

**c.461A>G, p.H154R**

PANTHER HMM: LIPASE (PTHR11610)

Substitution	preservation time	Message
H154R	1037	probably damaging

PSEP (position-specific evolutionary preservation) measures the length of time (in millions of years) a position in current protein has been preserved by tracing back to its reconstructed direct ancestors. The longer a position has been preserved, the more likely that it will have a deleterious effect. The thresholds we chose were: "probably damaging" (time > 450my, corresponding to a false positive rate of ~0.2 as tested on HumVar), "possibly damaging" (450my > time > 200my, corresponding to a false positive rate of ~0.4) and "probably benign" (time < 200my).

**c.788T>A, p.L263Q**

PANTHER HMM: LIPASE (PTHR11610)

Substitution	preservation time	Message
L263Q	455	probably damaging

PSEP (position-specific evolutionary preservation) measures the length of time (in millions of years) a position in current protein has been preserved by tracing back to its reconstructed direct ancestors. The longer a position has been preserved, the more likely that it will have a deleterious effect. The thresholds we chose were: "probably damaging" (time > 450my, corresponding to a false positive rate of ~0.2 as tested on HumVar), "possibly damaging" (450my > time > 200my, corresponding to a false positive rate of ~0.4) and "probably benign" (time < 200my).

**Figure S1** The pathogenicity prediction of patient's *LPL* mutants using PANTHER (Protein ANalysis THrough Evolutionary Relationships) classification system. The two mutants (c.461A>G; p.His154Arg and c.788T>A; p.Leu263Gln) were analyzed using PANTHER and their PSEP (position-specific evolutionary preservation) was calculated. According to the analysis, both mutants were predicted to be 'probably damaging'.

**c.461A>G, p.H154R**

Input	Protein_id	Codon change	Mutation	Type	Score	Prediction (cutoff=-2.5)	#Seq	#Cluster	Score	Prediction (cutoff=0.05)	Median_info	#SEQ
8,19810852, A,G	ENSP00000309757	GTC C[A/G]T CTC	H154R	Single AA Change	-7.65	Deleterious	243	30	0.001	Damaging	2.82	189

**c.788T>A, p.L263Q**

Input	Protein_id	Codon change	Mutation	Type	Score	Prediction (cutoff=-2.5)	#Seq	#Cluster	Score	Prediction (cutoff=0.05)	Median_info	#Seq
8,19813364, T,A	ENSP00000309757	CAG C[T/A]A GTG	L263Q	Single AA Change	-2.25	Neutral	243	30	0.025	Damaging	2.85	185

**Figure S2** The pathogenicity prediction of patient's *LPL* mutants using SIFT (Sorting Intolerant From Tolerant). The two mutants (c.461A>G; p.His154Arg and c.788T>A; p.Leu263Gln) were analyzed using SIFT and both were predicted to be 'damaging'.