1	Genome Medicine
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4	Detection of hematopoietic stem cell transcriptome in human fetal kidneys
5	and kidney organoids derived from human induced pluripotent stem cells
6	(iPSC)
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24 Abstract

Background: In mammalians, hematopoietic stem cells (HSC) arise in the dorsal aorta from the hemogenic endothelium, followed by their migration to fetal liver and to bone marrow. In zebrafish, kidney is the site of primary hematopoiesis. In humans, the presence of HSC in the fetal or adult kidney has not been established.

29 Methods: We analyzed the presence of HSC markers in human fetal kidneys by analysis of single-cell 30 datasets. We then analyzed in kidney organoids derived from iPSC, the presence of hematopoietic 31 markers using transcriptome analyses.

32 **Results:** 12 clusters were identified of stromal, endothelial, and nephron cell type-specific markers in

the two fetal stage (17 weeks) kidney datasets. Among these, expression of hematopoietic cells in

34 Cluster 9 showed expression of primitive markers. Moreover, whole transcriptome analysis of our iPSC-

derived kidney organoids revealed induction of the primitive hematopoietic transcription factor RUNX1

36 as found in the human fetal kidney cortex.

37 Conclusions: These finding support the presence of cells expressing HSC transcriptome in human
 38 kidney. The mechanisms of the appearance of the cells with the same transcriptional features during
 39 iPSC-derived kidney organoid generation requires further investigation.

40

41 Keywords: Transcriptome analysis, hematopoietic stem cells (HSC), human fetal kidney, human
42 kidney organoids, human induced pluripotent stem cells (iPSC)

44 Introduction

45 Hematopoietic stem cells (HSC) are characterized by their capacity of both self-renewal and 46 differentiation into blood and immune cell lineages throughout the life of the individual in a stem cell-47 regulating microenvironment, or HSC niche. HSC-niche interactions in bone marrow, liver and kidney have been extensively studied using vertebrate animal models, including mice, frogs, zebrafish, and 48 49 chickens [1,2]. During mammalian hematopoiesis, the most primitive hematopoietic cells migrate from 50 the aorta-gonad-mesonephros (AGM) region to the fetal liver and to the bone marrow which is the site of adult hematopoiesis [1]. However, the persistence of some degree of hematopoietic activity in adult 51 52 tissues is possible as this has been suggested by the discovery of donor-derived chimeric hematopoiesis 53 after liver transplantation showing the contribution of donor-derived cells to hematopoiesis [3]. To our 54 knowledge, there has been no study analyzing the possibility of donor-derived hematopoiesis after 55 kidney transplantation. It should be reminded that in the majority of cases, kidney transplants are 56 performed using kidneys from deceased donors [4,5]. HSC-kidney niche interactions have been studied 57 in many reports. For example, zebrafish kidney stromal cell lines can support and maintain early 58 hematopoietic precursors and differentiation of lymphoid, myeloid, and erythroid precursors [4].

Recent advances in single-cell RNA sequencing technology are leading to new discoveries and validation in fetal organs and organoids [5–7]. Here, we first analyzed the presence of transcriptional markers of HSC in fetal kidneys through analysis of a single-cell dataset described by Lindström NO et al [5–7]. We then performed a transcriptome analysis of iPSC-derived kidney organoids. We show that HSC-related markers can be detected in both in fetal kidneys and the human iPSC-derived kidney organoids.

65

66 **Results**

67 Human fetal kidney cortex harbors cells expressing hematopoietic transcripts

Single cell transcriptome is a powerful technology to investigate cell heterogeneity in a tissue.
Lindström NO et al [5–7] performed these experiments in cortexes tissues isolated from two human
fetal kidneys (17 weeks) by 10X genomics technology. This work allowed us to perform in silico

71 analyses. To this end, we merged and analyzed with Seurat package the 2 respective MTX files 72 generated by cell ranger in order to suppress batch error and performed downstream unsupervised 73 analysis. To build the common matrix of the two samples, genes which were found expressed in 74 minimum 5 cells by sample were conserved. After merging of the data from the two kidney samples, 75 the Seurat digital matrix comprised 7860 cells for 18119 transcripts. During batch correction with 76 canonical correlation, we observed that the 2 kidney samples were found well superposed in first 77 factorial map of canonical correlation (Fig. S1a) and the shared correlation strength decrease on the 78 thirty components of canonical correlation (Fig. S1b). tSNE analysis on the common variable genes on 79 the 40 principal components of the principal component analysis allowed to identify 12 clusters (Fig. 80 1a) reproducible in both kidneys (Fig. S1c). Major of the tSNE central cells comprising clusters 3,2,0,1 81 expressed mesoderm transcription factor TCF21 (Fig. 1a and Fig. S2), also expression of TCF21 is 82 positive in cells from cluster 6 which highly expressed matrix molecules such as Lumican (LUM) (Fig. 1a and Fig. S2) Decorin (DCN) and Collagens (COL3A1, COL1A1, COL1A2) (Fig. 1b). In cluster 4, 83 84 cells were found to be positive for KDR (Fig. 1a) and CD34 (data not shown), suggesting an expression profile corresponding to endothelial cells. Cells identified in cluster 7 have a high expression of 85 86 downstream NOTCH pathway transcription factor HEY1 such as cells from cluster 0 which are central 87 proximal from this position during tSNE analysis (Fig. 1a). Some cluster of cells which are left eccentric 88 (clusters 8 and 11) expressed tubular markers such as FXYD2 (Fig. 1a and Fig. S2) encoding the 89 sodium/potassium-transporting ATPase subunit gamma. Cluster of cells number 10, also left eccentric 90 during tSNE analysis expressed some podocyte markers such as PTPRO: Protein Tyrosine Phosphatase, 91 Receptor Type O (Fig. 1a and Fig. S2), but also SOST: Sclerostin and PODXL: podocalyxin like (Fig. 92 1b). Cluster of cells number 5 expressed specifically the renin molecule a well-known renal molecule 93 (Fig. 1a and Fig. S2). These results suggest that tSNE analysis performed post canonical analysis in 94 these 2 merged samples reflect the cell diversity compatible with kidney organ at this stage of 95 development described in the original paper [8]. Surprisingly, in unsupervised tSNE analysis of human kidney cortex, we found the left-top eccentric cluster number 9 (Fig. 1a) which is principally defined 96 97 by the specific expression of SRGN (Fig. 1a, Fig. 2a and Table S1). Serglycin (SRGN) is known to be

a hematopoietic cell granule proteoglycan. In this cluster of cells, there is also a specific expression of 98 99 hematopoietic cluster of differentiation such as PTPRC alias CD45 and CD44 (Fig. 2b). Some 100 molecules such as CD74 and HLA-DRA implicated in antigen presenting cells functionalities are also 101 expressed in this cluster of cells (Fig. 2c). Interestingly, a fraction of cells from cluster 9 also expressed 102 primitive hematopoietic transcription factors such as SPI1 (alias PU.1) and RUNX1 (Fig. 2d). Some of 103 the cells from the same cluster also expressed CXCR4 receptor which is well known to be expressed 104 on primitive human hematopoietic cells for their homing function. This original results on cluster 9 105 suggest the presence of cells with hematopoietic transcriptome with some of them expressing primitive 106 markers in the human kidney cortex at fetal stage (17 weeks).

107

108 Generation and characterization of iPSC-derived kidney organoids.

Human iPSC-derived kidney organoids have been generated as previously described [9]. Briefly, iPSC aggregates were generated in E8 media and Geltrex matrix leading to spontaneous formation of complex kidney organoids at days 12-14 of the culture. (Fig. 3a). We characterized iPSC-derived kidney organoids using whole-mounting staining with confocal imaging. As can be seen in Fig. 3b, glomerulilike structures, which contained cells that stained for the nephron marker Nephrin were easily identified [10]. Moreover, ultrastructure analyses revealed cell-cell junctions and the podocyte foot process formation in kidney organoids (Fig. 3c).

116

117 Detection of a hematopoietic transcriptome program iPSC-derived kidney organoids

We performed, in duplicate, whole transcriptome analysis of iPSC derived kidney organoids as compared to native iPSC with Clariom S human technology. After RMA normalization, we identified 3546 differentially expressed genes (DEG) with LIMMA algorithm (Fig. 4a) comprising 1432 upregulated genes. This DEG profile allowed to discriminate experimental sample groups by unsupervised classification (Fig. 4b). After functional enrichment on WikiPathway database, we identified a hematopoietic program in iPSC-derived kidney organoids. Especially, we uncovered an up regulation of RUNX1 and CD34 corresonding to genes expressed in hematopoietic stem cells and that of FLI1, 125 CXCR4, MXI1 downstream at erythrocyte and megakaryocyte progenitor levels. There was also a 126 repression of MYB megakaryocytic repressor (Fig. 4c). These results suggest the implication of a 127 hematopoietic transcriptional program in our iPSC-derived kidney organoids and especially induction 128 of the primitive hematopoietic transcription factor RUNX1 which was also detectable at the single cell 129 level (Fig. 2d) in human ex vivo fetal kidney cortex.

130

131 Discussion

The involvement of kidney in hematopoiesis has been clearly demonstrated in zebrafish [11]. In 132 133 humans, the most primitive hematopoietic cells arise from mesodermal lineage in AGM through 134 hemogenic endothelium [12]. Kidney is also a tissue developed from mesoderm but the presence of cells with HSC transcriptome has not been studied. Here, we first analyzed the HSC markers in fetal 135 kidney through analysis of fetal kidney single cell dataset analyses. In human fetal kidney cortex, we 136 137 found some cells expressing RUNX1 in a cluster of cells which harbored expression hematopoietic 138 markers (Cluster 9 on Fig. 1a and 1b). In cluster 9 of human fetal kidney sc-RNAseq, high expression of hematopoietic markers was confirmed by the presence of Serglycin (SRGN)-positive cells (Fig. 2a) 139 140 as well as cells expressing PTPRC alias CD45 Leukocyte Common Antigen and CD44 (receptor of 141 hyaluronic acid) (Fig. 2b). Serglycin (alias hematopoietic proteoglycan core protein) is a protein found 142 in secretory granules of myeloid cells as well as in platelets. Our analysis showed also the presence of 143 cells positive for MHC class II molecule HLA-DRA and CD74 (Fig. 2c) and most interestingly, cells expressing of hematopoietic transcription factors SPI1 and RUNX1 (Fig. 2d). Finally, in this cluster 9 144 145 of fetal kidney we found a higher expression of CXCR4 receptor of CXCL12 implicated in migration properties of HSCs (Fig. 2e). All these results allowed to suggest the presence of cells harboring 146 147 hematopoietic transcriptome in human fetal kidney.

We then analyzed the transcriptome of iPSC-derived kidney organoids and performed differential expression analysis of the kidney organoid versus parental iPSCs. Microarray analysis revealed important regulation of transcriptional program of these cells during their differentiation (Fig. 4a). This differentially expressed program allowed to discriminate group samples by unsupervised classification

(Fig. 4b). After functional enrichment performed on up-regulated genes during the differentiation 152 153 process of the iPSC-derived kidney organoids, we observed the induction of HSC markers such as 154 RUNX1 and CD34 (Fig. 4c). It is well established that RUNX1 along with a cis-regulatory elements integrating the GATA, ETS, and SCL transcriptional networks, plays a major role in HSC generation 155 156 [13]. We also found induction of FLI1 during the differentiation of iPSC-derived kidney organoid. SPI1 157 (alias PU.1), the main target downstream RUNX1 [14] is also a master regulator of hematopoiesis as 158 it prevents excessive HSC division and exhaustion by controlling the transcription of multiple cellcycle regulators [15]. Association of SPI1 and RUNX1 are comprised in a combination of 7 159 160 transcription factors which are sufficient to convert hemogenic endothelium into hematopoietic stem and progenitor cells that engraft myeloid, B and T cells in primary and secondary mouse recipients [16]. 161 In transcriptome analyses of iPSC-derived kidney organoids, we found an up-regulation of MYB which 162 163 is known to participate to cell fate decisions between erythropoiesis and megakaryopoiesis in human 164 hematopoiesis [17]. Amongst the hematopoietic transcripts identified in human fetal kidney cortex, we 165 have also detected the expression of which, CXCR4 in relation with its ligand CXCL12, is involved in 166 homing of hematopoietic cells to the bone marrow [18].

Our data has some limitations including the fact we can not exclude the presence of mesodermal cells 167 168 undergoing the fate of hematopoietic differentiation during our kidney organoid differentiation. Secondly, we could not identify the presence of cells with HSC functionality (self-renewal; 169 differentiation) in the current experiments. However these data suggest that at some point during 170 embryonic development, a special "kidney niche" could appear transiently in humans. The 171 172 identification of such a niche or its molecular counterparts could be of major interest to amplify human HSC for transplantation purposes, such has been described in zebrafish [4,19]. It is known that zebrafish 173 174 embryonic stromal trunk (ZEST) cells derived from the HSC emergence site are functionally similar to 175 the mammalian AGM niche cells. Moreover, ZEST cells and kidney cell lines have similar signaling 176 properties. [19,20]. Our results suggest that a "kidney microenvironmental niche" niche could be of 177 interest to generate conditions for HSC culture and expansion.

178

179 Materials and Methods

180 • KEY RESOURCES TABLE

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Antibodies		
Nephrin	Abcam	ab85379
DAPI	Sigma-aldrich	D9542
Chemicals, Peptides, and Recombinant		
Proteins		
Essential 8 basal medium	Thermo Fisher	A1516901
	Scientific	
Essential 8 supplement	Thermo Fisher	A1517101
	Scientific	
Geltrex® LDEV-Free Reduced Growth	Thermo Fisher	A1413202
Factor Basement Membrane Matrix	Scientific	
ROCK inhibitor	Global stem	GSR-6102
REAGENT or RESOURCE	SOURCE	IDENTIFIER
Experimental Models : Cell Lines		
Human iPSC: PB33	Human	-
Osmium tetroxide solution	Sigma-aldrich	75632
Glutaraldehyde grade I	Sigma-aldrich	G5882
Software and Algorithms		
ImageJ		

181

182 Generation of iPSC

183 The iPSC line used is this study was generated using Sendaï virus-mediated gene transfer of the four

184 "Yamanaka" factors as previously described (9).

185

186 Generation of Kidney organoids

iPSCs were maintained on Geltrex (Stem Cell Technologies, Inc) coated flat culture dish in E8 media 187 (Stem Cell Technologies, Inc) according to manufacturer's guidelines. Colonies were manually 188 189 harvested at 60-80% confluence. Cells were then collected and dissociated into single cells using EDTA. 190 Cells (1x10⁶ or 1x10⁵/well) were put onto ultra low attachment 24 well or 96 well plate (Corning, 191 Inc) to allow them to form aggregated in suspension with ROCK inhibitor (2-5 µmol). Cell aggregates were cultured in E8 medium (Stem Cell Technologies) with daily medium change for 6-7 days. Control 192 193 iPSC-A (iPSC-aggregates) were plated on a Geltrex (Stem Cell Technologies) in 96 well plate or 8 well 194 culture chamber. And then aggregates were treated E8 medium (Stem Cell Technologies) with daily 195 medium change for 12-14 days. Images were taken using a NIKON microscope.

196

197 Whole-mount immunostaining of 3D kidney organoids

Kidney organoids cultured on 96-well culture dishes were washed with phosphate-buffered saline (PBS),
fixed with 4% paraformaldehyde in PBS for 120 min, permeabilized with 0.2% Triton X-100 (Sigma)
in PBS and blocked in 10% serum. For nephrin staining, the antibody (Nephrin (Cat#ab85379; Abcam)
was diluted in PBS containing 10% serum and washed in PBS. Samples were incubated with secondary
antibodies in antibody dilution buffer, then washed in PBS. Nuclei were labeled with DAPI mounting
medium. Visualization and capture were realized with a Zeiss confocal microscope.

204

205 Transmission Electron Microscopy (TEM)

Kidney organoids were gently centrifuged, and pelleted before the TEM process as follows. The cells were fixed in 2.5% glutaraldehyde in phosphate-buffered saline (PBS) for 1h at 4°C, washed in PBS, and fixed in 1% osmium tetroxide in PBS for 1h. They were dehydrated in ascending series of graded ethyl alcohols, then in acetone. Each sample was infiltrated with the resin before being embedded in epoxy resin and polymerized for 72h. Semi-thin sections of about 0.5 to 1 μ m were obtained and colored with Toluidine blue before being examined via a light microscope with an associated digital camera, hooked to a computer for image processing and editing (Leica DC 300). Ultra thin sections of about
60/90 nm were contrasted with heavy metals (uranyl acetate and lead citrate) and were examined using
a Jeol 1010 transmission electron microscope at an accelerated voltage of 80kV. Images were
photographed on digital images Gatan Digital Micrograph : brure Erlangen 500w : camera and edited
by Image J and Microsoft Power Point.

217

218 Human fetal single cell transcriptome analysis

219 Dataset GSE112570 of Single Cell RNA-Sequencing allow to explore cellular heterogeneity of human 220 kidney cortical nephrogenic niche [8]. Experiments were performed with technology 10X Genomics single-cell RNA sequencing on two human kidney samples (17 weeks) respectively indexed in Gene 221 222 Expression Omnibus (GEO) database: GSM3073088, GSM3073089. Molecular index was realized: Chromium Single Cell 3' v2 single cell RNA-Seq of poly A selected mRNA kit (10X Genomics) and 223 Sequencing was processed on NextSeq 500 (Illumina). Bioinformatics base call by bcl2fastq v. 2.17; 224 225 reads were mapped using STAR 2.5.1b (Genome: GRCh37) and count tables were generated using the 226 Cell Ranger software version 1.3.1. Downstream bioinformatics single cell transcriptome analyses were performed in R software version 3.4.3. Digital matrix were built with both 10X MTX files and merged 227 228 in Seurat R-package version 2.3.0 [5] with package dependencies of matrix version 1.2-12, cowplot 229 0.9.2 and ggplot2 version 2.2.1 [21]. Batch correction was performed with canonical correlation on 230 thirty dimensions before mathematical dimension reduction with tSNE algorithm. Also, dplyr library 231 version 0.7.4 was used to generate intermediate table of best genes by cluster. Bioinformatics code to 232 perform these single cell analyses was deposed at the following web address:

233 <u>https://github.com/cdesterke/hsckidney/</u>.

234 Kidney organoid microarray analysis

Microarray Clariom S human was done on process total RNA from human WT iPSC and its derived kidney organoids in duplicates [9]. Expression matrix was built with CEL files generated on Affymetrix Station and normalized by RMA method with TAC version 4.0 software (Appliedbiosystems) (Irizarry et al., 2003). Differential expressed genes were estimated with linear models for microarray data

- 239 (LIMMA) algorithm by using a false discovery rate threshold less 5 percent [22]. Functional enrichment
- analysis on differential expressed genes was performed on WikiPathway database.
- 241

242 Author Contributions

JWH and AGT conceived, designed, analyzed data and wrote the manuscript. JWH performed all organoids experiments and performed confocal laser scanning microscopy with analysis. JLD performed TEM, CD analyzed bioinformatics data, ABG, FG, AGT analyzed data and supervised the project. JWH, CD and AGT wrote the paper.

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303	Figures	

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Fig. 1 Cell heterogeneity in human fetal kidney cortex by single cell transcriptome.

- **a** tSNE plot with eleven cell clusters from the combined analysis of the merged fetal kidney cortex (2
- 307 human kidneys 17 weeks; 7860 cells) after canonical correlation.
- **b** Heatmap with the expression pattern of the top five cluster-specific genes in 11 clusters identified in
- 309 human fetal kidney cortex.



Figure 2

Fig. 2 Hematopoietic transcripts detected in human fetal kidney cortex by single cell RNA sequencing.

- 329 **a** Violinplot of SRGN expression.
- **b** Violinplot of hematopoietic clusters of differentiation (PTPRC Alias CD45).
- 331 c Violinplot of expression of transcripts of differentiated hematopoietic cells (HLA-DRA: HLA-DR
- 332 Alpha).
- d Violinplot of expression of SPI1 (PU.1) and RUNX1.
- 334 e Violinplot of expression for CXCR4 receptor.

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336 Fig. 3 Characterization of human iPSC-derived kidney organoids.

- **a** Optical image of iPSC-derived kidney organoids at day+14. Scale bar : 100 μm.
- 338 **b** Confocal analysis and whole-mount staining for Nephrin in iPSC-derived kidney organoids showing
- nephron vesicles. Scale bar : 50 μm.
- 340 c Representative electron microscopy image of podocytes in iPSC-derived kidney organoid at day+ 14
- showing podocytes (P), podocyte foot process (Pfp) and cell-cell junctions (cj). Scale bar : 1 μm.



Figure 4

343 Fig. 4 Transcriptional program induced in kidney organoid derived from human iPSC.

- **a** Scatterplot of differential expressed genes found in transcriptome of kidney organoid versus iPSC.
- **b** Expression heatmap with unsupervised classification performed on differentially expressed genes
- induced during kidney organoid differentiation from iPSC.
- c Functional enrichment performed on WikiPathway database showing potential implication
 hematopoietic stem cell function during differentiation of kidney organoid derived from human iPSC.

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363 Supplemental Information



Sup fig 1

Fig. S1. Canonical correlation with batch correction between the two foetal kidneys process in single cell transcriptome.

- 367 (a) Factorial map showing superposition of the cells from the respective kidney during the canonical368 correlation.
- 369 **(b)** Profile of the shared correlation strength between the respective kidneys (30 dimensions); tSNE plot
- 370 post canonical correlation on the merged 2 kidneys.
- 371 (c) t-SNE dimension reduction of single cell transcriptome from human fetal kidney after batch
- 372 correction, cells from each kidney (respectively green and red) are plotted with t-SNE dimension
- 373 reduction algorithm and their distribution in the map confirmed a good batch correction during the
- analyses (canonical correlation with Seurat R-package).

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Sup fig 2

377 Fig. S2. Violinplot of cluster markers found in single cell sequencing after merging the fetal cortex

378 of two human kidneys.

379

BRON serghcein 0.0000 0.0255 0.037 0.039 FCERIO Fergment of Epi receptor in 0.4000 0.0000 0.0255 0.025 0.027 All coronin IA 0.0000 0.0000 0.0000 0.028 0.028 0.021 HA. main biscompatibility 8.5907 1.5564 0.322294 0.255 0.063 B mbbiter bistomenubility 3.57143 6.4711 1.1289 1.1289 0.858 0.019 CYR4 coropic, class I, B 7.13743 6.4711 1.1289 0.858 0.109 CYR4 coropic, class I, B 7.13743 6.4711 1.138077 0.385 0.109 CP74 moleculu 3.349	gene symbol	description	p val	p_val_a dj	avg_logFC cluster 9 / other clusters	percent of cells positives in cluster 9	percent of cells positives in others clusters
SROP SPECPA 0.0000 0.0000 0.0000 0.0000 TYROBD binding protein 0.0000 0.0000 0.842 0.003 AFIE 1 opendo 0.0000 0.0000 0.875 0.003 AFIE 1 opendo 0.0000 0.0000 0.875 0.003 COROL - 0.0000 0.0000 0.0000 0.825 0.007 COROL - 0.0000 0.0000 0.0000 0.825 0.028 Lysosomal protein 0.0000 0.0000 0.0000 0.0001 0.833 0.012 RLA major biolecompathility 8.5907 1.5543 3.328299 0.758 0.044 ARICIN Babori biolecompathility 3.5934 0.822 0.063 0.068 CXCRA Complex, class I, B 7.577 1.5517 1.719804 0.825 0.063 CYCRA complex, class I, C 0.444 3.4741 0.834 0.892 0.193 HLA-SE <td>SDCN</td> <td>• • • • • • • •</td> <td>0.00000</td> <td>0.00000</td> <td>2 5101000</td> <td>0.008</td> <td>0.011</td>	SDCN	• • • • • • • •	0.00000	0.00000	2 5101000	0.008	0.011
TYROB binding protein 0e:00 0e:00 0.0000 0.0000 AFI 1 0e:00 0.0000 0.0000 0.0000 PCERIO refinent of Lig receptor lg 0e:00 0.0000 0.025 0.025 COROI consini IA 0e:00 0.0000 0.025 0.028 A consini IA 0e:00 0.0000 1.856739 0.883 0.012 LAPIMS transcembrane 5 0.0000 1.856739 0.883 0.028 DRA complex_class I, DR aph 2.578 3.3328299 0.758 0.043 DRA complex_class I, DR aph 2.571 2.327066 0.808 0.0068 CXCR receford- Ke214 2.328299 0.758 0.043 DRA rajor bistocompatibility 5.7343 6.4721 0.825 0.068 CXCR receford- Ke244 1.1733 1.778307 0.888 0.193 CD4 Optimultal 3.94034 6.3295 0.908 0.219	SKGN	TYRO protein tyrosine kinase	0.00000	0.00000	3.5101006	0.908	0.011
allogarå infamumatory field 0.00000 0.00000 0.6470 0.875 0.039 PCERIO Fe fragment of [16 receptor 16 0.0000 0.0000 1.825761 0.825 0.007 COROT 0.0000 0.0000 1.952294 0.825 0.028 LAPTMS masmenhenze5 0.000 1.8565739 0.833 0.012 LAPTMS masmenhenze5 0.000 1.8565739 0.833 0.012 RAIGDI Rio Coll dissociation 1.63458 1.9126 - - - RAIGDI Rio Coll dissociation 1.63458 1.9126 - - - - RAIGDI Rio Coll dissociation 5.16156 9.35224 -	TYROBP	binding protein	0e+00	0e+00	2.6363035	0.842	0.003
PCR10 Fe fragment of IgE receptor Ig 0.00000 0.00000 0.0257601 0.825 0.007 COR01 acconsin IA 0.00000 0.00000 0.825 0.028 LAPTM iransembranes 0.00000 0.00000 0.8853 0.012 LAPTM iransembranes 0.0000 0.00000 0.8853 0.012 LAPTM iransembranes 0.0000 0.0000 0.8853 0.012 LAPTM iransembranes 0.0000 0.0000 0.883 0.012 RARILOR Roof Op dissocnition 1.0545 1.9129 0.738 0.044 RARILOR Roof Op dissocnition 1.0545 5.9120 2.2276666 0.808 0.0668 CXCAR receptor 4 8-214 5-213 1.7383077 0.888 0.109 major histocompatibility 5.0433 1.7383077 0.888 0.109 CYA CO74 mole Calsa 1, B 7-157 1.132072 0.908 0.219 detine tolde protein 2.23 2.54544 0	AIF1	allograft inflammatory factor 1	0.00000 0e+00	0.00000 0e+00	2.5726665	0.875	0.039
CORD1 Ontonin IA Oct-000 Possponal protein Out-00 Possponal protein Out-00 Possponal protein Out-00 Restrict Protein Restrict Protein Out-00 Restrict Protein Out-00 Restrict Protein Restrin Restrict Protein Restrin <td>FCER1G</td> <td>Fc fragment of IgE receptor Ig</td> <td>0.00000 0e+00</td> <td>0.00000 0e+00</td> <td>2.0257601</td> <td>0.825</td> <td>0.007</td>	FCER1G	Fc fragment of IgE receptor Ig	0.00000 0e+00	0.00000 0e+00	2.0257601	0.825	0.007
A Contain LA One Col 0.000 1.522.9 0.023 LATTMS transmembrane pathbility 0.0000 1.5567379 0.883 0.012 LATTMS transmembrane pathbility 0.0000 1.5567379 0.883 0.012 DRA complex: class IL DR alpha 0.0246 1.1780844 0.825 0.044 ARHGD1 No GDP discosiation 46:240 0.0236 1.1780844 0.825 0.063 CXCR receptor 4 8:211 0.2327 1.1780844 0.825 0.063 CXCR receptor 4 8:211 0.2327 1.1780847 0.063 CXCR receptor 4 8:211 0.2327 0.888 0.068 major histocompathbility 3:0148 5:4424 1.2382085 0.998 0.219 actin related protein 2:3 2:54694 4:64480 46:1480 46:1480 46:1480 CYBA cytochrome b:243 alpha chain 4:676 9:091 0.226 0.758 0.184 CYBA cytoc	CORO1	coronin 1 A	0.00000	0.00000	1.052204	0.825	0.028
LAPTUA ILAD 	A	lysosomal protein	0.00000	0.00000	1.952294	0.823	0.028
ILA major assocination 6.3906 1.5394 3.328299 0.758 0.044 ARHGD Rho GDP dissociation 10.348 19.119	LAPTM5	transmembrane 5	0e+00	0e+00	1.8567379	0.883	0.012
ARHGDI Rho GDP dissociation 1.05485 1.91129 Note of the second se	DRA	complex, class II, DR alpha	8.39007 3e-278	4e-273	3.3328299	0.758	0.044
D Initiation descension 16/200 17/05/00 0.022 0.0030 CXCR4 receptor 4 8e-214 5e-210 2.3270686 0.808 0.068 major histocompatibility 3.57343 6.4771 1.533 1.7383077 0.858 0.109 CD74 molecule 3.49344 6.32974 0.4853 0.892 0.103 major histocompatibility 3.00488 5.44453 0.892 0.103 0.103 extra clast protein 2/3 2.54694 4.61480 0.008 0.219 extra clast protein 2/3 2.54694 4.61480 0.800 0.183 extra clast protein 2/3 3.5484 0.009 0.226 0.758 0.184 EZR ezrin 2.669 3.665193 0.800 0.226 B2M beta-2-microglobulin 2.627 1.26857 0.975 0.874 FTL ferrith light chain 9-52 1.26457 0.975 0.837 GPX1 glutathione peroxidase 1 76-47 96-43	ARHGDI B	Rho GDP dissociation	1.05485	1.91129 0a 236	1 7160804	0.825	0.063
CXCR receptor 4 8 2:210 2:327086 0.808 0.068 mip biscompability 3.734 6.7471 1:53 1.7383077 0.558 0.109 CD74 CD74 molecule 9e-115 0.6111 3.0782853 0.892 0.103 mip biscompathility 3.048 5.44454 0.4290 0.634 0.4491 ARPC1B complex, submit 1B 5.4032 9.7884 0.4300 0.183 CYBA cytochrome b-245 alpha chain 4e-70 9.686 1.4584647 0.800 0.184 EZR carin 2.649 2.645 1.3655193 0.800 0.226 B2M beta-2-microglobulin 2.624 8.558 1.695188 0.992 0.874 FTI ferritin light chain 9.527 7.648 2.2176857 0.983 0.991 FYI profilin 4.547 1.018237 0.975 0.837 GYI glutathione peroxidae 7.47139 4.2176857 0.983 0.903	Б	C-X-C motif chemokine	5.16156	9.35224	1./109804	0.823	0.005
HLA-B complex, class 1, 8 7e-17 1e-153 1.7383077 0.858 0.109 CD74 CD74 molecule 9e-115 0e-111 3.078285 0.892 0.193 major histocompatibility 3.00488 5.44454 0.089 0.219 actin related protein 2/3 2.54094 4.61480 0.000 0.183 ARCIB complex submit IB 4e-90 9e-86 1.458467 0.800 0.183 CYBA cytochrome b-245 alpha chim 4e-76 9e-72 1.268269 0.758 0.814 EZR ezrin 2.690 3.6511 1.665193 0.800 0.226 B2M beta-2-microglobulin 2.6223 4.7519 0.991 0.991 FTI ferritin light chain 9e-52 7e-44 2.2176857 0.983 0.991 glutathione peroxidas 7e-47 9e-43 1.647589 0.883 0.556 GPX1 glutathione peroxidas 7e-41 0.907703 0.983 0.991 Artizyme1	CXCR4	receptor 4	8e-214	5e-210	2.3270686	0.808	0.068
CD74 CD74 nolecule 349344 6.32978 0.892 0.193 major histocompatibility 3.00488 5.44454 0.808 0.219 HLA-C complex, class 1, C 0.694 3.690 1.6342965 0.908 0.219 ARPC1B complex, class 1, C 0.694 3.690 1.6342965 0.800 0.183 CYBA extochrome b-245 alpha chain 4e-70 9e-72 1.268269 0.758 0.184 CYBA extochrome b-245 alpha chain 4e-76 9e-72 1.268269 0.800 0.226 EZR exrin 2e-63 3.6451 1.365193 0.800 0.226 EZR exrin 2e-64 3.6451 1.268267 0.983 0.991 B2M beta-2-microglobulin 2e-52 7e-48 2.176857 0.983 0.991 FTL ferritin light chain 9e-52 7e-44 1.018237 0.975 0.837 GPX1 glutathione peroxidas 1 7e-47 9e-43 1.647589 0	HLA-B	major histocompatibility complex, class I, B	3.57343 7e-157	6.47471 1e-153	1.7383077	0.858	0.109
CD/4 De1/11 De1/11 <thde1 11<="" th=""> <thde1 11<="" th=""> <thde1 11<="" th=""></thde1></thde1></thde1>	CD74	CD74 malaquia	3.49344	6.32978 0a 111	2 0792952	0.802	0.102
HLA-C complex, clash, C 0.e94 3.e-90 1.642965 0.908 0.219 ARPC1B complex subunit 1B 4e-90 9e-86 1.4584647 0.800 0.183 CYBA cytochrome b-245 alpha chait 4e-76 9e-72 1.268269 0.758 0.184 CYBA cytochrome b-245 alpha chait 4e-76 9e-72 1.268269 0.758 0.184 CYBA cytochrome b-245 alpha chait 4e-76 9e-72 1.268269 0.902 0.874 EZR czrin 2.60234 4.7519 0.800 0.226 FTL ferritin light chain 9e-52 7e-48 2.2176857 0.983 0.991 FTL ferritin light chain 9e-52 7e-48 2.2176857 0.883 0.556 GPX1 glutathione proxidase1 7e-47 9e-43 1.018237 0.993 0.903 GPX1 glutathione proxidase1 7e-47 9e-43 1.018678 0.917 0.663 GPX1 attraber chy rotyotin 23	CD/4	major histocompatibility	3.00488	5.44454	5.0782855	0.892	0.195
actin related protein 2/3 2.54694 4.61480 0 0.800 0.183 CYBA cytochrome b-245 alpha chait 4-76 9-72 1.268269 0.758 0.184 EZR cytochrome b-245 alpha chait 4-76 9-72 1.268269 0.758 0.184 EZR czrin 2-69 3-65 1.3665193 0.800 0.226 B2M beta-2-microglobulin 2-622 8-781 1.695188 0.992 0.874 FTI ferritin light chain 9-52 7-648 2.2176857 0.983 0.991 FTI ferritin light chain 9-52 7-648 2.176857 0.983 0.556 GPX1 glutathione peroxidase 1 7-647 9-643 1.647889 0.883 0.556 GPX1 glutathione peroxidase 1 7-647 9-643 1.647889 0.883 0.903 ARPC3 complex subunit 3 6-44 9-40 1.0166798 0.917 0.663 St13 domain binding 2.34788 4.25412	HLA-C	complex, class I, C	0e-94	3e-90	1.6342965	0.908	0.219
CYBA statum 5.40233 9.78848 0.758 0.184 CYBA cytochrome b-245 alpha chai 4c-76 9-c72 1.28209 0.758 0.184 EZR ezrin 2c-69 3c-65 1.3665193 0.800 0.226 B2M beta-2-microglobulin 2c-62 8c-58 1.6959188 0.992 0.874 FTL ferritin light chain 9c-52 7c-48 2.2176857 0.803 0.991 FTL profilin 4c-51 4c-47 1.1018237 0.975 0.837 GPX1 glutathione peroxidase 1 7c-47 9c-43 1.647589 0.883 0.556 Ornithine decarboxylase 2.8807 5.21967 0.997703 0.983 0.903 ARPC3 complex submit 3 9c-44 9c-40 1.0166798 0.917 0.663 ARPC3 complex submit 3 9c-44 9c-30 1.2094052 0.908 0.559 SATI accytitransferase 1 6c-41 5c-37 2.4500195	ARPC1B	complex subunit 1B	2.54694 4e-90	4.61480 9e-86	1.4584647	0.800	0.183
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	CVDA	and always 1, 245 alwha alwin	5.40233	9.78848	1 2(82(0	0.759	0.194
EZR exrin 2e-69 3e-65 1.3665193 0.800 0.226 B2M beta-2-microglobulin 2e-62 8e-58 1.6959188 0.992 0.874 FTL ferritin light chain 9e-52 7.e48 2.2176857 0.983 0.991 FTL ferritin light chain 9e-52 7.e48 2.2176857 0.983 0.991 PFN1 profilin 1 de-51 4e-47 1.1018237 0.975 0.837 GPX1 glutathione peroxidase 1 7e-47 9e-43 1.647589 0.883 0.903 OAZI antizyme 1 6e-45 7e-41 0.9077703 0.983 0.903 Complex suburit 3 9e-44 9e-40 1.0166798 0.917 0.663 SH3060 SH3 domain binding 2.34718 4.27412 ARPC3 complex suburit 3 9e-44 9e-40 1.0066798 0.917 0.663 SH3060 SH3 domain binding 2.34718 4.26494	CIDA	cytochrome 0-245 alpha chain	3.36348	6.09429	1.208209	0.758	0.164
B2M beta-2-microglobulin 2e-62 8:58 1.6959188 0.992 0.874 FTL ferritin light chain 9e-52 7e-48 2.2176857 0.983 0.991 FTL ferritin light chain 9e-52 7e-48 2.2176857 0.983 0.991 FTL ferritin light chain 9e-52 7e-48 2.2176857 0.975 0.837 GPX1 glutathione peroxidase 1 7e-47 9e-43 1.647589 0.883 0.556 Ormithine decarboxylase 2.8077 5.21967 0.977703 0.983 0.903 actin related protein 2/3 2.4718 4.47935 0.907703 0.983 0.559 SH3BGR SH3 domain binding 2.4718 4.47935 0.908 0.559 SH3 domain binding 2.4718 4.25412 0.908 0.559 0.908 0.559 SH3 domain binding 2.43748 4.25412 0.908 0.559 0.908 0.559 SAT1 acetryltransferase 1 6e-37 2.4506195	EZR	ezrin	2e-69	3e-65	1.3665193	0.800	0.226
FTL ferritin light chain 9-52 7-248 2.2176857 0.983 0.991 PFN1 profilin 1 4c-51 4c47 1.1018237 0.975 0.837 GPX1 glutathione peroxidase 1 7c-47 9c43 1.647589 0.883 0.556 OAZ1 antizyme 1 6c-45 7c-41 0.907703 0.983 0.903 actin related protein 2/3 2.47218 4.47935 - - - ARC3 complex subunit 3 9c-44 9c-49 1.0166798 0.917 0.663 SH3BGR SH3 domain binding 2.34788 4.25112 - - - L3 glutamate rich protein lik 3 3c-43 9c-39 1.2094052 0.908 0.559 SAT1 acetyltransferase 1 6c-41 5c-37 2.4506195 0.883 0.584 TMSB4X thymosin beta 4 X-linked 6c-39 8c-35 0.9379118 1.000 0.9977 TMSB4X thymosin beta 4 X-linked 6c-39 8c-35 <td>B2M</td> <td>beta-2-microglobulin</td> <td>3.75702 2e-62</td> <td>6.80734 8e-58</td> <td>1.6959188</td> <td>0.992</td> <td>0.874</td>	B2M	beta-2-microglobulin	3.75702 2e-62	6.80734 8e-58	1.6959188	0.992	0.874
PFN1 profilin 1 3.77142 6.83344 0.975 0.837 GPX1 glutathione peroxidase 1 7c.47 9c.43 1.1018237 0.975 0.837 GPX1 glutathione peroxidase 1 7c.47 9c.43 1.647589 0.883 0.556 OAZI antizyme1 6c.45 7c.41 0.907703 0.983 0.903 actin related protein 2/3 2.47118 4.47935 0.907703 0.983 0.903 SHBGR SH3 domain binding 2.34784 4.25412 0.907703 0.908 0.559 SAT1 acetyltransferase 1 6c.41 5e.37 2.4506195 0.883 0.584 SAT1 acetyltransferase 1 6c.41 5e.37 2.4506195 0.883 0.584 TMSB4X hymosin beta 4 X-linked 6c.39 7.31927 0.9379118 1.000 0.997 Tropomyosin 3 9c-39 7c.35 0.9303993 0.867 0.486 SQSTM1 sequestosome 1 1e-37 5e-33 1.2387851	FTL	ferritin light chain	2.62243 9e-52	4.75159 7e-48	2.2176857	0.983	0.991
PFN1 profilm 1 4e-31 4e-47 1.1018237 0.975 0.887 GPX1 glutathione peroxidase 1 7e-47 9e-43 1.647589 0.883 0.556 orrithine decarboxylase 2.88077 5.21967 9 9 9 9 actin related protein 2/3 2.47218 4.47935 9	2224		3.77142	6.83344			
GPX1 glutathione peroxidase 1 7e-47 9e-43 1.647589 0.883 0.556 ornithine decarboxylase 2.88077 5.21967 0.907703 0.983 0.903 actin related protein 2/3 2.47218 4.47935 0.907703 0.983 0.903 ARPC3 complex subunit 3 9e-44 9e-40 1.0166798 0.917 0.663 SH3BGR SH3 domain binding 2.34788 4.25412 Sh13 domain binding 2.34788 4.25412 SAT1 acetyltransferase 1 6e-41 5e-37 2.4506195 0.883 0.5584 TMSB4X thymosin beta 4 X-linked 6e-39 8e-35 0.9303993 0.867 0.486 TPM3 tropomyosin 3 9e-39 7e-33 1.2387851 0.833 0.377 SQSTM1 sequestosome 1 1e-36 4e-32 0.9370998 0.908 0.695 McCar paraspeckle assembly 1.67148 3.02875	PFN1	profilin l	4e-51 2.41810	4e-47 4.38136	1.1018237	0.975	0.837
OAZI antizyme 1 6e-45 7.e-41 0.9077703 0.983 0.903 ARPC3 complex subunit 3 9e-44 1.0166798 0.917 0.663 SH3GC3 SH3 domain binding 2.34788 4.24721 4.47935 0.903 L3 glutamate rich protein like 3 3e-43 9e-39 1.2094052 0.908 0.559 SAT1 acetyltransferase 1 6e-41 5e-37 2.4506195 0.883 0.584 TMSBAX thymosin beta 4 X-linked 6e-39 8e-35 0.9303993 0.867 0.486 TPM3 tropomyosin 3 9e-39 7.e-35 0.9303993 0.867 0.486 SQSTM1 sequestosme 1 1e-37 5e-33 1.2387851 0.833 0.377 actin related protein 2/3 1.54151 2.79306 NEAT1 transcript 1 0e-33 3.e249 0.917 0.674 REL proto-oncogene, NF-kB 7.49099 3.61814 <	GPX1	glutathione peroxidase 1	7e-47	9e-43	1.647589	0.883	0.556
actin related protein 2/3 complex subunit 3 2.47218 4.47935 Methods 0.016798 0.917 0.663 SH3B0GR SH3 domain binding glutamate rich protein like 3 3e-43 9e-39 1.2094052 0.908 0.559 SAT1 acetyltransferase 1 6e-41 5e-37 2.4506195 0.883 0.584 SAT1 acetyltransferase 1 6e-41 5e-37 2.4506195 0.883 0.594 TMSB4X thymosin beta 4 X-linked 6e-39 8e-35 0.9379118 1.000 0.997 TPM3 tropomyosin 3 9e-39 7.235 0.9303993 0.867 0.486 SQSTM1 sequestosome 1 1e-37 5e-33 1.2387851 0.833 0.377 ARPC2 complex subunit 2 1.54151 2.79306 0.9008 0.695 MEAT1 transcript 1 0e-36 4e-32 0.9370998 0.9017 0.674 SUSTM1 sequestosome 1 16.7148 3.02855 1.104068 0.917 0.674 CST3 <td< td=""><td>OAZ1</td><td>antizyme 1</td><td>2.88077 6e-45</td><td>5.21967 7e-41</td><td>0.9077703</td><td>0.983</td><td>0.903</td></td<>	OAZ1	antizyme 1	2.88077 6e-45	5.21967 7e-41	0.9077703	0.983	0.903
ARPC2 Complex studint 3 26-44 96-40 1.0100/98 0.917 0.003 SH3BGR SH3 domain binding 2.34788 4.25412 0.908 0.559 spermidine/spermine N1- 4.57738 8.29376 0.883 0.584 sacetyltransferase 1 6e-41 5e-37 2.4506195 0.883 0.584 TMSB4X thymosin beta 4 X-linked 6e-39 8e-35 0.9379118 1.000 0.997 TPM3 tropomyosin 3 9e-39 7e-35 0.9303993 0.867 0.486 SQSTMI sequestosome 1 1e-37 5e-33 1.2387851 0.833 0.377 actin related protein 2/3 1.54151 2.79306 0.9303998 0.908 0.695 nuclear paraspeckle assembly 1.67148 3.02855 0.917 0.674 CST3 cystain C 7e-33 2e-29 2.1934329 0.917 0.674 CST3 cystain C 7e-33 2e-29 2.1934329 0.792 0.581 REL subunit 5e-33 3e-28 1.104068 0.758 <td< td=""><td>A DDC2</td><td>actin related protein 2/3</td><td>2.47218</td><td>4.47935</td><td>1.0166708</td><td>0.017</td><td>0.663</td></td<>	A DDC2	actin related protein 2/3	2.47218	4.47935	1.0166708	0.017	0.663
L3 glutamate rich protein like 3 3e-43 9e-39 1.2094052 0.908 0.559 SAT1 acetyltransferase 1 6e-41 5e-37 2.4506195 0.883 0.584 TMSB4X thymosin beta 4 X-linked 6e-39 8e-35 0.9379118 1.000 0.997 TMSB4X thymosin beta 4 X-linked 6e-39 8e-35 0.9303993 0.867 0.486 TPM3 tropomyosin 3 9e-39 7e-35 0.9303993 0.867 0.486 SQSTM1 sequestosome 1 1e-37 5e-33 1.2387851 0.833 0.377 ARPC2 complex subunit 2 1e-36 4e-32 0.9370998 0.908 0.695 NEAT1 transcript 1 0e-36 4e-32 1.6546878 0.917 0.674 CST3 cystatin C 7e-33 2e-29 2.1934329 0.792 0.581 REL proto-oncogene, NF-kB 7.40909 1.35729 6.257 0.975 0.993 TPT1 controlled 1 0e-	SH3BGR	SH3 domain binding	2.34788	4.25412	1.0100798	0.917	0.005
SAT1 acetyltransferase 1 6-41 5-e37 2.4506195 0.883 0.584 TMSB4X thymosin beta 4 X-linked 6e-39 8e-35 0.9379118 1.000 0.997 TPM3 tropomyosin 3 9e-39 7e-35 0.9303993 0.867 0.486 SQSTM1 sequestosome 1 1e-37 5e-33 1.2387851 0.833 0.377 actin related protein 2/3 1.54151 2.79306 ARPC2 complex subunit 2 1e-36 4e-32 0.9370998 0.908 0.695 nuclear paraspeckle assembly 1.67148 3.02855 . NEAT1 transcript 1 0e-36 4e-32 1.6546878 0.917 0.674 CST3 cystatin C 7e-33 2e-29 2.1934329 0.792 0.581 REL proto-oncogene, NF-kB 3.61814 TPT1 controlled 1 0e-32 4e-28 0.5573017 1.000 <td>L3</td> <td>glutamate rich protein like 3</td> <td>3e-43</td> <td>9e-39</td> <td>1.2094052</td> <td>0.908</td> <td>0.559</td>	L3	glutamate rich protein like 3	3e-43	9e-39	1.2094052	0.908	0.559
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	SAT1	acetyltransferase 1	4.57738 6e-41	8.29376 5e-37	2.4506195	0.883	0.584
HMSB4X thymosin beta 4 X-linked 6e-39 8e-35 0.9379118 1.000 0.997 TPM3 tropomyosin 3 9e-39 7.31927 -			2.35164	4.26094	0.0270110	1.000	0.007
TPM3 tropomyosin 3 9e-39 7e-35 0.9303993 0.867 0.486 SQSTM1 sequestosome 1 1.9626 2.16750 - <t< td=""><td>TMSB4X</td><td>thymosin beta 4 X-linked</td><td>4.03955</td><td>8e-35 7.31927</td><td>0.93/9118</td><td>1.000</td><td>0.997</td></t<>	TMSB4X	thymosin beta 4 X-linked	4.03955	8e-35 7.31927	0.93/9118	1.000	0.997
SQSTM1 sequestosome 1 1.9626 2.16/50 0.833 0.377 actin related protein 2/3 complex subunit 2 1.54151 2.79306 0.908 0.695 ARPC2 complex subunit 2 1e-36 4e-32 0.9370998 0.908 0.695 nuclear paraspeckle assembly 1.67148 3.02855 0.917 0.674 NEAT1 transcript 1 0e-36 4e-32 1.6546878 0.917 0.674 CST3 cystatin C 7e-33 2e-29 2.1934329 0.792 0.581 REL subunit 5e-33 3e-28 1.104068 0.758 0.357 TPT1 controlled 1 0e-32 4e-28 0.5573017 1.000 0.999 HSPD1 heat shock protein family D 3e-31 7e-26 0.7874673 0.975 0.933 FTH1 ferritin heavy chain 1 8e-29 6e-25 1.4701043 1.000 0.999 LBA52 product 1 9e-28 9e-24 0.4379137 0.983 0.994 <	TPM3	tropomyosin 3	9e-39	7e-35	0.9303993	0.867	0.486
actin related protein 2/3 complex subunit 2 1.54151 le-36 2.79306 4e-32 0.908 0.695 NRPC2 nuclear paraspeckle assembly transcript 1 1.67148 3.02855 0.917 0.674 NEAT1 transcript 1 0e-36 4e-32 1.6546878 0.917 0.674 CST3 cystatin C 7e-33 2e-29 2.1934329 0.792 0.581 REL subunit 5e-33 3e-28 1.104068 0.758 0.357 TPT1 controlled 1 0e-32 4e-28 0.5573017 1.000 0.999 HSPD1 heat shock protein family D 3e-31 7e-26 0.784673 0.975 0.933 FTH1 ferritin heavy chain 1 8e-29 6e-25 1.4701043 1.000 0.999 UBA52 product 1 9e-28 9e-24 0.4379137 0.983 0.994	SQSTM1	sequestosome 1	1.19626 1e-37	2.16750 5e-33	1.2387851	0.833	0.377
ARPC2 complex subunit 2 1e-36 4e-32 0.937/0998 0.908 0.698 0.695 nuclear paraspeckle assembly 1.67148 3.02855 - <	ADDCO	actin related protein 2/3	1.54151	2.79306	0.0270000	0.000	0.005
NEAT1 transcript 1 0e-36 4e-32 1.6546878 0.917 0.674 CST3 cystatin C 7e-33 2e-29 2.1934329 0.792 0.581 CST3 cystatin C 7e-33 2e-29 2.1934329 0.792 0.581 REL subunit 5e-33 3e-28 1.104068 0.758 0.357 TPT1 controlled 1 0e-32 4e-28 0.5573017 1.000 0.999 HSPD1 heat shock protein family D 3e-31 7e-26 0.7874673 0.975 0.933 FTH1 ferritin heavy chain 1 8e-29 6e-25 1.4701043 1.000 0.999 UBA52 product 1 9e-28 9e-24 0.4379137 0.983 0.994	ARPC2	nuclear paraspeckle assembly	1.67148	4e-32 3.02855	0.9370998	0.908	0.695
CST3 cystain C 76-33 2e-29 2.1934329 0.792 0.581 REL roto-oncogene, NF-kB 7.49099 1.35729	NEAT1	transcript 1	0e-36	4e-32	1.6546878	0.917	0.674
REL proto-oncogene, NF-kB 7.49099 1.35729 6 6 6 REL subunit 5e-33 3e-28 1.104068 0.758 0.357 Image: REL proto-oncogene, NF-kB 5e-33 3e-28 1.104068 0.758 0.357 Image: REL proto-oncogene, NF-kB 5e-33 3e-28 1.104068 0.758 0.357 Image: REL proto-oncogene, NF-kB 1.07574 1.94913 1.94913 0.357 0.999 TPT1 controlled 1 0e-32 4e-28 0.5573017 1.000 0.999 HSPD1 heat shock protein family D 3e-31 7e-26 0.7874673 0.975 0.933 FTH1 ferritin heavy chain 1 8e-29 6e-25 1.4701043 1.000 0.999 Image: Rel protein fusion 2.63523 4.77478 1.000 0.999 1.000 UBA52 product 1 9e-28 9e-24 0.4379137 0.983 0.994	CST3	cystatin C	1.99687 7e-33	3.61814 2e-29	2.1934329	0.792	0.581
tumor protein, translationally- controlled 1 1.07574 1.94913 4e-28 1.000 0.999 HSPD1 heat shock protein family D 6.13724 1.11200 3e-31 0.7874673 0.975 0.933 FTH1 ferritin heavy chain 1 8e-29 6e-25 1.4701043 1.000 0.999 UBA52 product 1 9e-28 9e-24 0.4379137 0.983 0.994	REL	REL proto-oncogene, NF-kB subunit	7.49099 5e-33	1.35729 3e-28	1.104068	0.758	0.357
IP11 controlled I 0e-32 4e-28 0.55/301/ 1.000 0.999 HSPD1 heat shock protein family D 3e-31 7e-26 0.7874673 0.975 0.933 FTH1 ferritin heavy chain 1 8e-29 6e-25 1.4701043 1.000 0.999 ubiquitin A-52 residue ribosomal protein fusion 2.63523 4.77478 6.4379137 0.983 0.994	7071	tumor protein, translationally-	1.07574	1.94913	0.5572017	1 000	0.000
HSPD1 heat shock protein family D 3e-31 7e-26 0.7874673 0.975 0.933 FTH1 1.73854 3.15007 1.000 0.999 FTH1 ferritin heavy chain 1 8e-29 6e-25 1.4701043 1.000 0.999 ubiquitin A-52 residue ribosomal protein fusion 2.63523 4.77478 4.77478 4.77478 9e-24 0.4379137 0.983 0.994	TEL	controlled 1	0e-32 6.13724	4e-28	0.5573017	1.000	0.999
FTH1 ferritin heavy chain 1 8e-29 6e-25 1.4701043 1.000 0.999 ubiquitin A-52 residue ribosomal protein fusion 2.63523 4.77478 1.4701043 1.000 0.999 UBA52 product 1 9e-28 9e-24 0.4379137 0.983 0.994	HSPD1	heat shock protein family D	3e-31	7e-26	0.7874673	0.975	0.933
ubiquitin A-52 residue ribosomal protein fusion2.635234.774780.43791370.983UBA52product 19e-289e-240.43791370.9830.994	FTH1	ferritin heavy chain 1	1.73854 8e-29	3.15007 6e-25	1.4701043	1.000	0.999
UBA52 product 1 2.05325 4.7/478 0.4379137 0.983 0.994		ubiquitin A-52 residue	2 62522	1 77170			
	UBA52	product 1	2.03323 9e-28	9e-24	0.4379137	0.983	0.994

	MCL1, BCL2 family	9.75888	1.76821			
MCL1	apoptosis regulator	7e-28	3e-23	0.9316168	0.758	0.393
HSPH1	heat shock protein family H	4.92136 8e-26	8.91702 7e-22	0.8444851	0.942	0.796
	ribosomal protein lateral stalk	7.35494	1.33264			
RPLP1	subunit P1	2e-26	2e-21	0.3610463	1.000	1.000
COTL1	protein 1	5.24024 6e-25	1e-21	1.0506476	0.817	0.520
G. 13.61		1.19590	2.16685			0.000
CALM1	calmodulin l	2e-23	5e-19 4 26443	0.7064824	0.900	0.609
CLIC1	1	1e-23	6e-19	0.7654192	0.850	0.560
LISDE1	haat ahaalt matain family E	8.89503 0a 22	1.61169	0.6220022	0.075	0.026
HSPEI	eukarvotic translation	3.57260	6.47320	0.0329032	0.975	0.936
EEF1B2	elongation factor 1 beta 2	7e-22	6e-18	0.580957	0.933	0.876
UBC	ubiquitin C	1.03192 8e-21	1.86975 1e-17	0 8486491	0.992	0.950
CDC		3.13017	5.67156	0.0100101	0.972	0.750
ATP5E	FAU	8e-21	9e-17	0.4818868	0.967	0.966
FAU	ribosomal protein S30 fusion	2.20199 2e-20	3.98979 0e-16	0.3237957	0.992	0.998
	NPC intracellular cholesterol	2.95118	5.34724			
NPC2	transporter 2 ribosomal protein lateral stalk	1e-20 4 54839	6e-16 8 24124	1.1277988	0.783	0.594
RPLP2	subunit P2	7e-18	1e-14	0.2593048	0.992	1.000
SEDD1	stress associated endoplasmic	1.03484	1.87502 7a 12	0.4802011	0.967	0.660
SERPI	reticulum protein 1	1.15185	2.08704	0.4892011	0.807	0.009
PABPC1	poly	5e-15	5e-11	0.4134638	0.967	0.948
SLC25A	solute carrier family 25	1.77520	3.21649	0 5403144	0.808	0.737
5	eukaryotic translation	2.33957	4.23907	0.5405144	0.000	0.757
EIF1	initiation factor 1	3e-14	2e-10	0.3121184	1.000	0.998
SELK		2.54124 0e-14	4.60447 3e-10	0.7817369	0.842	0.716
	S100 calcium binding protein	6.34918	1.15040			
S100A11	A11	7e-14	9e-09	0.8247093	0.758	0.633
SERF2	small EDRK-rich factor 2	9.11/04 4e-14	7e-09	0.2917475	0.992	0.986
MODIA		1.15830	2.09873	0.5100016		0.405
NOPIO	NOP10 ribonucleoprotein	4e-13 3.75832	1e-09 6.80970	0.5102016	0.758	0.487
RPS28	ribosomal protein S28	5e-13	9e-09	0.2564121	1.000	1.000
CAP7B	capping actin protein of	4.34631 3e-13	7.87508 4e-09	0 5952878	0.758	0.592
CALT		8.45317	1.53163	0.3932878	0.758	0.392
RPS29	ribosomal protein S29	6e-13	1e-08	0.2746119	1.000	1.000
DNAJB1	family	1.98858 2e-12	3.60311 3e-08	0.5654268	0.933	0.841
		2.47872	4.49120			
SDCBP	syndecan binding protein	7e-12	5e-08	0.6616057	0.758	0.557
BTG1	1	2.74009 2e-12	4.90380 0e-08	0.8923802	0.775	0.601
DCAD		9.04875	1.63954	0.((05145	0.022	0.7(7
PSAP	prosaposin	3.68232	3e-07 6.67200	0.6605145	0.833	0.767
DUSP1	dual specificity phosphatase 1	5e-11	4e-07	0.4921929	0.817	0.564
COX411	cytochrome c oxidase subunit	5.71414 4e-11	1.03534 6e-06	0 2968962	0.933	0.936
007411	ubiquitin conjugating enzyme	1.19968	2.17370	0.2708702	0.755	0.750
UBE2D3	E2 D3	1e-10	2e-06	0.3807076	0.883	0.792
A1	family class A member 1	5.50009 0e-10	3.97943 4e-06	0.4127855	1.000	0.999
	_	5.38698	9.76067			
PCBP1	poly	2e-10	2e-06	0.4278739	0.842	0.716
YBX1	Y-box binding protein 1	0e-10	4e-05	0.3772188	0.833	0.837
CEL 1	aofilin 1	7.88459	1.42860	0.2672521	0.083	0.074
CrLI		1.05218	1.90645	0.20/2331	0.703	0.7/4
ACTB	actin beta	7e-09	8e-05	0.3932285	1.000	0.999

ĺ	1	3.33086	6.03519			1
PGK1	phosphoglycerate kinase 1	6e-09	6e-05	0.4577908	0.758	0.643
	SUB1 homolog,	3.34726	6.06490			
SUB1	transcriptional regulator	4e-09	9e-05	0.3576456	0.908	0.857
		3.75381	6.80154			
H3F3B	H3 histone family member 3B	7e-09	1e-05	0.3144709	0.992	0.993
	DnaJ heat shock protein	2.32612	4.21471			
DNAJB6	family	9e-07	3e-03	0.4016447	0.925	0.868
		3.19623	5.79126			
CSTB	cystatin B	7e-07	1e-03	0.4852028	0.767	0.624
		1.30452	2.36367			
RHOA	ras homolog family member A	7e-06	2e-02	0.2910496	0.858	0.814
		2.97978	5.39907			
HSPA1A	heat shock protein family A	5e-06	2e-02	0.331032	0.942	0.994
		3.51673	6.37197			
HSPB1	heat shock protein family B	7e-06	5e-02	0.4753915	0.925	0.941
	GC-rich promoter binding	5.38740	9.76144			
GPBP1	protein 1	6e-06	1e-02	0.4378892	0.800	0.769
	eukaryotic translation	2.65684	4.81392			
EIF4A1	initiation factor 4A1	0e-05	8e-01	0.2558842	0.958	0.966
	serine and arginine rich	1.01351	1.00000			
SRSF7	splicing factor 7	1e-03	0e+00	0.3631672	0.800	0.726
		1.38276	1.00000			
GPX4	glutathione peroxidase 4	5e-03	0e+00	0.2528755	0.817	0.758
		2.66107	1.00000			
ENO1	enolase 1	9e-02	0e+00	0.2645355	0.742	0.769

381

382 Table S1-Table presenting differential expressed genes found in cluster 9 as compared to others

383 clusters in human fetal kidney cortex.