

Whole-exome sequencing identifies susceptibility genes and pathways for idiopathic pulmonary fibrosis in the Chinese population

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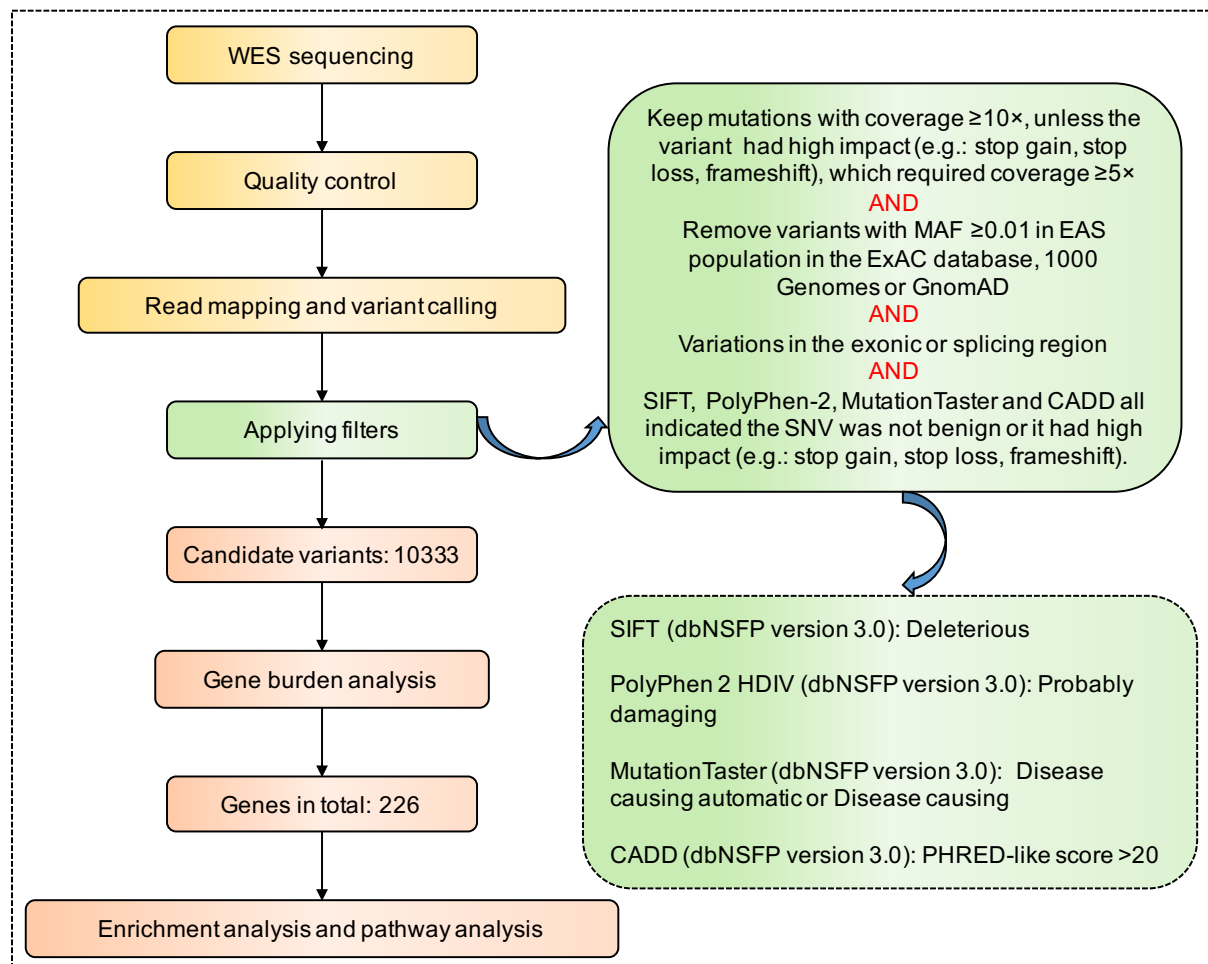
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Fig S1 Flowchart of the study design for the rare variant analysis.



Four filters used to identify deleterious variants and the thresholds of four software (SIFT, PolyPhen-2, MutationTaster and CADD) used to identify deleterious variants were shown in green box above. MAF=mutant allele frequency, EAS=East Asian, ExAC=Exome Aggregation Consortium,

GnomAD=Genome Aggregation Database.

Fig S2 Principal Component Analysis of 110 IPF samples and 60 healthy control samples.

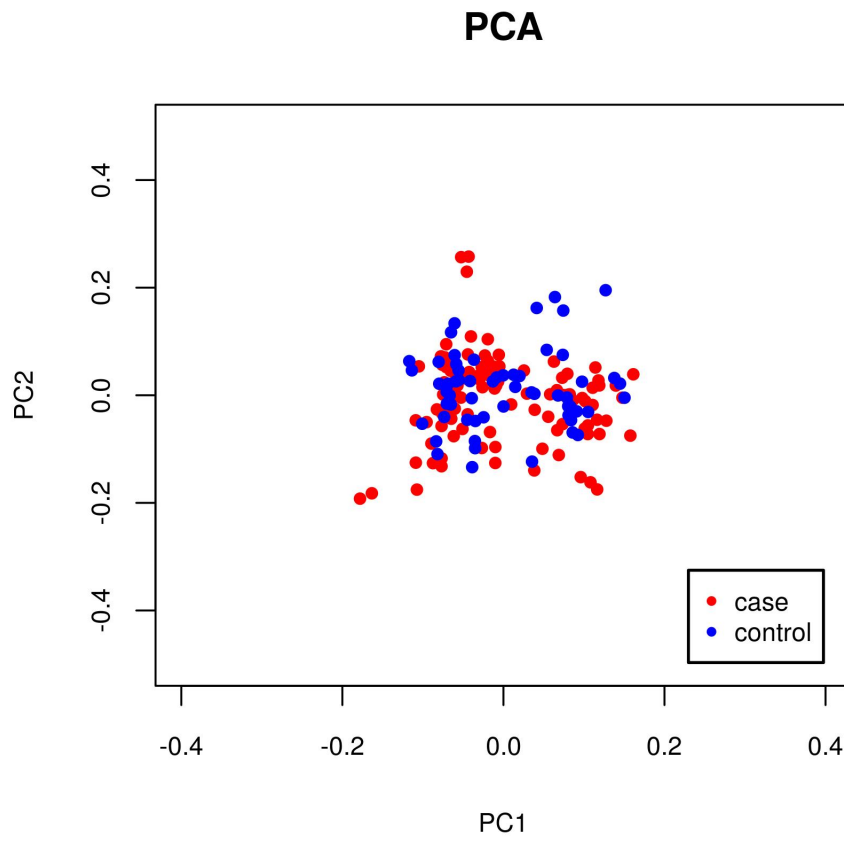


Fig S3: Coverage of variants identified in HLA regions.

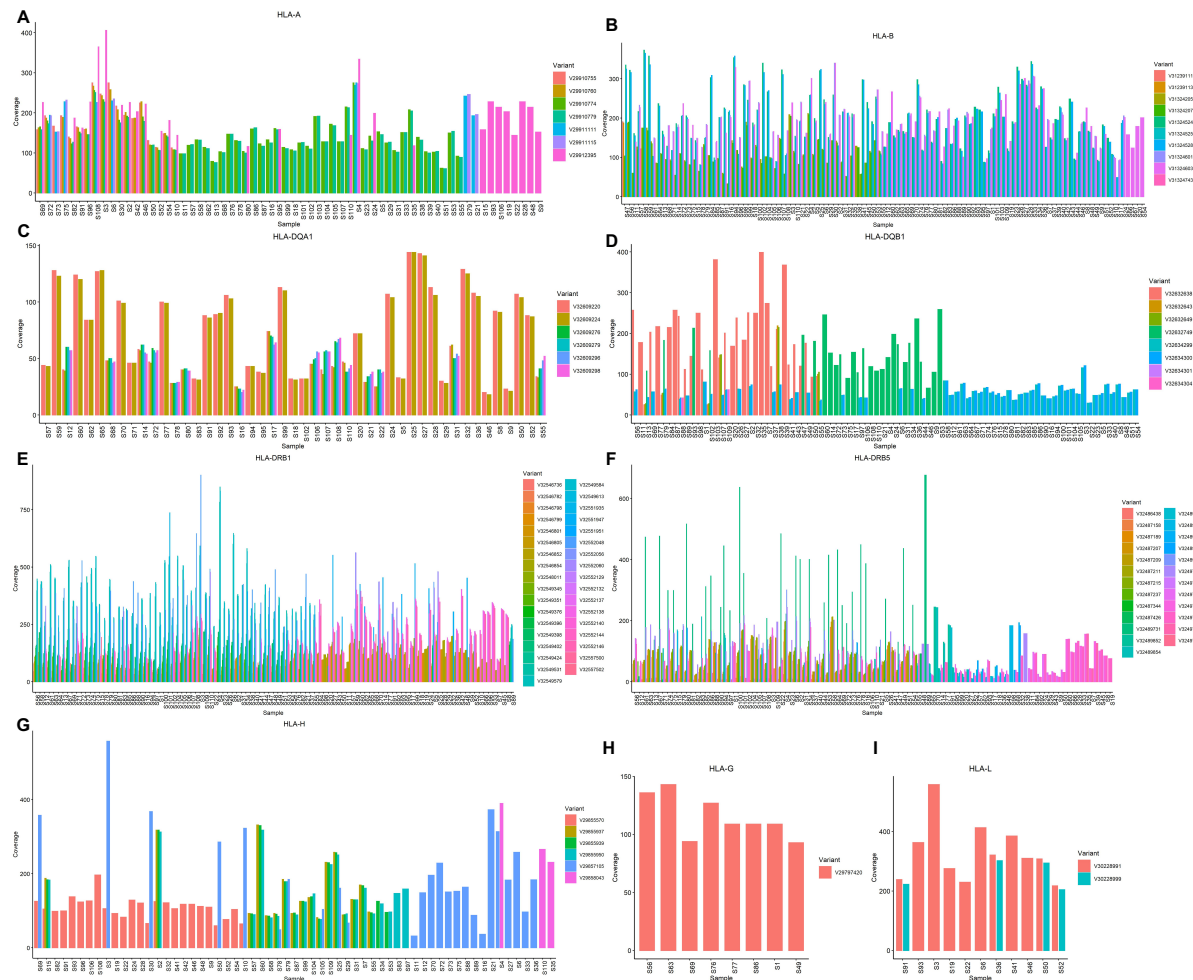


Table S1 226 candidate genes enriched with rare deleterious variants.

Gene	Variant_count	P-FDR from SKAT
<i>DDX11L1</i>	1	0.015737394
<i>OR4F5</i>	1	0.046780623
<i>KLHL17</i>	1	0.000952768
<i>RNF207</i>	2	0.041229025
<i>PRAMEF1</i>	3	6.28E-14
<i>PRAMEF2</i>	4	0.022339276
<i>MSTIL</i>	11	4.24E-14
<i>AX748283</i>	4	0.00019935

<i>BC038455</i>	2	0.00250716
<i>UBXN11</i>	7	0.000488736
<i>KIAA1522</i>	4	0.004535233
<i>TIE1</i>	5	3.18E-05
<i>TTC39A</i>	2	7.70E-06
<i>FAM72D</i>	1	1.61E-14
<i>LOC100288142</i>	2	0
<i>PDE4DIP</i>	5	2.47E-05
<i>SEC22B</i>	3	0.014669238
<i>NBPF12</i>	1	1.14E-06
<i>NBPF14</i>	2	0
<i>NBPF16</i>	1	0
<i>HRNR</i>	10	3.61E-06
<i>NES</i>	4	0.000175388
<i>HSPA6</i>	6	0.008187631
<i>KIAA0040</i>	4	0.023411563
<i>PTPRVP</i>	5	0.013689552
<i>CEP170</i>	2	0.0049815
<i>OR2T3</i>	1	0.046780623
<i>OR2T5</i>	1	1.10E-09
<i>OR2T29</i>	1	0.001969812
<i>BC046483</i>	5	3.06E-05
<i>PTCHD3</i>	3	0.042739341
<i>AGAP4</i>	2	0.005652204
<i>FAM178A</i>	1	0.016902956
<i>FANK1</i>	1	0.046780623
<i>PIDD</i>	1	0.008161304
<i>C11orf40</i>	4	0.008633502
<i>OR51A4</i>	3	0.015471737
<i>LINC00294</i>	1	0.00448289
<i>MDK</i>	13	2.07E-06
<i>FOLH1</i>	1	0.046780623

<i>METTL12</i>	3	0.042041974
<i>SLC22A9</i>	1	0.015535744
<i>ESRRA</i>	5	2.96E-11
<i>TRIM64B</i>	2	0.047976413
<i>CASP5</i>	2	0.04837382
<i>AK130852</i>	10	0.015737394
<i>LRTM2</i>	1	0.038442492
<i>PHC1</i>	1	0.000201375
<i>TAS2R46</i>	2	0.011392102
<i>PRB3</i>	4	7.16E-09
<i>PRB4</i>	2	0.028334864
<i>PRB1</i>	3	0.000246804
<i>SLCO1A2</i>	1	0.046780623
<i>KRT6B</i>	2	4.24E-14
<i>LOC283335</i>	1	7.99E-10
<i>STAT2</i>	1	0.046780623
<i>BC033961</i>	1	0.005627372
<i>KIAA1033</i>	1	0.046780623
<i>GATC</i>	1	0.038442492
<i>CAMKK2</i>	5	0.036283865
<i>KNTC1</i>	5	0.046459129
<i>SKA3</i>	4	0.01867057
<i>PARP4</i>	4	1.84E-08
<i>PABPC3</i>	15	1.84E-09
<i>C14orf23</i>	4	0.018754551
<i>WDR89</i>	8	0.008225472
<i>DKFZp686O16217</i>	2	0.009454911
<i>ELK2AP</i>	1	9.00E-05
<i>FLJ00382</i>	1	0.00115614
<i>GOLGA6L6</i>	3	0.00031415
<i>LOC283710</i>	2	0.000172033
<i>CHRNA7</i>	3	0.011065819

<i>MAPKBP1</i>	4	0.025202021
<i>SORD</i>	3	0.028334864
<i>CSK</i>	1	0.044777337
<i>CSPG4</i>	2	7.17E-06
<i>DNM1P41</i>	3	0.036629748
<i>PCSK6</i>	2	0.00115614
<i>WASH3P</i>	2	0.016387193
<i>SSTR5-AS1</i>	4	0.004535233
<i>TSR3</i>	2	0.048466823
<i>GNPTG</i>	1	0.038442492
<i>NMRAL1</i>	1	0.038442492
<i>AK055785</i>	2	5.22E-08
<i>OTOA</i>	2	0.011519765
<i>LOC653786</i>	1	0.0049815
<i>ZNF629</i>	1	0.038442492
<i>CES1</i>	5	0.003593626
<i>PDPR</i>	4	0.000203198
<i>NPIPL2</i>	2	0
<i>CLEC18B</i>	5	0.02139066
<i>PLCG2</i>	3	0.042041974
<i>C16orf85</i>	2	0.018911871
<i>AK055272</i>	3	0.001218903
<i>AK302511</i>	1	0.036283865
<i>CNTROB</i>	2	0.048466823
<i>MEIS3P1</i>	1	3.18E-05
<i>TOM1L2</i>	3	0.009237796
<i>C17orf103</i>	1	9.37E-06
<i>KCNJ12</i>	4	4.89E-07
<i>GOSR1</i>	4	4.30E-05
<i>COPZ2</i>	2	3.45E-05
<i>BC033456</i>	2	4.63E-08
<i>USP32</i>	1	0.028334864

<i>TBC1D3P2</i>	2	2.47E-10
<i>CCDC40</i>	3	0.00135667
<i>AK127919</i>	1	3.18E-05
<i>SOGA2</i>	8	0.001314571
<i>KIAA1468</i>	2	0.002866685
<i>OR4F17</i>	1	3.72E-05
<i>REEP6</i>	1	0.046780623
<i>ATP8B3</i>	5	0.000892129
<i>KRI1</i>	3	0.038442492
<i>ANKLE1</i>	7	7.66E-06
<i>B3GNT3</i>	5	3.27E-05
<i>ZNF626</i>	2	0.018286361
<i>RHPN2</i>	1	4.01E-06
<i>U2AF1L4</i>	6	0.006639426
<i>LOC644189</i>	2	8.45E-06
<i>CD177</i>	2	3.64E-06
<i>KLC3</i>	5	0.000100495
<i>MYBPC2</i>	4	0.048113376
<i>SIGLEC10</i>	2	0.001619871
<i>ZNF880</i>	13	0.031549467
<i>ZNF83</i>	2	0.005301149
<i>LILRA6</i>	4	3.27E-05
<i>KIR2DL1</i>	3	3.77E-13
<i>KIR2DS4</i>	1	0.011649469
<i>MGC2752</i>	1	3.03E-07
<i>FAM136A</i>	2	4.76E-08
<i>RGPD1</i>	3	1.23E-05
<i>VWA3B</i>	3	0.029704755
<i>GCC2</i>	1	2.71E-06
<i>ANAPC1</i>	3	0.001666354
<i>RGPD5</i>	2	0.000575101
<i>HS6ST1</i>	2	0

<i>SMPD4</i>	5	0.008187631
<i>POTEE</i>	5	0
<i>PLA2R1</i>	1	0.046459129
<i>ITGA6</i>	3	0.043859594
<i>PRKRA</i>	2	0.00019935
<i>CCDC150</i>	4	0.000913164
<i>ANKRD44</i>	1	0.008633502
<i>FTCDNL1</i>	2	0.000355721
<i>PRR21</i>	2	0.013903322
<i>AQP12A</i>	2	0.008187631
<i>BC101234</i>	3	2.60E-09
<i>LOC339593</i>	1	0.01279849
<i>BFSP1</i>	3	0.00073135
<i>RIN2</i>	6	0.042739341
<i>LAMA5</i>	7	0.029704755
<i>BAGE3</i>	1	0.009431036
<i>POM121L7</i>	3	5.62E-12
<i>BCR</i>	2	3.15E-09
<i>AK026502</i>	2	6.28E-14
<i>TCN2</i>	2	0.046780623
<i>SYN2</i>	3	0.000188538
<i>VENTXP7</i>	3	0.000493286
<i>GOLGA4</i>	2	0.046780623
<i>MST1</i>	5	0.004535233
<i>LINC00636</i>	2	2.28E-06
<i>SDHAP2</i>	2	9.79E-08
<i>MUC4</i>	19	0.00870228
<i>ABCA11P</i>	1	0.021026873
<i>OTOP1</i>	3	4.89E-10
<i>USP17L10</i>	2	9.52E-14
<i>USP17L11</i>	4	0.009040961
<i>USP17L20</i>	1	0.028334864

<i>LPHN3</i>	1	0.016902956
<i>SLC9B1</i>	4	0
<i>DCHS2</i>	7	7.22E-05
<i>ENPP6</i>	1	0.016902956
<i>SDHA</i>	3	5.91E-05
<i>C9</i>	1	0.038442492
<i>LOC100272216</i>	3	0
<i>BTF3</i>	1	0.036629748
<i>ERAP1</i>	1	0.016902956
<i>PCDHB16</i>	1	0.046780623
<i>GPRIN1</i>	2	0.020850546
<i>LOC100132062</i>	1	6.04E-06
<i>FAM8A1</i>	2	0.00297184
<i>HLA-G</i>	1	0.038237787
<i>HLA-H</i>	7	2.17E-05
<i>AK309533</i>	6	7.51E-06
<i>HLA-A</i>	7	1.49E-12
<i>HLA-L</i>	2	0.018046635
<i>HLA-B</i>	11	0
<i>TNXB</i>	4	0.000128876
<i>HLA-DRB5</i>	26	0
<i>HLA-DRB1</i>	36	0
<i>HLA-DQA1</i>	6	2.26E-08
<i>HLA-DQB1</i>	8	0
<i>SYNGAP1</i>	5	0.001635482
<i>C6orf57</i>	1	0.044777337
<i>ANKRD6</i>	1	0.021026873
<i>GPR126</i>	4	2.02E-05
<i>FNDCl</i>	4	0.046780623
<i>LINC00473</i>	1	0.016632759
<i>TCP10L2</i>	1	0.000145558
<i>LFNG</i>	2	0.00038938

<i>ZNF890P</i>	2	0.007840158
<i>LOC402470</i>	1	0.009993988
<i>ZNF733P</i>	1	0.012159401
<i>ZNF107</i>	5	0.02238969
<i>MUC17</i>	9	4.33E-06
<i>RABL5</i>	4	0.000166946
<i>POLR2J3</i>	2	0
<i>RASA4</i>	4	0.018995754
<i>FAM185A</i>	1	3.18E-05
<i>FLJ45340</i>	2	3.18E-05
<i>FAM115C</i>	2	1.22E-05
<i>ARHGEF5</i>	7	0.005992449
<i>AGAP3</i>	7	3.98E-10
<i>KMT2C</i>	8	1.24E-13
<i>FAM86B1</i>	2	1.95E-11
<i>FAM86B2</i>	3	0.000493724
<i>LOC729732</i>	2	0.046780623
<i>NUDT18</i>	3	0.014594909
<i>CPNE3</i>	2	0.040883428
<i>FOXD4L3</i>	2	0.003288371
<i>OR13C5</i>	3	6.83E-09
<i>CEL</i>	2	0.000142615
<i>OLFM1</i>	1	0.028334864
<i>AK096249</i>	2	0.028334864
<i>RBMX</i>	1	0.001846669
<i>CD24</i>	4	0.01876791

Variant count: the number of deleterious variants detected in each gene. P-FDR: P values were from SKAT and corrected by false discovery rate (FDR).