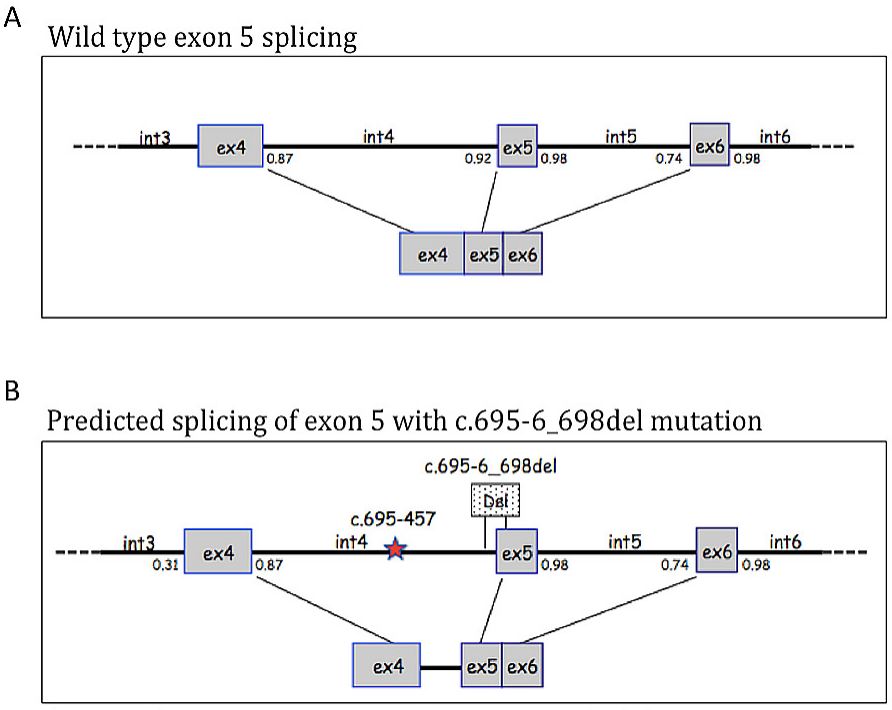
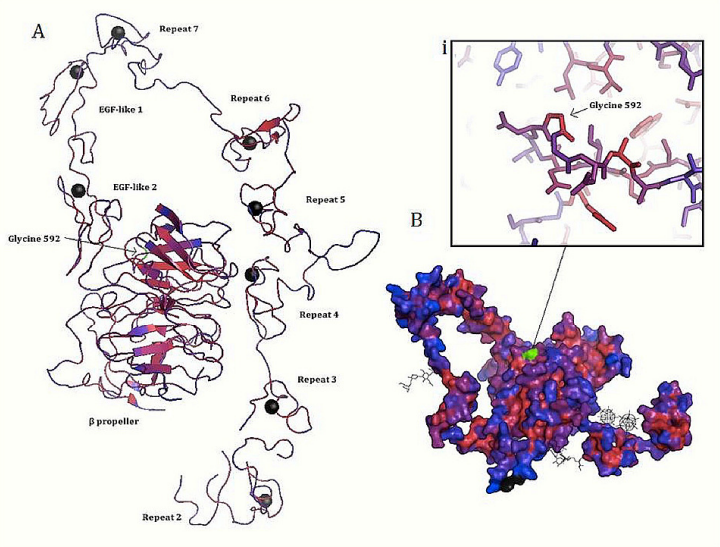
Supplementary Fig.S1:

In silico, splice site predictions using BDGP prediction tools (http://www.fruitfly.org/seq_tools/splice.html)[34]. A: Wild type *LDLR* scores for the acceptor/donor splice sites. B: *LDLR* mutation (c.695-6_698del) removes the exon 5 acceptor site and potentially activates an upstream cryptic site (c.695-457/8).



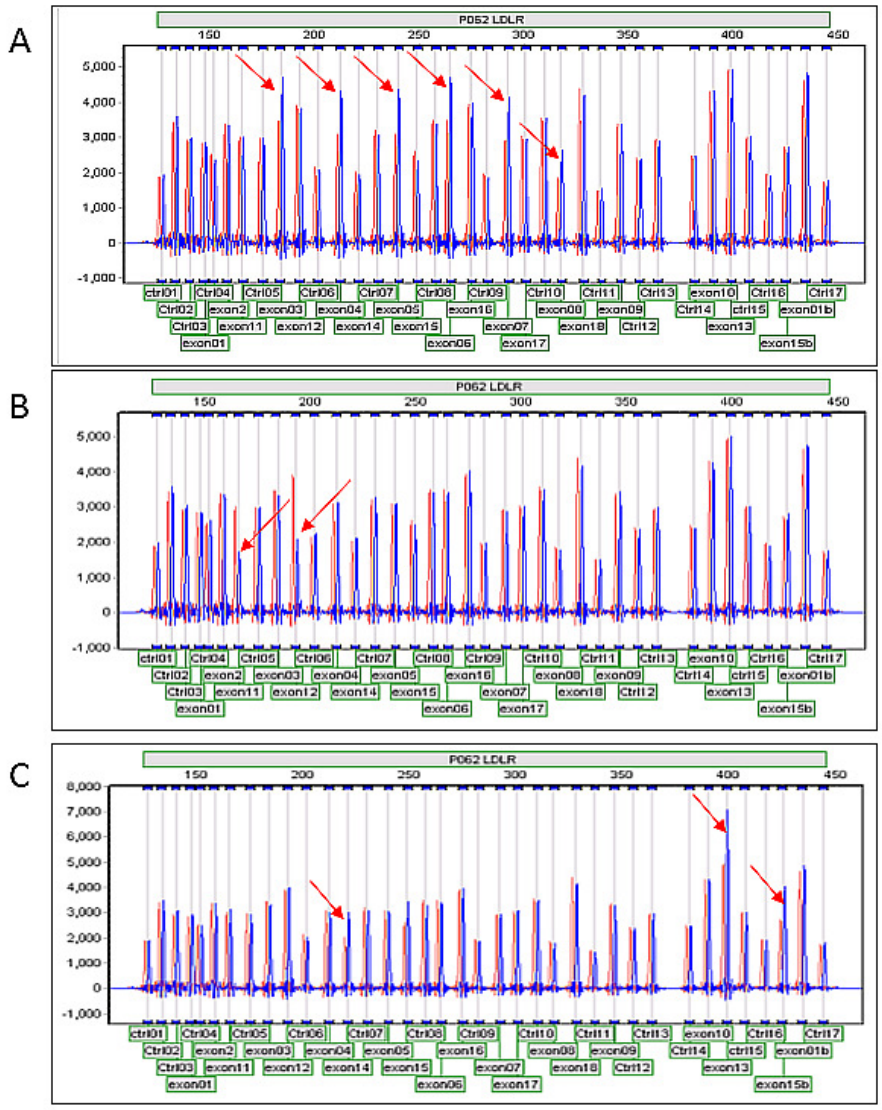
Supplementary Fig.S2:

Conservation score calculated over the entire available crystal structure of the LDL-R protein. Red shows high conservation, purple- moderate conservation, blue- poor conservation and black- no conservation. A. LDL-R protein displaying the calcium molecules (black spheres) and labeled regions including Glycine 592. B. Glycine 592 is on the surface of the protein and is highly conserved (see inset 'i').



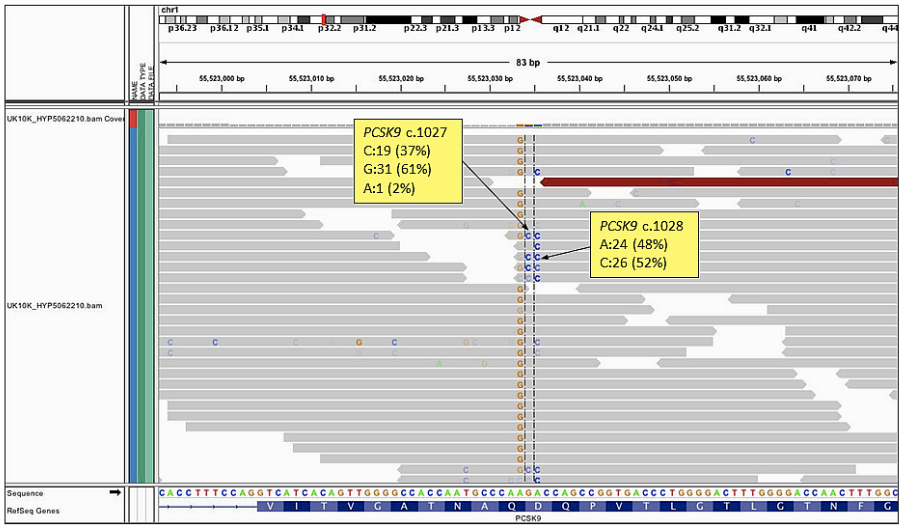
Supplementary Fig.S3:

MLPA results quantified by the fluorescence peak heights for the tested sample (blue) and normalised control (red). Red arrows mark peaks, in which the sample/control difference was significant. A: Heterozygous duplication of exons 3 to 8 in sample HYP5002209. B: Heterozygous deletion of exons 11 and 12 in sample HYP5062217. C: Heterozygous duplication of exons 13 to 15 in sample HYP5062219.



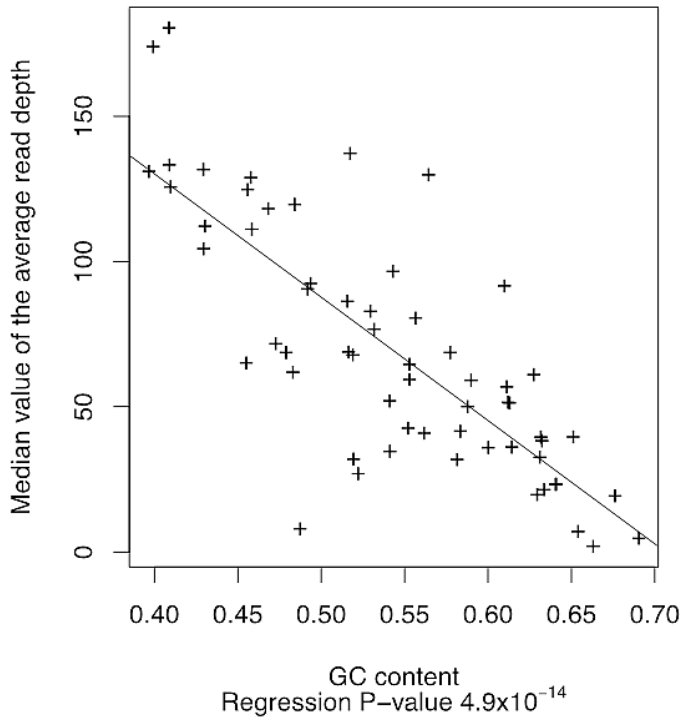
Supplementary Fig.S4:

Intergrative Genomic Viewer image of the coverage of *PCSK9* exon 7 region containing two false positive variants c.1027G>C and c.1028A>C. These artifacts were probably created during the amplification step in the sequence capture process.



Supplementary Fig.S5:

The negative correlation of the median read depth and the GC content for each targeted exon of the four FH genes (*LDLR*, *APOB*, *PCSK9* and *LDLRAP1*).



No. samples	Nucleotide change	Functional effect	Depth	Quality	PolyPhen	SIFT	Mutation Taster
1	c.148C>T	p.(R50W)	139	181	D	D	N
1	c.1199G>A	p(.R400H)	35	100	B	D	N
1	c.2938G>A	p.(A980T)	29	198	B	T	N
1	c.3931A>C	p.(K1311Q)	68	170	B	D	N

Table S1.

Summary of novel *APOB* variants, located outside of exons 26 and 29. 'Depth' refers to the depth coverage; 'Quality' values are Phred-like quality scores generated by SAMtools. D-damaging; B-benign; T-tolerated; N- polymorphism.