Supplemental data

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Supplemental Figure S1

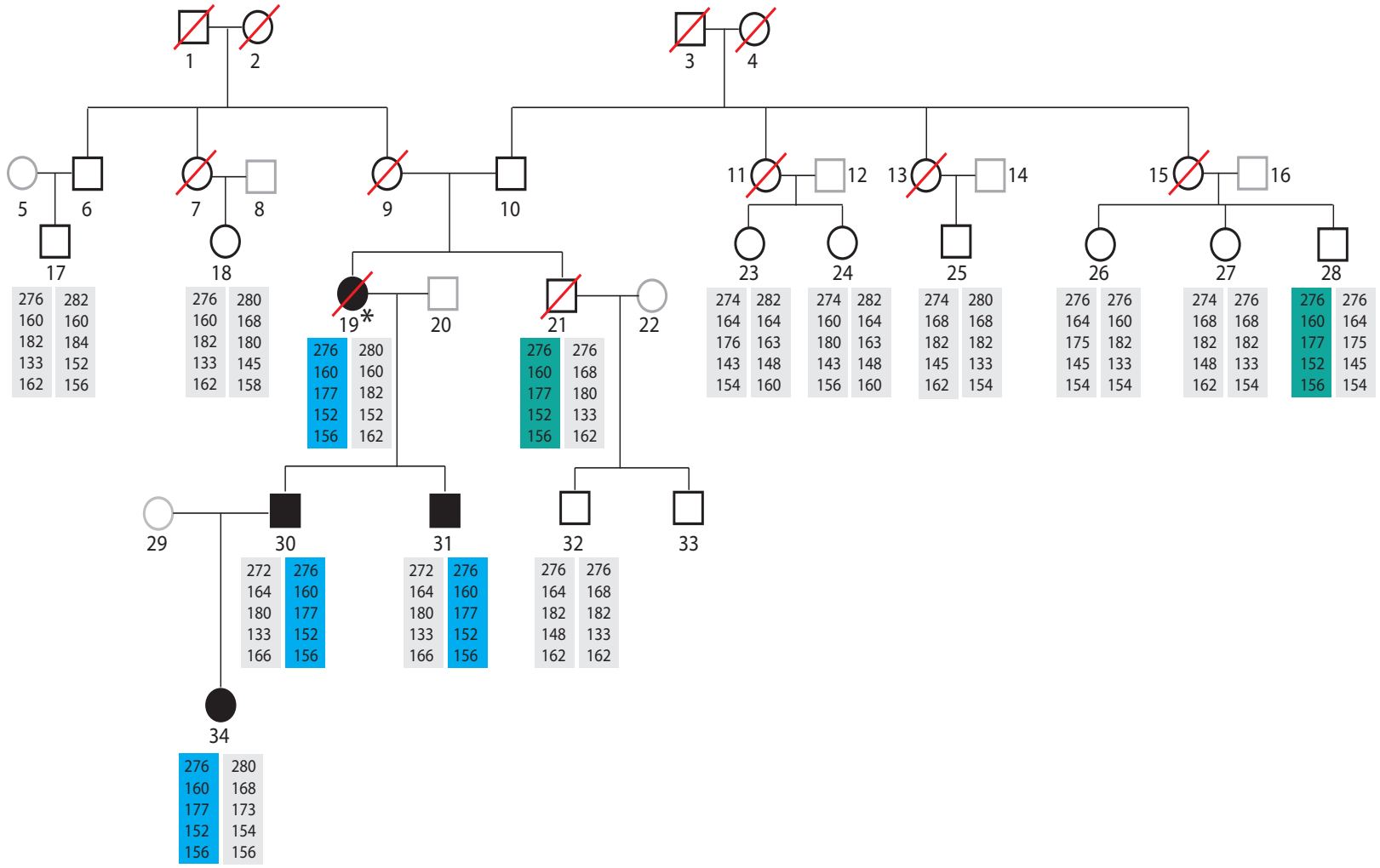
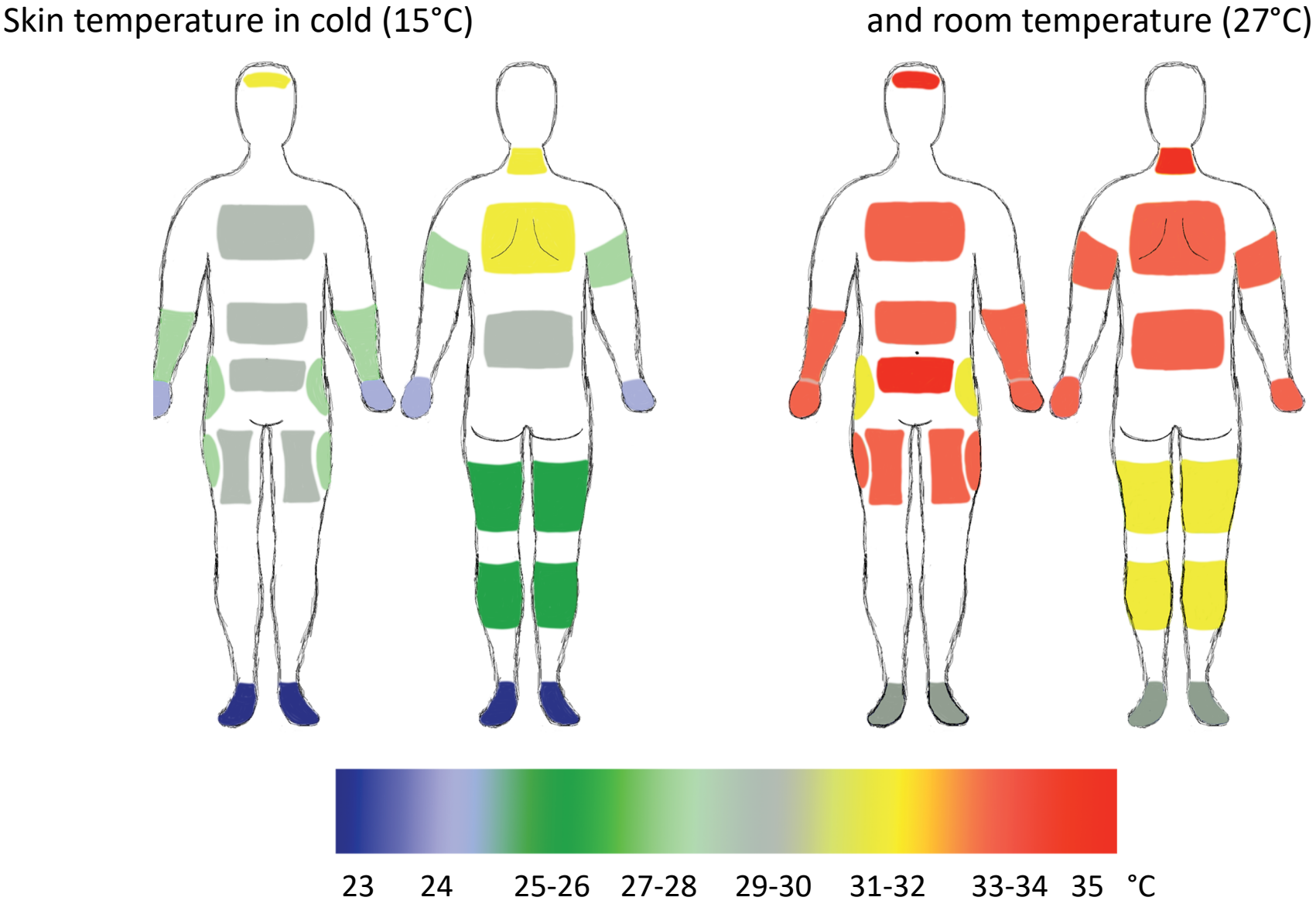


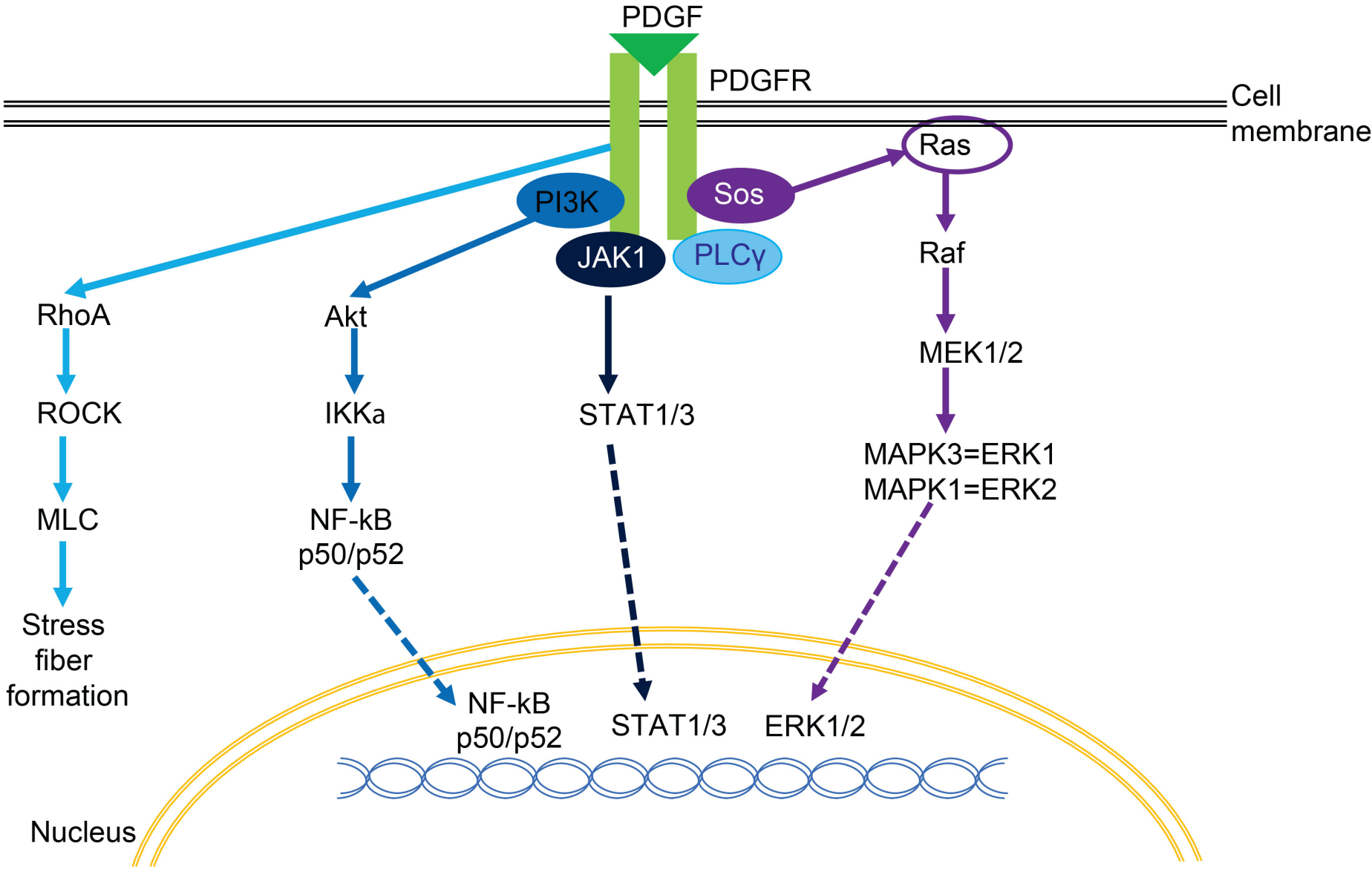
Figure of the pedigree of the original OPDKD family showing the results from haplotype analysis. While two healthy family members share the affected haplotype (marked in green) the *PDGFRB* mutation has occurred in the index patient (19*) proving that it is a *de novo* mutation (haplotype marked in blue).

Supplemental Figure S2



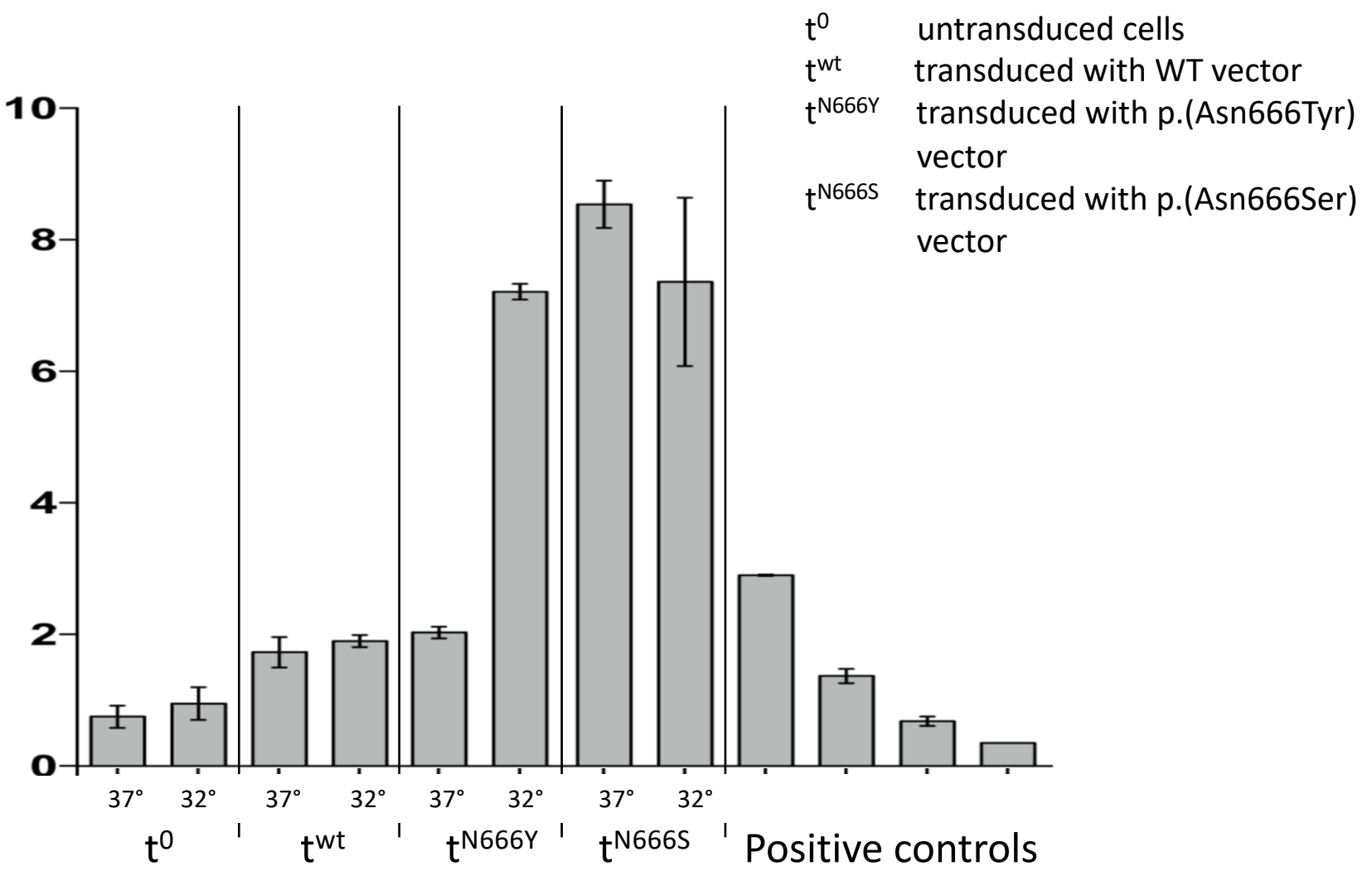
Schematic figure of skin temperature in various temperatures.
Based on Webb P. Temperatures of skin, subcutaneous tissue, muscle and core in resting men in cold, comfortable and hot conditions. *Eur J Appl Physiol Occup Physiol.* 1992;64(5):471-6.

Supplemental Figure S3



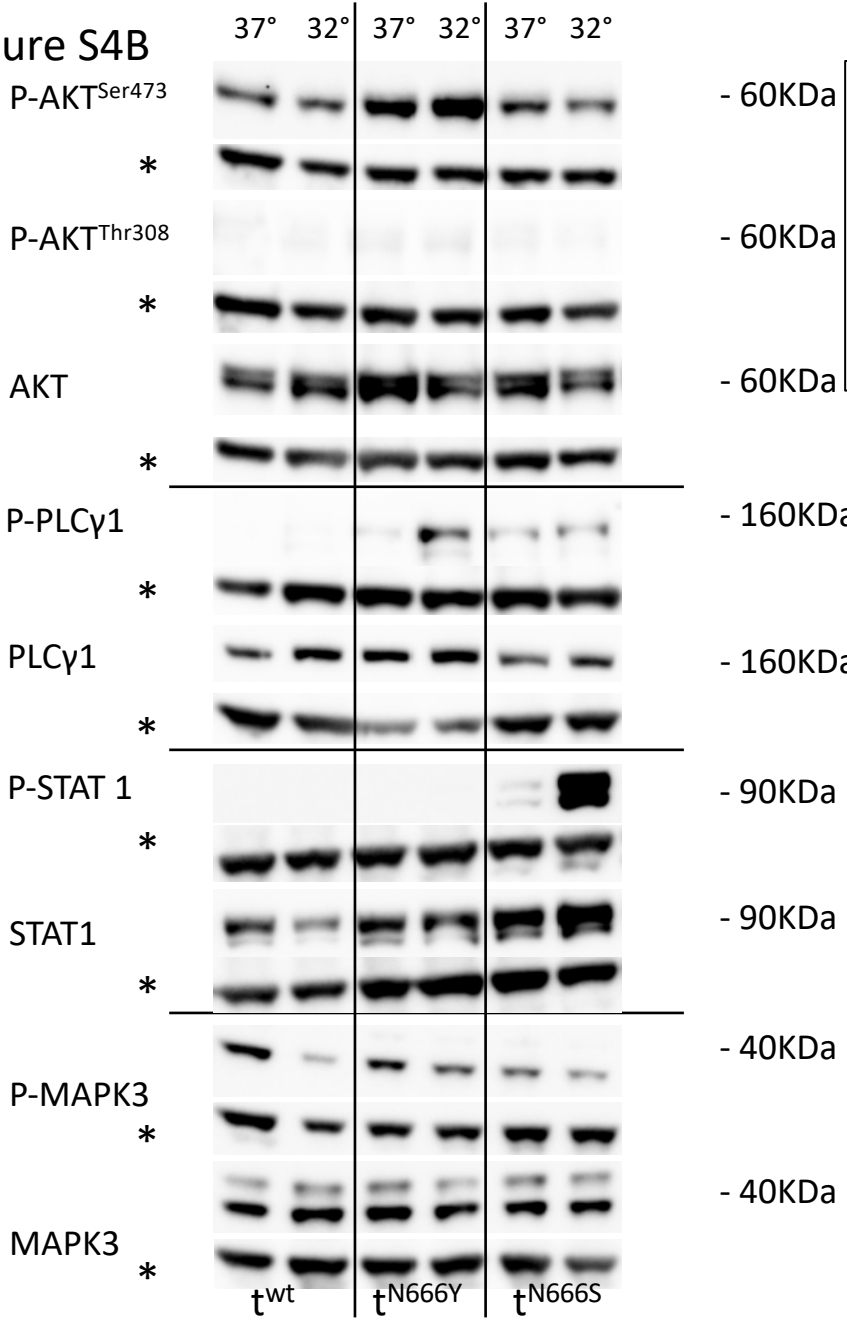
Overview PDGFR signaling. Adapted from Ying HZ, Chen Q, Zhang WY, Zhang HH, Ma Y, Zhang SZ, Fang J, Yu CH. PDGF signaling pathway in hepatic fibrosis pathogenesis and therapeutics. *Mol Med Rep.* 2017; 16(6):7879-89.

Supplemental Figure S4A



ELISA examination of total P-PDGFRβ in transduced Hela cells harvested after overnight serum starvation at 37° or 32° show greatly increased levels in p.(Asn666Tyr) transduced cells at 32° and in p.(Asn666Ser) transduced cells at both temperatures.

Supplemental Figure S4B



t^{wt}	transduced with WT vector
t^{N666Y}	transduced with p.(Asn666Tyr) vector
t^{N666S}	transduced with p.(Asn666Ser) vector
*	GAPDH

Transduced Hela cells harvested in serum (to detect also P-AKT) after overnight exposure to 37° or 32°. Increased levels of P-PLCγ1 and slighly increased P-AKT is seen in N666Y cells at 32°. Greatly increased levels of P-STAT1 is seen in N666S cells.

Supplemental Table S1

Variants retained after filtering

Chr	Start	End	Ref	Obs	Gene	ExonicFunc	cDNA Change	AAChange
19	55508765	55508766	TG	-	NLRP2	frameshift deletion	NM_001174082:exon11:c.2894_2895del	p.965_965del
17	37900375	37900375	G	C	GRB7	nonsynonymous SNV	NM_001030002:exon7:c.G716C	p.R239P
5	149503840	149503840	T	A	PDGFRB	nonsynonymous SNV	NM_002609:exon14:c.A1996T	p.N666Y
9	35813771	35813771	G	A	HINT2	nonsynonymous SNV	NM_032593:exon2:c.C92T	p.A31V
7	107603504	107603506	ACC	GTT	LAMB1	delins	NM_002291.2:exon15:c.1701_1703delinsCCA	p.V568H

The NLRP2 frameshift deletion was regarded an unlikely candidate as the gene in gnomAD is listed with pLI = 0, with 53 (expected 45) loss of function mutations distributed throughout the gene, i.e this gene will tolerate haploinsufficiency. Likewise, the HINT2 mutation is located in a non-conserved region of the protein and predicted to be tolerated/benign. In gnomAD it is recorded a number of SNV's in the immediate surroundings. In addition, it is postulated that HINT2 will tolerate haploinsufficiency. The GRB7 c.G716C mutation was not inherited by the affected granddaughter and was therefore excluded. The LAMB1 indel will change the moderately conserved amino acid Valine to Histidine. The various prediction software used by Alamut classifies is not in concordance, ranging from *uncertain*/*possibly damaging* (Align GVGD/PolyPhen-2 humvar) to *Deleterious*/*Disease Causing* (SIFT/MutationTester). In gnomAD several amino acids in the immediate vicinity is listed, including one affecting the same codon (p.Val568Phe). In addition, LAMB1 is in OMIM coupled to Lissencephaly (#150240) with autosomal recessive inheritance. It is thus unlikely that this mutation could cause this dominant inherited disease.

Supplemental Table S2

Microsatellite analysis of the PDGFRB locus

Name	Primer 1	Primer 2	Chr	Amplicon (bp)	Amplicon start	Amplicon end
D5S413	AGTCACCTTCTCTGTCTCCA	AGGCCTCATTCAAAATCTGT	5	272	14836 7356	14836 7627
D5S812	TACCACAGCAACCACAAAGA	GAGGAAAGCAAAGACCATGA	5	162	14900 8723	14900 8884
PDGFRB	***(Start) « ATG..... «***	***« .....TAG « (Stop)***	***5***	***(21285)***	***14949 5326***	***14951 6610***
D5S2015	TTGGCTAATGGGAGGCAACA	GCTACCTAAAGAACACAGTCATGGC	5	173	14957 8337	14957 8509
D5S636F	AAGGCATATGGGAAATATCTGT	CCACACCATTATGACATTTTCT	5	144	14989 6516	14989 6659
D5S2014	AGCTACTACCAGCAGCATTC	CTACATTATTATTATTGTGTGTCCG	5	160	14996 3917	14996 4076