

Supplementary Figure 1

Supplementary Fig. 1. PRSS35 is a secreted protein that decreased in HCC patients

a, Proteomic analysis and comparison of THLE3 and PLC secretome (with non-classical secreted proteins) presented as a volcano plot. The red transverse dashed line indicates adjusted *P*-value of 0.05. The left black longitudinal dashed line indicates a fold-change (FC) of 0.5 and the right black longitudinal dashed line indicates a FC of 2.0. Orange dots: significantly increased proteins in THLE3 secretome (P < 0.05, FC > 2.0). Green dots: significantly decreased proteins in THLE3 (P < 0.05, FC < 0.5). The experiment was repeated three times (left panel). Diagram of the screening strategy for PRSS35 being the most significantly decreased secreted protein in HCC (right panel)

b, Western blot analysis of intracellular (Lys: lysate) and extracellular (Sup: supernatant) PRSS35 protein levels with anti-N-PRSS35 antibody in PLC, HepG2 and Hep3B cells stably expressing PRSS35 or EV. Ponceau staining and β -actin served as loading control.

c, Schematic diagram of the antigen sequences of three PRSS35 antibodies.

d, PRSS35 protein levels were determined with three different antibodies by western blot using the paired human HCC tissues (T) and adjacent non-cancerous liver tissues (N). Ponceau staining and calnexin served as loading control. FL: full length. SF: short form.

e, Representative IHC images of PRSS35 staining in normal liver tissues (normal) and HCC specimens of different clinical stages I-IV (healthy donors, n=20; patients with HCC, stage I (n=12), II (n=92), III (n=38) and IV (n=16)). Antibody against C-PRSS35 was used (left panel). Statistical quantification of the mean optical density (MOD) values for PRSS35 staining in IHC assay (right panel).

f, Kaplan-Meier curves with univariate analyses of patients with low versus high PRSS35 expression.

g, Schematic diagram of the antigen sequences of antibody pairs used in ELISA kit.

h, The standard curve of PRSS35 ELISA kit. We set ten diluted concentrations of purified PRSS35 domain1 protein fragment and determined the corresponding OD450 to calculate the linearity information.

i, Western blot analysis of PRSS35 protein when knocking down HNF4A with different shRNAs or overexpressing HNF4A in HepG2 cells. β -actin served as a loading control. FL: full length. SF: short form

j, Quantitative real-time PCR analysis of PRSS35 mRNA levels when knocking down HNF4A with different shRNAs or overexpressing HNF4A in HepG2 cells (n=3 biologically replicates).

k, A diagram shows the sites and sequences of potential HNF4A responsive elements (HREs) in *PRSS35* gene (upper panel). Luciferase assays were performed to identify HREs in *PRSS35* gene (lower panel, n=3 biologically replicates).

Data are presented as the mean \pm s.e.m. (e) or \pm s.d (j, k). Statistical significance was determined by two-tailed unpaired Student's t-test (a, e) or log-rank test (f, j, k). The blotting experiments were repeated at least three times with biological replicates (b, d, i). Source data are provided as a Source Data file.



Supplementary Fig. 2. PRSS35 activated by FURIN functions as a protease

a, Bands from (2a) were analyzed by mass spectrometry to identify PRSS35 cleavage sites. PRSS35 cleavage of β -casein at K43-K44 was monitored by LC-MS through not identifying peptides containing amino acids in front of K44 in cleaved β -casein band, but identifying full length β -casein band. Identified peptides from full length β -casein and cleaved β -casein were shown.

b, Conserved cleavage motifs by proprotein convertases (PCs) in PRSS35 protein sequence of five species.

c, His-PRSS35-domain1 protein purified from *E. coli* was incubated with β -casein protein at 37°C overnight, followed by SDS-PAGE and coomassie brilliant blue staining (left panel). His-PRSS35-domain1 signal was determined by western blot with anti-His antibody and N-PRSS35 antibody (right panel). D1: PRSS35-domain1.

d, Diagram of prediction of signal peptide in PRSS35.

e, Fluorescent absorbance monitored over time as a measurement of active peptidase activity of PRSS35-domain1 (left panel, n=3 biologically replicates). Sequences of three fluorescent peptides (right panel).

f, *E. coli* purified His-D1 and β -casein protein were incubated with DMSO, serine protease inhibitor 1 (PMSF) or serine protease inhibitor 2 (cocktails) at 37°C overnight, followed by SDS-PAGE and coomassie brilliant blue staining. His-D1 signal was determined by western blot with anti-His antibody. D1: PRSS35 domain1, Serine protease inhibitor 2 (cocktails) included Aprotinin, Bestatin, Leupetin, Pepstatin, PMSF, E-64, and Phosphoramidon.

g, *E. coli* purified wild type His-D1 or mutated His-D1 protein (serine to alanine mutation) as indicated was incubated with β -casein protein at 37°C overnight, followed by SDS-PAGE and coomassie brilliant blue staining. wild type His-D1 and His-D1-mutation signals were determined by western blot with anti-His antibody.

Data are presented as the mean \pm s.d. (e). Statistical significance was determined by two-way ANOVA (e). The blotting experiments were repeated at least three times with biological replicates (c, f, g). Source data are provided as a Source Data file.



Supplementary Fig. 3. PRSS35 suppresses neutrophil migration by degrading CXCL2

a, Growth curves of HepG2, PLC, Hepa1-6, and Hep3B cells stably expressing EV or PRSS35 (mPRSS35). Cell numbers were determined by trypan blue counting (n=5 biologically replicates).

b, Equal numbers of Hepa1-6 cells overexpressing EV or Flag-mPRSS35 were injected subcutaneously into C57BL/6J mice. Tumor weight was measured at 35 days after injection (n=6 biologically replicates).

c, Plasmids expressing YAP-5SA alone or YAP-5SA plus mPRSS35 together with PB transposase plasmids were delivered into ICR mice by hydrodynamic injection. YAP-5SA induced liver tumorigenesis was analyzed approximately 100 days after injection. RFP served as a control. Livers were harvested and imaged at the end of the experiment.

d, Geno-typing result of *mPRSS35* knockout mice. 154bp was deleted in *mPRSS35* knockout mice.

e, Body, liver and spleen weight of WT and *PRSS35*-KO mice (n=5 biologically replicates).

f, Triglyceride (TG), total cholesterol (TCHO) and glucose (Glu) in serum of WT and *PRSS35*-KO mice (n=5 biologically replicates).

g, Aspartic transaminase (AST) and alanine aminotransferase (ALT) concentrations in serum of WT and *PRSS35*-KO mice (n=5 biologically replicates).

h, Hematoxylin staining (H&E) of liver tissues from WT and *PRSS35*-KO mice.

i, Photograph of spleen and liver of WT and PRSS35-KO mice.

j, The neutrophil infiltration in the liver tissues of WT and *PRSS35*-KO mice (n=3 biologically replicates).

k, Plasmids expressing YAP-5SA or RFP together with PB transposase plasmids were delivered into mPRSS35-KO or WT C57BL/6J mice by hydrodynamic injection (n=6 in each group). YAP-5SA induced liver tumorigenesis was analyzed approximately 100 days after injection. Livers were harvested and imaged at the end of the experiment.

l, mRNA levels of the possible PRSS35-degrading substrates detected by transcriptomics.

m, Validation of the purity of isolated neutrophils from peripheral blood of healthy C57BL/6J mice by flow cytometry.

Data are presented as the mean \pm s.d. (a, b, e, f, g, j). Statistical significance was determined by two-way ANOVA (a, b, j). Source data are provided as a Source Data file.



Supplementary Figure 4







Supplementary Fig. 4. PRSS35 inhibits HCC development by suppressing CXCL2-mediated neutrophil NETs formation

a, Hepa1-6 cells stably expressing EV, mCXCL2, Flag-mPRSS35, or mCXCL2 plus Flag-mPRSS35 were injected subcutaneously into C57BL/6J mice. Photograph showed tumors at the end of experiment (left panel). Tumors were extracted and weighted at the end of the experiment (right panel, n=6 biologically replicates).

(**b**, **c**, **d**, **e**) Plasmids expressing YAP-5SA alone or YAP-5SA plus mCXCL2 shRNAs together with plasmids expressing PB transposase were delivered into *mPRSS35*-KO or WT C57BL/6J mice by hydrodynamic injection. YAP-5SA induced liver tumorigenesis was analyzed approximately 100 days after injection. **b**, Photograph showed tumors at the end of experiment. **c**, Representative FACS analysis of neutrophil in tumors was shown. **d**, Western blot analysis of mCXCL2 and H3Cit protein levels in tumor lysates. Ponceau staining served as a loading control. **e**, Serum NETs levels in mice with HCC *in situ* were measured by MPO-DNA ELISA kit (n=5 biologically replicates).

f, Serum NETs levels were measured by mouse H3Cit ELISA kit using the sera from the mouse experiment in Figure 4d (left panel, n=3 biologically replicates) and Figure 4k (right panel, n=3 biologically replicates).

(g, h, i) Hepa1-6 cells stably expressing EV or Flag-mPRSS35 were injected subcutaneously into C57BL/6J mice, followed by intratumor and peritumoral injection of Ly6G antibody or IgG antibody nine days later. g, Photograph showed tumors at the end of experiment (left panel). Tumors were extracted and weighted at the end of the experiment (right panel, n=6 biologically replicates). h, Representative FACS analysis of neutrophil in tumors was shown. i, Representative IHC analysis of Ly6G expression in tumors (left panel). Statistical quantification of Ly6G-positive area/total area in IHC assay (right panel, n=5 biologically replicates).

j, Hepa1-6 cells stably expressing control empty vector (EV) or Flag-mPRSS35 were injected subcutaneously into C57BL/6J mice, followed by daily intraperitoneal injection of DNase I five days later. Photograph showed tumors at the end of the experiment (upper panel). Tumors were extracted and weighted at the end of the experiment (lower panel, n=5 biologically replicates).

k, Western blot analysis of mCXCL2, Flag-mPRSS5 and H3Cit protein levels in tumors. β -actin served as a loading control.

l, The neutrophils in tumors was detected by Flow cytometry (n=3 biologically replicates).

m, Representative IHC images (left panel) and quantification (right panel, n=5 biologically replicates) of neutrophils in the tumors using anti-Ly6G staining.

n, Serum NETs levels were measured by H3Cit ELISA kit ((n=3 biologically replicates).

o, FACS sequential gating strategies for FACS experiments in Figure 4c, Extended Figure 3j, m, Extended Figure 4c, h.

p, Working model of PRSS35 suppressing HCC progression.

Data are presented as the mean \pm s.d. (a, e, f, g, i, j, l, m, n). Statistical significance was determined by two-way ANOVA (a, e, f, g, j, l, n) or two-tailed unpaired Student's t-test (i, m). The blotting experiments were repeated at least three times with biological replicates (d, k). Source data are provided as a Source Data file.

Supplementary Table 1. Clinicopathological characteristics of clinical samples and expression profile of PRSS35 in liver cancer

Characteristics	Number of cases (%)
Age (years)	
≤50	95 (60.1)
>50	63 (39.9)
AFP	
≤400ug/ul	97 (61.4)
>400ug/ul	61 (38.6)
Gender	
Female	17 (10.8)
Male	141 (89.2)
Tumor size	
≤3 cm	21 (13.3)
>3 cm	137 (86.7)
Tumor node	
≤1	120 (75.9)
>1	38 (24.1)
HBsAg	
negative	38 (24.1)
positive	120 (75.9)
Cirrhosis	
Absent	34 (21.5)
Present	124 (78.5)
Vascular Invasion	
Absent	98 (62.0)
Present	60 (38.0)
Vital status	· ·
Alive	53 (33.5)
Dead	105 (66.5)
Clinical stage	
I	12 (7.6)
II	92 (58.2)
III	38 (24.1)
IV	16 (10.1)
T classification	· ·
I	12 (7.6)
П	92 (58.2)
III	38 (24.1)
IV	16 (10.1)
N classification	· ·
N0	2 (1.3)
N1	156 (98.7)
M classification	
ΜΟ	1 (0.6)
M1	157 (99.4)
PRSS35	
Low expression	81 (51.3)
High expression	77 (48.7)

Abbreviationas: HBsAg, hepatitis B surface antigen; AFP, alpha fetoprotein.

Supplementary Table 2. Correlation between PRSS35 expression and clinicopathological Characteristics of liver cancer patients

Variable	Total	PRSS35	expression	Chi-square test
		low	high	p-value
Age (years)				
≤50	63	37	26	
>50	95	44	51	0.126
Gender				
Female	17	12	5	
Male	141	69	72	0.092
Tumor node				
≤1	120	63	57	
>1	38	18	20	0.581
Tumor size (cm)				
≤3	21	8	13	
>3	137	73	64	0.195
Vascular Invasion				
Absent	98	53	45	
Present	60	28	32	0.366
AFP (ug/ul)				
≤400	97	51	46	
>400	61	30	31	0.678
HBsAg				
negative	38	17	21	
positive	120	64	56	0.356
Cirrhosis				
Absent	34	17	17	
Present	124	64	60	0.868
Vital status				
Alive	53	25	28	
Dead	105	56	49	0.464
Clinical stage				
I	12	0	12	
I -IV	146	81	65	<0.001

Abbreviationas: HBsAg, hepatitis B surface antigen; AFP, alpha fetoprotein.

Supplementary Table 3. Spearman analysis of the correlation between PRSS35 and clinicopathological characteristics

Variables	PRSS35 expression le	evel
varidbles	Spearman Correlation	p-Value
Survival time	0.312	<0.001
Vital status	-0.023	0.773
Clinical stage	-0.15	0.06
Tumor size	-0.106	0.184

Supplementary Table 4. Oligonucleotide sequences of shRNA

Oligonucleotide sequence of shRNAs					
Genes	Sequence				
	CCGGCCTGTCCCTCTAAAGCAATAACTCGAGTTATTGCTTTAGAGGGACA				
shFURIN-1	GGTTTTTG				
	CCGGCCACATGACTACTCCGCAGATCTCGAGATCTGCGGAGTAGTCATG				
shFURIN-2	TGGTTTTTG				
	CCGGGCCAAGGGTTGACTTCAAGAACTCGAGTTCTTGAAGTCAACCCTT				
shCXCL2-1 (Mouse)	GGCTTTTTG				
	CCGGCCACTCTCAAGGGCGGTCAAACTCGAGTTTGACCGCCCTTGAGAG				
shCXCL2-2 (Mouse)	TGGTTTTTG				
	CCGGACTGAACAAAGGCAAGGCTAACTCGAGTTAGCCTTGCCTTTGTTC				
shCXCL2-3 (Mouse)	AGTTTTTTG				

Supplementary Table 5. The information of serum samples from 149 liver cancer patients and 73 healthy donors

1 female 67 HCC 51 male 63 HCC 101 male 56 HCC 2 female 42 HCC 53 male 41 HCC 102 male 43 3 male 43 HCC 53 male 43 HCC 104 female 45 HCC 5 male 43 HCC 55 male 54 HCC 104 female 65 HCC 6 female 52 HCC 58 male 64 HCC 107 male 53 HCC 7 male 64 HCC 107 male 54 HCC 108 male 74 HCC 10 male 74 HCC 58 male 74 HCC 118 female 53 HCC 11 male 74 HCC 63 male 74 HCC 113 female 71 HCC 13 male 45 HCC 66 male 73 HCC 113 male 73 HCC 14 male 45 HCC 66 f	Patient	Gender	Age (years)	Tumor	Patient	Gender	Age (years)	Tumor	Patient	Gender	Age (years)	Tumor
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20 male 55 HCC 70 male 67 HCC 120 male 54 HCC 21 female 46 HCC 71 male 70 HCC 121 male 46 HCC 22 male 68 HCC 72 male 64 HCC 122 male 56 HCC 23 male 54 HCC 73 male 49 HCC 123 female 54 HCC 24 male 54 HCC 74 male 85 HCC 124 male 50 HCC 25 male 70 HCC 75 male 67 HCC 126 female 50 HCC 26 male 61 HCC 77 male 71 HCC 126 female 50 HCC 29 female 56 HCC 79 male 71 <td>19</td> <td>female</td> <td>70</td> <td>HCC</td> <td>69</td> <td>male</td> <td>56</td> <td>HCC</td> <td>119</td> <td>male</td> <td>46</td> <td>HCC</td>	19	female	70	HCC	69	male	56	HCC	119	male	46	HCC
1female46HCC71male70HCC121male46HCC22male68HCC72male64HCC122male56HCC23male70HCC73male49HCC123female54HCC24male54HCC74male85HCC124male46HCC25male73HCC75male67HCC125female50HCC26male70HCC76male63HCC126female57HCC27female61HCC77male71HCC127female46HCC28female58HCC79male64HCC129male48HCC29female56HCC79male61HCC130female66HCC30male59HCC80male61HCC131male66HCC31male53HCC83female74HCC133male55HCC33female61HCC83female74HCC133male54HCC34female61HCC84male66HCC134female72HCC34female61HC	20	male	55	HCC	70	male	67	HCC	120	male	54	HCC
22 male 68 HCC 72 male 64 HCC 122 male 56 HCC 23 male 70 HCC 73 male 49 HCC 123 female 54 HCC 24 male 54 HCC 74 male 85 HCC 124 male 46 HCC 25 male 73 HCC 75 male 67 HCC 125 female 50 HCC 26 male 70 HCC 76 male 63 HCC 126 female 57 HCC 27 female 61 HCC 77 male 76 HCC 128 female 70 HCC 28 female 58 HCC 79 male 64 HCC 129 male 48 HCC 30 male 59 HCC 80 male 61 HCC 131 male 64 HCC 133 male 55 HCC </td <td>21</td> <td>female</td> <td>46</td> <td>HCC</td> <td>71</td> <td>male</td> <td>70</td> <td>HCC</td> <td>121</td> <td>male</td> <td>46</td> <td>HCC</td>	21	female	46	HCC	71	male	70	HCC	121	male	46	HCC
23 male 70 HCC 73 male 49 HCC 123 female 54 HCC 24 male 54 HCC 74 male 85 HCC 124 male 46 HCC 25 male 73 HCC 75 male 67 HCC 125 female 50 HCC 26 male 61 HCC 77 male 61 HCC 127 female 46 HCC 27 female 51 HCC 77 male 71 HCC 127 female 46 HCC 28 female 56 HCC 79 male 64 HCC 129 male 48 HCC 30 male 53 HCC 81 male 47 HCC 131 male 66 HCC 133 male 55 HCC 31 male 51 HCC 83 female 74 HCC 133 male 54 HCC	22	male	68	HCC	72	male	64	HCC	122	male	56	HCC
24male54HCC74male85HCC124male46HCC25male73HCC75male67HCC125female50HCC26male70HCC76male63HCC126female57HCC27female61HCC77male71HCC127female46HCC28female58HCC78male76HCC128female70HCC29female56HCC79male64HCC130female66HCC30male59HCC80male61HCC131male66HCC31male53HCC81male47HCC131male66HCC32male73HCC82female72HCC133male55HCC33female61HCC83female74HCC133male55HCC34female61HCC85female54HCC134female72HCC34female61HCC85female64HCC135male54HCC35male51HCC85female64HCC136male62HCC35male55 <t< td=""><td>23</td><td>male</td><td>70</td><td>HCC</td><td>73</td><td>male</td><td>49</td><td>HCC</td><td>123</td><td>female</td><td>54</td><td>HCC</td></t<>	23	male	70	HCC	73	male	49	HCC	123	female	54	HCC
25 male 73 HCC 75 male 67 HCC 125 female 50 HCC 26 male 70 HCC 76 male 63 HCC 126 female 57 HCC 27 female 61 HCC 77 male 71 HCC 128 female 50 HCC 28 female 56 HCC 79 male 64 HCC 129 male 48 HCC 30 male 53 HCC 80 male 61 HCC 130 female 66 HCC 31 male 53 HCC 81 male 47 HCC 131 male 66 HCC 32 male 73 HCC 82 female 74 HCC 133 male 55 HCC 33 female 61 HCC 83 female 74 HCC 133 male 55 HCC 34 female	24	male	54	HCC	74	male	85	HCC	124	male	46	HCC
26male 70 HCC 76 male 63 HCC 126 female 57 HCC 27 female 61 HCC 77 male 71 HCC 127 female 46 HCC 28 female 58 HCC 78 male 76 HCC 128 female 70 HCC 29 female 56 HCC 79 male 64 HCC 129 male 48 HCC 30 male 59 HCC 80 male 61 HCC 130 female 66 HCC 31 male 53 HCC 81 male 47 HCC 131 male 66 HCC 32 male 73 HCC 82 female 72 HCC 132 male 48 HCC 33 female 61 HCC 83 female 74 HCC 133 male 55 HCC 34 female 61 HCC 83 female 54 HCC 134 female 72 HCC 36 male 55 HCC 86 male 64 HCC 135 male 54 HCC 37 female 47 HCC 83 female 54 HCC 135 male 62 HCC 38 male 86 HCC 88 male 82 HCC 138 male 62 HCC 39 male 48 HCC<	25	male	73	HCC	75	male	67	HCC	125	female	50	HCC
27female 61 HCC 77 male 71 HCC 127 female 46 HCC 28 female 58 HCC 78 male 76 HCC 128 female 70 HCC 29 female 56 HCC 79 male 64 HCC 129 male 48 HCC 30 male 59 HCC 80 male 61 HCC 130 female 66 HCC 31 male 53 HCC 81 male 47 HCC 131 male 66 HCC 32 male 73 HCC 82 female 72 HCC 132 male 48 HCC 33 female 41 HCC 83 female 74 HCC 133 male 55 HCC 34 female 61 HCC 84 male 66 HCC 134 female 72 HCC 35 male 51 HCC 85 female 54 HCC 135 male 54 HCC 36 male 55 HCC 86 male 64 HCC 136 male 62 HCC 37 female 47 HCC 87 male 70 HCC 137 female 62 HCC 39 male 86 HCC 88 male 82 HCC 139 female 62 HCC 40 female 54 HC	26	male	70	HCC	76	male	63	HCC	126	female	57	HCC
28female58HCC78male76HCC128female70HCC29female56HCC79male64HCC129male48HCC30male59HCC80male61HCC130female66HCC31male53HCC81male47HCC131male66HCC32male73HCC82female72HCC132male48HCC33female61HCC83female74HCC133male55HCC34female61HCC84male66HCC134female72HCC35male51HCC85female54HCC135male54HCC36male55HCC86male61HCC136male62HCC36male55HCC87male61HCC137female62HCC38male86HCC89male61HCC139female73HCC40female54HCC89male65HCC140male62HCC39male48HCC89male65HCC140male64HCC40female54HCC<	27	female	61	HCC	77	male	71	HCC	127	female	46	HCC
29female56HCC79male64HCC129male48HCC30male59HCC80male61HCC130female66HCC31male53HCC81male47HCC131male66HCC32male73HCC82female72HCC132male48HCC33female41HCC83female74HCC133male55HCC34female61HCC84male66HCC134female72HCC35male51HCC85female54HCC135male54HCC36male55HCC86male64HCC136male62HCC36male55HCC87male70HCC137female62HCC37female48HCC89male61HCC139female73HCC38male86HCC90female65HCC140male62HCC40female54HCC91male62HCC141male54HCC41male76HCC91male68HCC141male54HCC43male55HCC <td>28</td> <td>female</td> <td>58</td> <td>HCC</td> <td>78</td> <td>male</td> <td>76</td> <td>HCC</td> <td>128</td> <td>female</td> <td>70</td> <td>HCC</td>	28	female	58	HCC	78	male	76	HCC	128	female	70	HCC
30male59HCC80male61HCC130female66HCC31male53HCC81male47HCC131male66HCC32male73HCC82female72HCC132male48HCC33female41HCC83female74HCC133male55HCC34female61HCC84male66HCC134female72HCC35male51HCC85female54HCC135male68HCC36male55HCC86male64HCC136male68HCC37female47HCC87male61HCC137female62HCC38male86HCC88male82HCC138male62HCC39male48HCC89male61HCC139female73HCC40female54HCC90female65HCC140male64HCC41male76HCC91male62HCC139female73HCC42female54HCC91male65HCC140male54HCC43male55HCC<	29	female	56	HCC	79	male	64	HCC	129	male	48	HCC
31male 53 HCC 81 male 47 HCC 131 male 66 HCC 32 male 73 HCC 82 female 72 HCC 132 male 48 HCC 33 female 41 HCC 83 female 74 HCC 133 male 55 HCC 34 female 61 HCC 84 male 66 HCC 134 female 72 HCC 35 male 51 HCC 85 female 54 HCC 135 male 54 HCC 36 male 55 HCC 86 male 64 HCC 136 male 68 HCC 37 female 47 HCC 87 male 70 HCC 137 female 62 HCC 38 male 86 HCC 88 male 82 HCC 139 female 62 HCC 39 male 48 HCC 90 female 65 HCC 140 male 62 HCC 41 male 76 HCC 91 male 62 HCC 140 male 50 HCC 42 female 66 HCC 92 female 68 HCC 140 male 50 HCC 44 male 54 HCC 93 male 45 HCC 141 male 50 HCC 44 male 55 HCC <t< td=""><td>30</td><td>male</td><td>59</td><td>HCC</td><td>80</td><td>male</td><td>61</td><td>HCC</td><td>130</td><td>female</td><td>66</td><td>HCC</td></t<>	30	male	59	HCC	80	male	61	HCC	130	female	66	HCC
32male73HCC82female72HCC132male48HCC33female41HCC83female74HCC133male55HCC34female61HCC84male66HCC134female72HCC35male51HCC85female54HCC135male54HCC36male55HCC86male64HCC136male68HCC37female47HCC87male70HCC137female62HCC38male86HCC88male82HCC138male62HCC39male48HCC90female65HCC140male62HCC41male76HCC91male62HCC141male54HCC42female55HCC92female68HCC140male50HCC43male55HCC93male45HCC143male49HCC44male54HCC93male59HCC144male65HCC43male54HCC94female59HCC144male65HCC44male54HCC	31	male	53	HCC	81	male	47	HCC	131	male	66	HCC
33female41HCC83female74HCC133male55HCC34female61HCC84male66HCC134female72HCC35male51HCC85female54HCC135male54HCC36male55HCC86male64HCC136male68HCC37female47HCC87male70HCC137female62HCC38male86HCC88male82HCC138male62HCC39male48HCC89male61HCC139female73HCC40female54HCC90female65HCC140male62HCC41male76HCC91male62HCC141male54HCC42female66HCC92female68HCC141male54HCC43male55HCC93male45HCC143male49HCC44male54HCC94female59HCC144male65HCC45male60HCC95male82HCC145male56HCC45male59HCC <td>32</td> <td>male</td> <td>73</td> <td>HCC</td> <td>82</td> <td>female</td> <td>72</td> <td>HCC</td> <td>132</td> <td>male</td> <td>48</td> <td>HCC</td>	32	male	73	HCC	82	female	72	HCC	132	male	48	HCC
34female61HCC84male66HCC134female72HCC35male51HCC85female54HCC135male54HCC36male55HCC86male64HCC136male68HCC37female47HCC87male70HCC137female62HCC38male86HCC88male82HCC138male62HCC39male48HCC89male61HCC139female73HCC40female54HCC90female65HCC140male62HCC41male76HCC91male62HCC141male54HCC43male55HCC92female68HCC142male50HCC44male54HCC93male45HCC143male65HCC44male54HCC95male82HCC145male56HCC45male60HCC95male59HCC143male65HCC46male59HCC96male45HCC146female56HCC47male42HCC	33	female	41	HCC	83	female	74	HCC	133	male	55	HCC
35male51HCC85female54HCC135male54HCC36male55HCC86male64HCC136male68HCC37female47HCC87male70HCC137female62HCC38male86HCC88male82HCC138male62HCC39male48HCC89male61HCC139female73HCC40female54HCC90female65HCC140male62HCC41male76HCC91male62HCC141male54HCC43male55HCC92female68HCC142male49HCC44male54HCC94female59HCC144male56HCC45male60HCC95male82HCC145male56HCC46male59HCC96male45HCC146female56HCC47male42HCC97male56HCC147male63HCC	34	female	61	HCC	84	male	66	HCC	134	female	72	HCC
36male55HCC86male64HCC136male68HCC37female47HCC87male70HCC137female62HCC38male86HCC88male82HCC138male62HCC39male48HCC89male61HCC139female73HCC40female54HCC90female65HCC140male62HCC41male76HCC91male62HCC141male54HCC42female66HCC92female68HCC142male50HCC43male55HCC93male45HCC143male65HCC44male54HCC95male82HCC144male65HCC45male60HCC95male82HCC145male56HCC46male59HCC96male45HCC146female56HCC47male42HCC97male56HCC147male63HCC	35	male	51	HCC	85	female	54	HCC	135	male	54	HCC
37female47HCC87male70HCC137female62HCC38male86HCC88male82HCC138male62HCC39male48HCC89male61HCC139female73HCC40female54HCC90female65HCC140male62HCC41male76HCC91male62HCC141male54HCC42female66HCC92female68HCC142male50HCC43male55HCC93male45HCC144male65HCC44male54HCC95male82HCC145male65HCC44male54HCC93male45HCC144male65HCC45male60HCC95male82HCC145male56HCC46male59HCC96male45HCC146female56HCC47male42HCC97male56HCC147male63HCC	36	male	55	HCC	86	male	64	HCC	136	male	68	HCC
38male86HCC88male82HCC138male62HCC39male48HCC89male61HCC139female73HCC40female54HCC90female65HCC140male62HCC41male76HCC91male62HCC141male54HCC42female66HCC92female68HCC142male50HCC43male55HCC93male45HCC143male49HCC44male54HCC94female59HCC144male65HCC45male60HCC95male82HCC145male56HCC46male59HCC97male56HCC147male63HCC	37	female	47	HCC	87	male	70	HCC	137	female	62	HCC
39male48HCC89male61HCC139female73HCC40female54HCC90female65HCC140male62HCC41male76HCC91male62HCC141male54HCC42female66HCC92female68HCC142male50HCC43male55HCC93male45HCC143male49HCC44male54HCC94female59HCC144male65HCC45male60HCC95male82HCC145male56HCC46male59HCC97male56HCC147male63HCC	38	male	86	HCC	88	male	82	HCC	138	male	62	HCC
40female54HCC90female65HCC140male62HCC41male76HCC91male62HCC141male54HCC42female66HCC92female68HCC142male50HCC43male55HCC93male45HCC143male49HCC44male54HCC94female59HCC144male65HCC45male60HCC95male82HCC145male56HCC46male42HCC97male56HCC147male63HCC	39	male	48	HCC	89	male	61	HCC	139	female	73	HCC
41male76HCC91male62HCC141male54HCC42female66HCC92female68HCC142male50HCC43male55HCC93male45HCC143male49HCC44male54HCC94female59HCC144male65HCC45male60HCC95male82HCC145male56HCC46male59HCC96male45HCC146female56HCC47male42HCC97male56HCC147male63HCC	40	female	54	HCC	90	female	65	HCC	140	male	62	HCC
42female66HCC92female68HCC142male50HCC43male55HCC93male45HCC143male49HCC44male54HCC94female59HCC144male65HCC45male60HCC95male82HCC145male56HCC46male59HCC96male45HCC146female56HCC47male42HCC97male56HCC147male63HCC	41	male	76	HCC	91	male	62	HCC	141	male	54	HCC
43male55HCC93male45HCC143male49HCC44male54HCC94female59HCC144male65HCC45male60HCC95male82HCC145male56HCC46male59HCC96male45HCC146female56HCC47male42HCC97male56HCC147male63HCC	42	female	66	HCC	92	female	68	HCC	142	male	50	HCC
44 male 54 HCC 94 female 59 HCC 144 male 65 HCC 45 male 60 HCC 95 male 82 HCC 145 male 56 HCC 46 male 59 HCC 96 male 45 HCC 146 female 56 HCC 47 male 42 HCC 97 male 56 HCC 147 male 63 HCC	43	male	55	HCC	93	male	45	HCC	143	male	49	HCC
45male60HCC95male82HCC145male56HCC46male59HCC96male45HCC146female56HCC47male42HCC97male56HCC147male63HCC	44	male	54	HCC	94	female	59	HCC	144	male	65	HCC
46male59HCC96male45HCC146female56HCC47male42HCC97male56HCC147male63HCC	45	male	60	HCC	95	male	82	HCC	145	male	56	HCC
47 male 42 HCC 97 male 56 HCC 147 male 63 HCC	46	male	59	HCC	96	male	45	HCC	146	female	56	HCC
	47	male	42	HCC	97	male	56	HCC	147	male	63	HCC

48	male	66	HCC	98	male	61	HCC	148	female	35	HCC
49	male	47	HCC	99	male	66	HCC	149	female	66	HCC
50	male	62	HCC	100	female	78	HCC				

Supplementary Table 5 continued

Healthy donor	Gender	Age(years)	Healthy donor	Gender	Age(years)
1	male	47	38	male	35
2	female	31	39	male	42
3	female	31	40	male	37
4	male	41	41	male	36
5	female	27	42	male	38
6	female	29	43	female	34
7	male	28	44	female	48
8	female	29	45	male	31
9	female	49	46	male	43
10	female	45	47	female	54
11	male	32	48	male	45
12	female	47	49	female	50
13	male	47	50	male	58
14	male	29	51	female	30
15	female	19	52	female	50
16	female	32	53	male	51
17	female	56	54	female	51
18	female	52	55	female	43
19	male	27	56	male	53
20	male	28	57	female	38
21	female	42	58	female	24
22	female	38	59	male	61
23	male	36	60	male	66
24	female	35	61	female	34
25	female	38	62	male	71
26	female	47	63	male	66
27	male	26	64	male	35
28	male	86	65	male	84
29	male	35	66	male	48
30	male	39	67	female	37
31	female	42	68	male	53
32	female	47	69	male	24
33	male	36	70	male	33
34	male	64	71	male	32
35	male	44	72	female	31
36	male	37	73	female	37
37	female	55			



b



f







С





Source data-Supplementary Figure 4



k

