAAGGATACTTAGTGCACTGC |      |      |      |      | 5950 |
| AHR_Neanderthal.seq                   | ACGTTTGTCTGTATTTGTAAGTGCCAAACAAAGGATACTTAGTGCACTGC |      |      |      |      | 5950 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  |      |      |      |      | 2547 |
| AHR_Modern_Hubbard.seq                |  |      |      |      |      | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  |      |      |      |      | 2547 |

|                                       |  |      |      |      |      |      |
|---------------------------------------|--|------|------|------|------|------|
|                                       | 5960   | 5970 | 5980 | 5990 | 6000 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TACATTGTGGGATTTATTTCTAGATGATGTGCACATCTAAGGATATGGAT |      |      |      |      | 6000 |
| AHR_Modern.seq                        | TACATTGTGGGATTTATTTCTAGATGATGTGCACATCTAAGGATATGGAT |      |      |      |      | 6000 |
| AHR_Neanderthal.seq                   | TACATTGTGGGATTTATTTCTAGATGATGTGCACATCTAAGGATATGGAT |      |      |      |      | 6000 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  |      |      |      |      | 2547 |
| AHR_Modern_Hubbard.seq                |  |      |      |      |      | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  |      |      |      |      | 2547 |

|                                       |  |      |      |      |      |      |
|---------------------------------------|--|------|------|------|------|------|
|                                       | 6010   | 6020 | 6030 | 6040 | 6050 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | GTGTCTAATTTAGTCTTTTCTGTACCAGGTTTTCTTACAATACCTGAA |      |      |      |      | 6050 |
| AHR_Modern.seq                        | GTGTCTAATTTAGTCTTTTCTGTACCAGGTTTTCTTACAATACCTGAA |      |      |      |      | 6050 |
| AHR_Neanderthal.seq                   | GTGTCTAATTTAGTCTTTTCTGTACCAGGTTTTCTTACAATACCTGAA |      |      |      |      | 6050 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  |      |      |      |      | 2547 |
| AHR_Modern_Hubbard.seq                |  |      |      |      |      | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  |      |      |      |      | 2547 |

|                                       |   |      |      |      |      |      |
|---------------------------------------|---|------|------|------|------|------|
|                                       | 6060  | 6070 | 6080 | 6090 | 6100 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | GACTACCAGTATTTCTAGTGTATATGAAAGCTTTCAACAT TACTATGCAC |      |      |      |      | 6100 |
| AHR_Modern.seq                        | GACTACCAGTATTTCTAGTGTATATGAAAGCTTTCAACAT TACTATGCAC |      |      |      |      | 6100 |
| AHR_Neanderthal.seq                   | GACTACCAGTATTTCTAGTGTATATGAAAGCTTTCAACAT TACTATGCAC |      |      |      |      | 6100 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |   |      |      |      |      | 2547 |
| AHR_Modern_Hubbard.seq                |   |      |      |      |      | 2547 |
| AHR_Neanderthal_Hubbard.seq           |   |      |      |      |      | 2547 |

|                                       |   |      |      |      |      |      |
|---------------------------------------|---|------|------|------|------|------|
|                                       | 6110  | 6120 | 6130 | 6140 | 6150 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | AAACTAGTGT TTTTCGATGTTACTAAATTTTAGGTAATGCTTT CATGGC |      |      |      |      | 6150 |
| AHR_Modern.seq                        | AAACTAGTGT TTTTCGATGTTACTAAATTTTAGGTAATGCTTT CATGGC |      |      |      |      | 6150 |
| AHR_Neanderthal.seq                   | AAACTAGTGT TTTTCGATGTTACTAAATTTTAGGTAATGCTTT CATGGC |      |      |      |      | 6150 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |   |      |      |      |      | 2547 |
| AHR_Modern_Hubbard.seq                |   |      |      |      |      | 2547 |
| AHR_Neanderthal_Hubbard.seq           |   |      |      |      |      | 2547 |

|                                       |  |      |      |      |      |      |
|---------------------------------------|--|------|------|------|------|------|
|                                       | 6160   | 6170 | 6180 | 6190 | 6200 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TTTTTTCTTCAAAATGT TACT GCTT ACAT AT AT CAT GCAT AGAT TTTT GC |      |      |      |      | 6200 |
| AHR_Modern.seq                        | TTTTTTCTTCAAAATGT TACT GCTT ACAT AT AT CAT GCAT AGAT TTTT GC |      |      |      |      | 6200 |
| AHR_Neanderthal.seq                   | TTTTTTCTTCAAAATGT TACT GCTT ACAT AT AT CAT GCAT AGAT TTTT GC |      |      |      |      | 6200 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |  |      |      |      |      | 2547 |
| AHR_Modern_Hubbard.seq                |  |      |      |      |      | 2547 |
| AHR_Neanderthal_Hubbard.seq           |  |      |      |      |      | 2547 |

|                                       |   |      |      |      |      |      |
|---------------------------------------|---|------|------|------|------|------|
|                                       | 6210  | 6220 | 6230 | 6240 | 6250 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TT AAAGT AT GAT TT ATA AT AT CCT CAT T AT CAAAGT TGT ATACAAT AATA |      |      |      |      | 6250 |
| AHR_Modern.seq                        | TT AAAGT AT GAT TT ATA AT AT CCT CAT T AT CAAAGT TGT ATACAAT AATA |      |      |      |      | 6250 |
| AHR_Neanderthal.seq                   | TT AAAGT AT GAT TT ATA AT AT CCT CAT T AT CAAAGT TGT ATACAAT AATA |      |      |      |      | 6250 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |   |      |      |      |      | 2547 |
| AHR_Modern_Hubbard.seq                |   |      |      |      |      | 2547 |
| AHR_Neanderthal_Hubbard.seq           |   |      |      |      |      | 2547 |

|                                       |                             |      |      |
|---------------------------------------|-----------------------------|------|------|
|                                       | 6260                        | 6270 |      |
| AHR_002_Hum_ENST00000242057.8.seq     | TATAAT AAAATAACAAATATGAATAA |      | 6276 |
| AHR_Modern.seq                        | TATAAT AAAATAACAAATATGAATAA |      | 6277 |
| AHR_Neanderthal.seq                   | TATAAT AAAATAACAAATATGAATAA |      | 6277 |
| AHR_002_Hum_ENST00000242057.8_CDS.seq |                             |      | 2547 |
| AHR_Modern_Hubbard.seq                |                             |      | 2547 |
| AHR_Neanderthal_Hubbard.seq           |                             |      | 2547 |



# Supplementary Data SD7

## SD7\_AHR\_5'-UTR\_185Variant.docx

### Conservation of ancient hominin AHR 5'-UTR 185G variant within primates

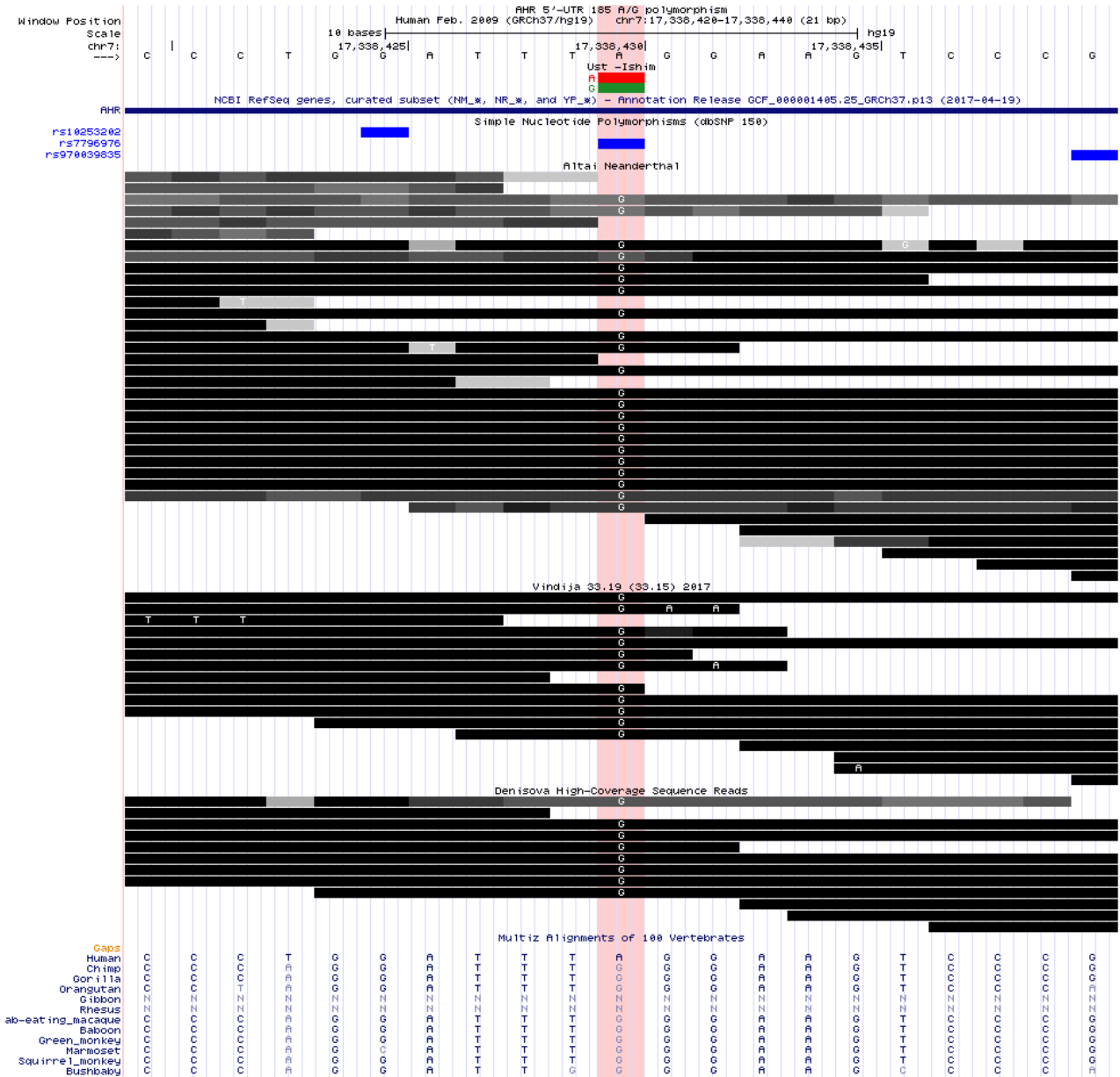


Fig. SD7. Using the UCSC Genome Browser the AHR mRNA exon 1 sequence around the 185A/G variant site (red highlighting) from the modern human reference genome (assembly GRCh37/hg19; upper track) was aligned with the variants (VCF-format) observed in the genome of an ancient anatomically modern human (45 kya) found at Ust'-Ishim in Siberia (Fu et al., 2014) (second track), documenting that this individual is heterozygous A/G at position 185. The third track demonstrates that the sequence shown is part of the RefSeq human AHR mRNA sequence NM\_001621.4. The fourth track shows that the 185A/G variant is known in present-day humans as reference single nucleotide polymorphism (SNP) rs7796976 in dbSNP. The three tracks below show the alignment of the sequence reads obtained from the Altai-Neanderthal (Prüfer et al., 2014), Vindija-Neanderthal (Prüfer et al., 2017) and Denisovan (Meyer et al., 2012) genome, respectively, comprising only 185G reads. The bottom track displays the primate section of the "Multiz Alignments of 100 Vertebrates" available in the UCSC Genome Browser, showing that the 185G variant is highly conserved within primates, and the 185A variant is a newly derived allele, unique for the modern human lineage, with an allele frequency of 21% (dbSNP, build 151, rs7796976).

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