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Supplemental Data

Rare Coding Variants in *ANGPTL6* Are Associated with Familial Forms of Intracranial Aneurysm

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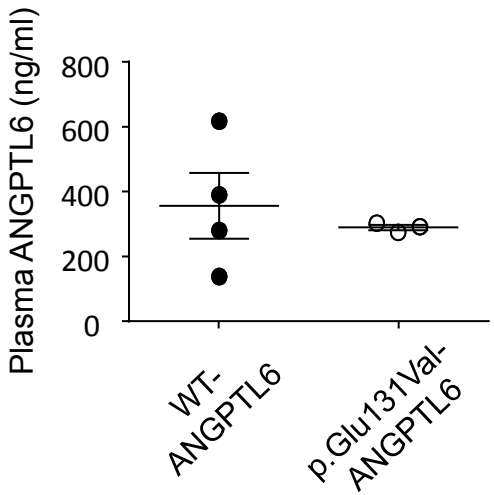
Supplemental Figure 1

Analysis of serum levels of ANGPTL6 in controls (WT-ANGPTL6) and individuals expressing the p.Glu131Val-ANGPTL6 (heterozygous).



Supplemental Table 2: Association tests on rare coding variants in *ANGPTL6*

Statistical test	Number of carriers		Allele count		p-value	OR	CI 95%
	IA cases	Internal controls	IA cases	gnomAD NFE individuals			
SKAT	6/95	8/404	-	-	0.0233	-	-
CAST	6/95	8/404	-	-	0.0331	3.326	[0.927-11.242]
FISHER	-	-	6/190	169/15018	0.0227	2.865	[1.023-6.485]

Supplemental Table 3: Full list of rare coding variants* detected in *ANGPTL6* among IA cases and reference individuals

GRCh37/ hg19 position	rsID	REF allele	ALT allele	Protein Consequence (ENSP00000253109)	Transcript Consequence (ENST00000253109)	Annotation	Allele Count in cases (n=95)	Allele Count in internal controls (n=404)	Allele Count (gnomAD NFE)	MAF (gnomAD NFE)
19:10203293	.	G	C	p.Ala462Gly	c.1385C>G	missense	0	0	1	6.68E-05
19:10203300	rs769022609	T	A	p.Lys460Ter	c.1378A>T	stop gained	1	0	0	-
19:10203324	rs200825170	G	A	p.Arg452Cys	c.1354C>T	missense	0	0	1	6.68E-05
19:10203363	rs201518909	G	A	p.Arg439Ter	c.1315C>T	stop gained	0	0	2	1.33E-04
19:10203375	rs150235799	C	T	p.Gly435Ser	c.1303G>A	missense	0	0	1	6.67E-05
19:10203390	rs769478685	C	T	p.Gly430Ser	c.1288G>A	missense	0	0	1	6.67E-05
19:10203416	rs548381762	T	C	p.His421Arg	c.1262A>G	missense	0	0	1	6.69E-05
19:10203432	rs146282548	C	G	p.Gly416Arg	c.1246G>C	missense	0	1	9	6.02E-04
19:10203434	rs372960335	C	T	p.Arg415Gln	c.1244G>A	missense	0	1	1	6.69E-05
19:10203435	rs377498859	G	A	p.Arg415Trp	c.1243C>T	missense	0	0	1	6.69E-05
19:10203444	.	G	C	p.Leu412Val	c.1234C>G	missense	0	0	2	1.34E-04
19:10204027	rs776568403	G	T	p.Ser407Tyr	c.1220C>A	missense	0	0	1	6.67E-05
19:10204052	rs568396237	C	T	p.Val399Met	c.1195G>A	missense	0	0	1	6.67E-05
19:10204083	.	AAGAG	A	p.Ser387PhefsTer81	c.1160_1163delCTCT	frameshift	0	0	1	6.67E-05
19:10204132	.	T	C	p.His372Arg	c.1115A>G	missense	0	0	1	6.67E-05
19:10204137	rs761235613	G	T	p.Ser370Arg	c.1110C>A	missense	0	0	1	6.67E-05
19:10204142	rs754265148	C	T	p.Glu369Lys	c.1105G>A	missense	0	0	1	6.67E-05
19:10204187	rs779222736	C	G	p.Gly354Arg	c.1060G>C	missense	0	0	3	2.00E-04
19:10204205		G	A	p.Leu348Phe	c.1042C>T	missense	1	0	0	-
19:10204215	rs769287477	C	G	p.Glu344Asp	c.1032G>C	missense	0	1	0	-
19:10204229	rs138652863	G	A	p.Arg340Cys	c.1018C>T	missense	0	0	3	2.00E-04
19:10204239	.	C	G	p.Gln336His	c.1008G>C	missense	0	0	1	6.67E-05
19:10204377	.	G	C	p.His315Asp	c.943C>G	missense	0	0	1	6.66E-05
19:10204419	rs748744561	G	A	p.Arg301Trp	c.901C>T	missense	0	0	2	1.33E-04
19:10204440	rs201494217	C	T	p.Gly294Arg	c.880G>A	missense	0	0	1	6.66E-05
19:10204464	rs774043154	A	G	p.Trp286Arg	c.856T>C	missense	0	0	2	1.33E-04
19:10204469	rs201622589	G	C	p.Ser284Ter	c.851C>G	stop gained	0	0	24	1.60E-03
19:10204476	rs760163416	C	T	p.Val282Ile	c.844G>A	missense	0	0	1	6.66E-05
19:10204510	rs778164883	C	A	p.Gln270His	c.810G>T	missense	0	0	1	6.67E-05
19:10204512	rs372998779	G	C	p.Gln270Glu	c.808C>G	missense	0	0	3	2.00E-04
19:10204529	rs150117768	C	A	p.Arg264Leu	c.791G>T	missense	0	0	1	6.67E-05
19:10204530	rs182345321	G	A	p.Arg264Cys	c.790C>T	missense	0	0	5	3.33E-04
19:10205491	.	C	T	p.Glu236Lys	c.706G>A	missense	0	0	2	1.33E-04
19:10205553	rs138519545	T	C	p.Asp215Gly	c.644A>G	missense	0	0	1	6.66E-05
19:10205607	rs145558307	G	A	p.Pro197Leu	c.590C>T	missense	0	0	1	6.67E-05
19:10206662	rs200836122	T	C	p.Gln193Arg	c.578A>G	missense	0	0	13	8.68E-04
19:10206680	rs771739756	C	G	p.Gly187Ala	c.560G>C	missense	0	0	1	6.72E-05
19:10206686	.	C	A	p.Cys185Phe	c.554G>T	missense	0	0	1	6.68E-05
19:10206729		C	G	p.Val171Leu	c.511G>C	missense	0	1	0	-
19:10206761	rs771917209	A	C	p.Leu160Arg	c.479T>G	missense	0	0	1	6.70E-05
19:10206763	rs369847598	C	A	p.Gln159His	c.477G>T	missense	0	0	5	3.35E-04
19:10206774	rs770895499	G	A	p.Arg156Trp	c.466C>T	missense	0	0	1	6.72E-05
19:10206780	rs199549770	C	T	p.Ala154Thr	c.460G>A	missense	0	0	1	6.72E-05
19:10206782	rs770263825	G	GCGCGCTGAG CCTCGGCGGA	p.Ala153ValfsTer66	c.439_457dupTCCGCC GAGGCTCAGCGCG	frameshift	2	0	1	6.72E-05
19:10206787	rs776060868	C	CTGAGCCTCGG CGGACGCGT	p.Ala153ValfsTer66	c.434_452dupACGCGT CCGCCGAGGCTCA	frameshift	0	0	2	1.34E-04
19:10206801	rs779899913	A	G	p.Ser147Pro	c.439T>C	missense	0	0	1	6.76E-05
19:10206824	rs554909694	A	G	p.Leu139Pro	c.416T>C	missense	0	0	1	6.82E-05
19:10206824	rs554909694	A	T	p.Leu139His	c.416T>A	missense	0	0	1	6.82E-05

19:10206848	rs576667683	T	A	p.Glu131Val	c.392A>T	missense	2	2	39	2.67E-03
19:10206854	.	C	G	p.Gly129Ala	c.386G>C	missense	0	1	0	-
19:10206875	.	G	A	p.Ala122Val	c.365C>T	missense	0	0	1	6.92E-05
19:10206896	.	T	C	p.Gln115Arg	c.344A>G	missense	0	0	1	6.94E-05
19:10206915	.	G	A	p.Gln109Ter	c.325C>T	stop gained	0	0	1	7.00E-05
19:10206993	.	C	A	p.Ala83Ser	c.247G>T	missense	0	0	1	6.82E-05
19:10206995	.	A	T	p.Leu82Gln	c.245T>A	missense	0	0	1	6.81E-05
19:10206997	.	C	G	p.Arg81Ser	c.243G>C	missense	0	1	3	2.03E-04
19:10207001	.	T	C	p.Gln80Arg	c.239A>G	missense	0	0	1	6.77E-05
19:10207020	.	C	G	p.Glu74Gln	c.220G>C	missense	0	0	1	6.73E-05
19:10207035	.	C	T	p.Val69Ile	c.205G>A	missense	0	0	3	2.05E-04
19:10207035	.	C	A	p.Val69Phe	c.205G>T	missense	0	0	1	6.82E-05
19:10207053	.	C	G	p.Ala63Pro	c.187G>C	missense	0	0	2	1.35E-04
19:10207059	.	C	T	p.Glu61Lys	c.181G>A	missense	0	0	1	6.76E-05
19:10207076	rs560311003	T	G	p.Glu55Ala	c.164A>C	missense	0	0	1	6.77E-05
19:10207083	rs746538090	T	A	p.Thr53Ser	c.157A>T	missense	0	0	1	6.76E-05
19:10207103	rs560892001	C	T	p.Gly46Asp	c.137G>A	missense	0	0	2	1.34E-04
19:10207104	.	C	T	p.Gly46Ser	c.136G>A	missense	0	0	1	6.73E-05
19:10207225	rs751565560	C	T	p.Trp5Ter	c.15G>A	stop gained	0	0	1	6.69E-05

[*] *Rare variants were defined as having an MAF below 1% among the whole-genome sequenced individuals with European Non-Finnish ancestry available in gnomAD*