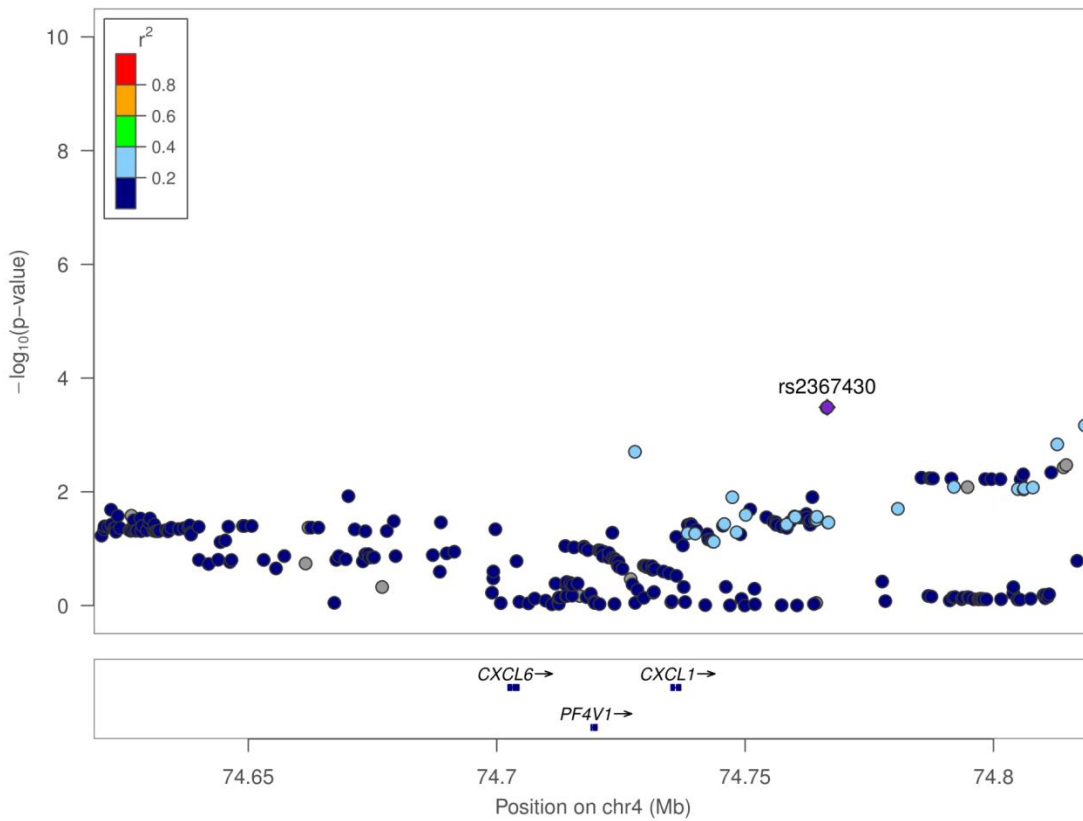


The PF4/PPBP/CXCL5 Gene Cluster Is Associated with Periodontitis

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Appendix



Appendix Figure. Association plot with AgP for the genomic region at *PFV1*. *PF4V1* and the adjacent genes *CXCL1* and *-6* show no association with AgP. The $-\log_{10}$ p-values of the analyzed SNPs were plotted as a function of the genomic SNP position (NCBI build 36, hg19/1000 Genomes 2012, CEU). SNP annotations were generated by LocusZoom.

Appendix Table. Summary of illumine base calling and alignments.

Gene ID	Name	Location	Value 1	Value2	log2, fold change	test stats	p_value	q_value
ENSMUSG00000026407	Cacna1s	1:136052749-136119822	21.734	8.175	-1.411	-2.423	0.00070	0.05518
ENSMUSG00000026691	Fmo3	1:162953801-162984528	0.713	4.360	2.612	3.356	0.00015	0.01744
ENSMUSG00000042686	Jph1	1:16994937-17097889	4.967	2.202	-1.174	-2.919	0.00060	0.04994
ENSMUSG00000007122	Casq1	1:172209893-172219868	49.357	13.029	-1.922	-4.775	0.00005	0.00719
ENSMUSG00000079588	Tmem182	1:40805600-40855944	8.593	2.844	-1.596	-3.426	0.00030	0.03074
ENSMUSG00000082209	Eif4a-ps4	1:60703917-60705656	10.115	0.267	-5.243	-5.127	0.00030	0.03074
ENSMUSG00000061816	Myl1	1:66924294-66945404	718.167	232.166	-1.629	-4.860	0.00005	0.00719
ENSMUSG00000026208	Des	1:75360328-75375012	90.506	40.440	-1.162	-3.071	0.00005	0.00719
ENSMUSG00000055866	Per2	1:91415983-91459330	11.875	20.675	0.800	2.338	0.00110	0.07610
ENSMUSG00000039891	Txlnb	10:17790521-17845665	9.364	3.798	-1.302	-3.197	0.00005	0.00719
ENSMUSG00000019787	Trdn	10:33083482-33476709	11.240	3.483	-1.690	-4.418	0.00005	0.00719
ENSMUSG00000020331	Hcn2	10:79716633-79736108	0.525	2.204	2.071	2.645	0.00145	0.09251
ENSMUSG00000020038	Cry1	10:85131701-85185054	4.175	10.333	1.307	3.495	0.00005	0.00719
ENSMUSG00000020722	Cacng1	11:107703217-107716522	15.432	4.204	-1.876	-4.178	0.00005	0.00719
ENSMUSG00000034227	Foxj1	11:116330703-116335399	2.864	9.582	1.742	3.769	0.00005	0.00719
ENSMUSG00000054986	Sec14l3	11:4064840-4077736	2.468	27.186	3.461	4.076	0.00005	0.00719
ENSMUSG00000061462	Obscn	11:58994255-59136402	17.902	8.959	-0.999	-2.183	0.00140	0.09073
ENSMUSG00000056598	Lrrc48	11:60353328-60394341	2.061	6.791	1.720	2.996	0.00020	0.02186
ENSMUSG00000087410	2310065F04Rik	11:67112460-67120080	4.550	0.677	-2.748	-3.010	0.00065	0.05250
ENSMUSG00000018566	Slc2a4	11:69942538-69948188	21.504	10.248	-1.069	-2.639	0.00050	0.04408
ENSMUSG00000020839	Tmigd1	11:76902158-76916587	14.073	4.736	-1.571	-2.558	0.00095	0.06862
ENSMUSG00000093483	AA465934	11:83291698-83294632	40.468	8.342	-2.278	-3.109	0.00030	0.03074

ENSMUSG00000038756	Ttl6	11:96133785-96165451	0.463	3.976	3.103	4.202	0.00015	0.01744
ENSMUSG00000007877	Tcap	11:98383810-98384953	395.954	159.427	-1.312	-4.080	0.00005	0.00719
ENSMUSG00000020889	Nr1d1	11:98740637-98775333	127.199	46.096	-1.464	-2.825	0.00005	0.00719
ENSMUSG00000021194	Chga	12:102554968-102565027	1.731	18.743	3.437	6.084	0.00005	0.00719
ENSMUSG00000011148	Adssl1	12:112620044-112641354	40.189	21.023	-0.935	-2.707	0.00010	0.01271
ENSMUSG00000071398	2410004P03Rik	12:17004957-17011727	1.438	5.114	1.830	2.988	0.00100	0.07160
ENSMUSG00000021087	Rtn1	12:72211751-72409054	3.409	12.147	1.833	2.835	0.00010	0.01271
ENSMUSG00000052374	Actn2	13:12269425-12340760	38.586	21.081	-0.872	-2.549	0.00055	0.04672
ENSMUSG00000021319	Sfrp4	13:19623174-19632821	27.219	48.059	0.820	2.626	0.00080	0.06073
ENSMUSG00000021373	Cap2	13:46501847-46649642	9.817	3.629	-1.436	-2.505	0.00040	0.03791
ENSMUSG00000047419	Cmya5	13:93040712-93144724	10.456	4.002	-1.386	-3.767	0.00005	0.00719
ENSMUSG00000068697	Myoz1	14:20649101-20656540	86.321	21.851	-1.982	-5.987	0.00005	0.00719
ENSMUSG00000039376	Synpo2l	14:20658945-20668354	4.544	1.626	-1.483	-2.969	0.00015	0.01744
ENSMUSG00000071540	3425401B19Rik	14:32659118-32685272	4.564	1.423	-1.682	-3.601	0.00005	0.00719
ENSMUSG00000021798	Ldb3	14:34526698-34588681	39.153	15.118	-1.373	-3.448	0.00005	0.00719
ENSMUSG00000072601	Ear1	14:43818764-43875517	7.832	23.142	1.563	2.964	0.00035	0.03436
ENSMUSG00000062148	Ear6	14:51853698-51854643	14.399	35.960	1.320	2.666	0.00035	0.03436
ENSMUSG00000018893	Mb	15:77015488-77057107	575.177	225.241	-1.353	-3.350	0.00005	0.00719
ENSMUSG00000005716	Pvalb	15:78191113-78206400	153.991	21.751	-2.824	-7.041	0.00005	0.00719
ENSMUSG00000022619	Mapk8ip2	15:89453912-89464468	0.256	2.661	3.380	2.153	0.00005	0.00719
ENSMUSG00000037579	Kcnh3	15:99224975-99242817	0.400	2.045	2.354	3.139	0.00085	0.06335
ENSMUSG00000023011	Faim2	15:99497004-99528017	0.741	5.091	2.780	5.093	0.00005	0.00719
ENSMUSG00000033383	Rtp1	16:23429132-23433960	0.360	4.927	3.775	4.859	0.00005	0.00719

ENSMUSG00000047531	Rtp2	16:23925547-23930787	0.337	3.911	3.537	4.077	0.00055	0.04672
ENSMUSG00000008658	Rbfox1	16:6809221-7412479	3.874	1.134	-1.773	-2.962	0.00005	0.00719
ENSMUSG00000040666	Sh3bgr	16:96200469-96228933	51.102	19.172	-1.414	-2.540	0.00035	0.03436
ENSMUSG00000002500	Rpl3l	17:24727819-24736143	28.551	14.058	-1.022	-2.568	0.00015	0.01744
ENSMUSG00000041062	Mslnl	17:25736039-25748330	0.339	5.282	3.961	4.812	0.00015	0.01744
ENSMUSG00000024033	Rsph1	17:31255018-31277356	4.204	12.485	1.570	3.141	0.00035	0.03436
ENSMUSG00000024298	Zfp871	17:32771235-32788287	2.232	0.824	-1.437	-2.345	0.00150	0.09423
ENSMUSG00000002289	Angptl4	17:33773749-33781575	10.651	21.913	1.041	2.500	0.00030	0.03074
ENSMUSG00000040694	Apobec2	17:48419230-48432728	32.790	10.702	-1.615	-4.411	0.00005	0.00719
ENSMUSG00000045761	Fam179a	17:71673260-71729669	3.227	7.066	1.131	2.322	0.00125	0.08231
ENSMUSG00000033966	Cdkl4	17:80523549-80563834	0.310	2.049	2.725	3.418	0.00070	0.05518
ENSMUSG00000024471	Myot	18:44334073-44355724	43.161	19.328	-1.159	-3.334	0.00005	0.00719
ENSMUSG00000024524	Gnal	18:67088335-67245830	1.910	11.019	2.529	4.656	0.00005	0.00719
ENSMUSG00000024743	Syt7	19:10389089-10453181	0.480	1.569	1.708	2.790	0.00050	0.04408
ENSMUSG00000033863	Klf9	19:23141225-23166911	36.241	20.087	-0.851	-2.466	0.00045	0.04032
ENSMUSG00000075289	Carns1	19:4164323-4175479	4.467	9.288	1.056	2.661	0.00065	0.05250
ENSMUSG00000049134	Nrap	19:56287136-56390037	12.737	6.077	-1.068	-2.695	0.00005	0.00719
ENSMUSG00000042179	Pnliprp1	19:58728886-58744169	109.166	26.743	-2.029	-5.419	0.00005	0.00719
ENSMUSG00000017817	Jph2	2:163336241-163397993	6.251	2.440	-1.357	-3.114	0.00020	0.02186
ENSMUSG00000017300	Tnnc2	2:164769897-164779967	672.302	264.126	-1.348	-3.101	0.00005	0.00719
ENSMUSG00000039155	Cdh26	2:178430530-178487366	1.852	6.862	1.890	3.222	0.00005	0.00719
ENSMUSG00000016349	Eef1a2	2:181147652-181157014	53.511	24.882	-1.105	-3.502	0.00005	0.00719
ENSMUSG00000026880	Stom	2:35313985-35336976	24.803	47.834	0.947	3.074	0.00010	0.01271

ENSMUSG00000026950	Neb	2:52136646-52338798	111.187	38.261	-1.539	-3.268	0.00005	0.00719
ENSMUSG00000027022	Xirp2	2:67446001-67526614	7.969	3.101	-1.362	-3.760	0.00005	0.00719
ENSMUSG00000075307	Klhl41	2:69670119-69684230	25.218	10.367	-1.282	-3.874	0.00005	0.00719
ENSMUSG00000027073	Prg2	2:84980460-84983632	91.222	234.501	1.362	4.792	0.00005	0.00719
ENSMUSG00000027895	Kcnc4	3:107438302-107458898	1.694	4.573	1.433	2.866	0.00080	0.06073
ENSMUSG00000040562	Gstm2	3:107981701-107986453	60.296	112.684	0.902	2.596	0.00005	0.00719
ENSMUSG00000027887	Sypl2	3:108211471-108226648	8.527	3.234	-1.399	-3.071	0.00005	0.00719
ENSMUSG00000033400	Agl	3:116739998-116808166	12.852	6.316	-1.025	-2.527	0.00085	0.06335
ENSMUSG00000090066	1110002E22Rik	3:138048760-138081506	1.660	0.475	-1.806	-2.357	0.00040	0.03791
ENSMUSG00000027744	Stoml3	3:53488726-53508502	4.582	55.750	3.605	7.557	0.00005	0.00719
ENSMUSG00000098912	RP23-199B2.4	3:88775215-88832547	3.071	0.480	-2.676	-2.383	0.00065	0.05250
ENSMUSG00000027932	Slc27a3	3:90385238-90389938	2.033	7.039	1.792	2.593	0.00070	0.05518
ENSMUSG00000042250	Pglyrp4	3:90726905-90741517	4.230	0.260	-4.024	-3.963	0.00070	0.05518
ENSMUSG00000038550	Gm129	3:95871521-95892005	28.204	12.574	-1.165	-2.858	0.00145	0.09251
ENSMUSG00000068854	Hist2h2be	3:96221120-96223738	2.420	9.708	2.004	4.718	0.00005	0.00719
ENSMUSG00000038403	Hfe2	3:96525184-96529216	15.510	4.839	-1.680	-4.273	0.00005	0.00719
ENSMUSG00000032643	Fhl3	4:124700700-124708611	30.323	12.460	-1.283	-3.277	0.00005	0.00719
ENSMUSG00000037139	Myom3	4:135759714-135815564	7.233	2.670	-1.438	-2.839	0.00010	0.01271
ENSMUSG00000086549	Gm13648	4:156034839-156059802	4.287	12.422	1.535	2.780	0.00095	0.06862
ENSMUSG00000028294	1700003M02Rik	4:34688558-34730206	0.727	3.904	2.425	2.296	0.00055	0.04672
ENSMUSG00000028441	1110017D15Rik	4:41505008-41517333	4.055	15.498	1.934	2.368	0.00150	0.09423
ENSMUSG00000073102	Drc1	5:30281387-30366708	0.784	3.301	2.075	2.951	0.00120	0.08031
ENSMUSG00000062077	Trim54	5:31116711-31137630	12.031	4.400	-1.451	-2.920	0.00095	0.06862

ENSMUSG00000063646	Jakmip1	5:37028334-37148001	0.973	4.212	2.114	1.744	0.00105	0.07357
ENSMUSG00000029268	Ugt2a1	5:87459489-87490871	2.147	32.384	3.915	6.222	0.00005	0.00719
ENSMUSG00000029273	Sult1d1	5:87554644-87569027	0.421	4.205	3.321	2.780	0.00060	0.04994
ENSMUSG00000029373	Pf4	5:90772434-90773381	72.774	129.142	0.827	3.564	0.00155	0.09590
ENSMUSG00000030110	Ret	6:118151747-118197744	1.742	0.671	-1.377	-2.503	0.00125	0.08231
ENSMUSG00000047228	BC048546	6:128539821-128581606	140.424	29.632	-2.245	-4.535	0.00005	0.00719
ENSMUSG00000042717	Ppp1r3a	6:14713821-14755274	3.575	1.038	-1.784	-4.076	0.00005	0.00719
ENSMUSG00000029683	Lmod2	6:24597770-24605414	21.356	8.389	-1.348	-3.558	0.00005	0.00719
ENSMUSG00000004347	Pde1c	6:56069820-56369634	0.812	3.257	2.004	3.389	0.00005	0.00719
ENSMUSG00000044086	Lmod3	6:97238527-97252780	5.799	2.313	-1.326	-2.432	0.00090	0.06647
ENSMUSG00000030996	Art1	7:102096878-102111148	29.924	12.777	-1.228	-2.984	0.00005	0.00719
ENSMUSG00000030897	Cnga4	7:105404567-105408738	0.357	5.207	3.867	4.751	0.00020	0.02186
ENSMUSG00000031026	Trim66	7:109449005-109508134	0.108	1.475	3.765	2.107	0.00005	0.00719
ENSMUSG00000030672	Mylpf	7:127211607-127214298	1266.740	492.558	-1.363	-3.770	0.00070	0.05518
ENSMUSG00000042828	Trim72	7:128002848-128011393	9.601	4.714	-1.026	-2.350	0.00130	0.08492
ENSMUSG00000030785	Cox6a2	7:128154375-128223816	136.454	65.121	-1.067	-2.954	0.00005	0.00719
ENSMUSG00000038801	Scgb1c1	7:140845564-140846768	12.860	76.515	2.573	7.406	0.00005	0.00719
ENSMUSG00000025488	Cox8b	7:140898942-140900446	200.858	109.052	-0.881	-4.873	0.00140	0.09073
ENSMUSG00000025515	Muc2	7:141746831-141754690	0.485	3.538	2.866	3.641	0.00040	0.03791
ENSMUSG00000031097	Tnni2	7:142441807-142444410	624.654	238.042	-1.392	-3.336	0.00005	0.00719
ENSMUSG00000061723	Tnnt3	7:142460808-142516009	835.862	289.943	-1.527	-2.394	0.00105	0.07357
ENSMUSG00000087090	Nctc1	7:142544608-142558596	3.531	0.983	-1.844	-2.673	0.00105	0.07357
ENSMUSG00000030401	Rtn2	7:19282661-19296164	42.636	21.444	-0.991	-2.581	0.00055	0.04672

ENSMUSG00000049685	Cyp2g1	7:26808926-26821197	2.810	44.860	3.997	8.174	0.00005	0.00719
ENSMUSG00000030592	Ryr1	7:29003339-29125151	11.401	4.075	-1.484	-4.133	0.00005	0.00719
ENSMUSG00000006651	Aplp1	7:30434980-30445582	8.682	17.559	1.016	2.863	0.00030	0.03074
ENSMUSG00000036915	Kirrel2	7:30447533-30457690	0.401	12.233	4.932	1.729	0.00010	0.01271
ENSMUSG00000066584	Scgb2b27	7:34011931-34013942	38.280	5.572	-2.780	-3.808	0.00030	0.03074
ENSMUSG00000038670	Mybpc2	7:44501698-44524669	29.459	6.822	-2.111	-5.628	0.00005	0.00719
ENSMUSG00000095276	Gm581	7:45176348-45179597	3.136	38.749	3.627	7.574	0.00005	0.00719
ENSMUSG00000038201	Kcna7	7:45405959-45411382	3.178	1.106	-1.523	-2.765	0.00120	0.08031
ENSMUSG00000030433	Sbk2	7:4956133-4964390	10.010	2.423	-2.047	-3.166	0.00020	0.02186
ENSMUSG00000055489	Ano5	7:51511028-51598709	1.452	0.495	-1.553	-2.860	0.00075	0.05828
ENSMUSG00000038663	Fsd2	7:81533307-81566944	3.450	1.166	-1.565	-2.894	0.00045	0.04032
ENSMUSG00000049791	Fzd4	7:89404365-89410110	5.806	2.655	-1.129	-2.729	0.00075	0.05828
ENSMUSG00000062826	Ces2f	8:104947355-104955962	8.207	3.307	-1.311	-2.766	0.00120	0.08031
ENSMUSG00000060019	Gm10073	8:106572965-106573461	57.321	17.529	-1.709	-5.388	0.00010	0.01271
ENSMUSG00000034467	Dynlrb2	8:116505014-116515896	7.594	28.043	1.885	4.446	0.00110	0.07610
ENSMUSG00000031980	Agt	8:124556533-124569706	7.583	2.522	-1.588	-3.128	0.00015	0.01744
ENSMUSG00000031530	Dusp4	8:34807296-34819894	8.074	3.856	-1.066	-2.594	0.00155	0.09590
ENSMUSG00000031791	Tmem38a	8:72572102-72587282	37.991	21.692	-0.808	-2.598	0.00100	0.07160
ENSMUSG00000002190	Clgn	8:83389866-83428552	0.284	2.891	3.348	3.814	0.00020	0.02186
ENSMUSG00000043154	Ppp2r3a	9:101104991-101251832	11.296	6.167	-0.873	-2.389	0.00080	0.06073
ENSMUSG00000003410	Elavl3	9:22015004-22052023	0.226	1.952	3.112	3.811	0.00035	0.03436
ENSMUSG00000049281	Scn3b	9:40269215-40291618	0.231	1.542	2.736	1.491	0.00055	0.04672
ENSMUSG00000070306	Ccdc153	9:44240676-44247306	4.212	12.842	1.608	3.200	0.00120	0.08031

ENSMUSG00000044938	Klhl31	9:77636499-77660127	3.026	0.958	-1.660	-3.626	0.00010	0.01271
ENSMUSG00000032452	Clstn2	9:97444394-98033181	0.312	2.209	2.825	3.706	0.00015	0.01744
ENSMUSG00000031312	Itgb1bp2	X:101449087-101453541	13.070	5.560	-1.233	-2.344	0.00145	0.09251
ENSMUSG00000023092	Fhl1	X:56731786-56793346	135.019	64.140	-1.074	-2.618	0.00045	0.04032
ENSMUSG00000082635	Gm14750	X:77988362-77992734	53.173	12.887	-2.045	-5.500	0.00010	0.01271

Supplement materials_Description of the study population

(1) **AgP (Germany).** The AgP patients were recruited from throughout Germany and Vienna, Austria and were described before (Schaefer et al. 2015). In brief, inclusion criteria for the AgP cases were no diabetes and >30% alveolar bone loss under the age of 36 years (mean age, 32; age range 18-35), documented by dental radiographs (N=717 AgP patients, 302 males and 415 females). The AgP control sample consisted of 4,213 controls (2,018 males, 2,191 females, four unknown, mean age=57 years, age range: 19-82) from North- and West-Germany. They were recruited from the Competence Network "FoCus - Food Chain Plus" (Muller et al. 2015), the Dortmund Health Study (DHS) (Berger 2012) and the Heinz Nixdorf Recall Studies 1-3 (HNR1-3) (Schmermund et al. 2002).

CP (USA). The American CP cohort was used as described in (Divaris et al. 2012) and consisted of European American participants of the Dental Atherosclerosis Risk In Communities (ARIC) study with moderate CP (n=1,961 cases; 939 females, 1,022 males; mean age=63 years) and

severe CP (n=785 cases; 279 females, 506 males; mean age=64 years). Individuals who were periodontally-healthy or had mild periodontitis were used as controls (N=1,864 controls; 1,197 females, 667 males; mean age=62 years) (The atherosclerosis risk in communities (aric) study: Design and objectives. The aric investigators 1989).

CP (Germany). The German CP cases and controls were first described in (Schaefer et al. 2011). 399 cases (157 males, 242 females, mean age at first diagnosis=60 years, age range: 36-59), which had >50% bone loss at ≥ 7 teeth sites diagnosed < the age of 60 years were included in this study. The controls (N=1,633, 932 males, 687 females, 14 unknown, mean age of blood donation=58 years, age range: 34-77) consisted of 728 population-representative controls (SPC) and 553 blood donors (BSP), which were collected in North-Germany at the Biobank popgen (Kiel, Germany) and an additional sample of 352 blood donors from Bavaria (Munich, Germany), which were diagnosed to be free of periodontitis.

Supplement material 1

Summary of illumine base calling and alignments

Genotype		Susc.1	Susc.2	Susc.3	Susc.4	Resis.1	Resis.2	Resis.3	Resis.4
Raw	<i>RIN</i>	7.6	7.1	7.3	7	8.1	7.9	7.4	6.3
	<i>Gender</i>	M	M	M	M	M	F	M	F
	<i>Total number of sequences</i>	20875025	21965937	21987585	22252577	22715559	23622044	20692167	22858649
g and Filtering	<i>Sequences after quality filtering</i>	18393145	19337466	19159466	19780962	19936553	20643897	18330333	20203438
	<i>Percent of bad quality</i>	11.89	11.97	12.86	11.11	12.23	12.61	11.41	11.62
Mapping	<i>Total aligned sequences</i>	18062361	19034898	18760038	19541772	19599315	20372563	18133993	19941773
	<i>Percent aligned</i>	98.20	98.44	97.92	98.79	98.31	98.69	98.93	98.70

Annotation	<i>Ensemble gene reads</i>	14270908	13995971	14770085	12260846	14819587	17001896	11363602	14914419
	<i>Ambiguous reads</i>	300035	272449	304427	201377	288014	329778	186175	277017
	<i>No feature reads</i>	1422505	1291706	1623479	1005522	1484980	1406996	836647	1239549
	<i>Ensemble genes with coverage of at least 10</i>	15414	15451	16423	15434	16153	15729	15394	15858

Libraries of cDNA (four resistant and four susceptible) were sequenced together to obtain around 20 million raw sequence reads per sample. These reads then passed cleaning and filtering, before mapping onto the genome.

The eight samples were sequenced together on the same lane of the Illumina GAllx flow. We chose only four of the samples for the next analysis (susc. 2, susc. 4 and resis. 1, resis 3).

Sus. = susceptible mouse phenotype from the F2 population.

Res. = resistant mouse phenotype from the F2 population.