

# New rare genetic variants of *LMF1* gene identified in hyperchylomicronemic patients

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## Supplemental Data

### Supplemental Legends for Figures

#### Supplemental Figure 1: Tests of different volume of medium for LPL activity assay

The LPL activity was dosed with 10 to 50  $\mu$ l of the same medium of cells co-transfected with LPL and WT LMF1.

#### Supplemental Figure 2: Tests of different incubation time after heparin addition in the cell medium

The LPL activity was dosed in the medium of cell co-transfected with LPL and WT LMF1 from 1 to 8 hours after addition of heparin in the cell culture medium.

### Supplemental Table 1: Primers used for *LMF1* gene sequencing

Gene region	Forward primer	Reverse Primer
Exon 1	5'-tgtgagcggggcctcc-3'	5'-gagaccgcgcggaggagt-3'
Exon 2	5'-gccccacattctgagctg-3'	5'-agtgacagcaagccctaagc-3'
Exon 3	5'-gcttcactcagtgggaaa-3'	5'-catactgggaaggctgatgg-3'
Exon 4	5'-ttgtgaaatgtgtgctcc-3'	5'-cgttattccccaaacaccac-3'
Exon 5	5'-cctgggaagctgttctgtc-3'	5'-caggggtgtgcaggactgag-3'
Exon 6	5'-cacaagcctctccctagcc-3'	5'-gccagcgtctctgtggac-3'
Exon 7	5'-cagctgggttcagttgtga-3'	5'-caccaccgactttctcct-3'
Exon 8	5'-gagccccacctggaagat-3'	5'-tctccccatatacccagctc-3'

<b>Exon 9</b>	5'-ctctcagtagcccctgacca-3'	5'-ccatctatgggcagaagagg-3'
<b>Exon 10</b>	5'-gagtggcacagccgtctc-3'	5'-cagcagacacctggatttg-3'
<b>Exon 11</b>	5'-ctgctgggggtctacctgt-3'	5'-agggcaaacttgctgag-3'

**Supplemental Table 2: Comparison of LPL and LMF1 mRNA expression and LPL activity in HEK cells non-transfected or co-transfected with LMF1 and LPL.**

mRNA expression was measured by RT-qPCR.

	Non-transfected HEK cells	HEK cells co-transfected with LMF1 and LPL
LPL mRNA	0.03 +/-0.01	187.96 +/- 49.42
LMF1 mRNA	0.02 +/- 0.01	2.67 +/- 0.82
LPL activity	2.82 +/- 0.36	23.58 +/- 2.12

**Supplemental Table 3: *LMF1* coding and non-coding variants identified in the hyperchylomicronemic cohort (n=385)**

HCM, hyperchylomicronemic; MAF, minor allele frequency; NA, not available

Exon	Position	Variant	Rs number	HCM cohort (n=385)		Control dyslipidemic cohort (n=144)		MAF in 1000 Genomes EUR (%)	MAF in ExAC Eur nonFinn (%)
				HTZ/HMZ	MAF (%)	HTZ/HMZ	MAF (%)		
1	c.-39_21del		rs36202798	219/39	33.5	21/3	11.1	23.0	1.0
1	c.-21G>T		rs13334376	110/7	15.2	0/0	0	23.0	12.1
1	c.95C>T	p.Ala32Val	rs199831082	1/0	0.1	0/0	0	0.0	0.0
1	c.107G>A	p.Gly36Asp	rs111980103	21/1	2.9	29/2	11.5	9.0	21.0
1	c.117C>A	p.Gly39Gly	rs373824481	1/0	0.1	0/0	0	0.0	0.0
2	c.194-28T>C		rs3751666	229/58	37.3	73/23	41.3	37.7	38.1
2	c.234C>G	p.Leu78Leu	rs149929337	5/0	0.6	0/0	0	0.5	0.2
2	c.255T>C	p.Leu85Leu	rs12448005	50/6	7.3	17/2	7.3	5.8	7.1
2	c.306G>A	p.Thr102Thr	rs3751667	149/19	21.8	51/9	20.8	20.8	22.8
2	c.396C>T	p.Leu132Leu	rs375877835	1/0	0.1	0/0	0	0.0	0.0
2	c.411G>A	p.Ser137Ser	rs117150036	9/0	1.2	2/0	0.7	1.4	2.1
2	c.413C>G	p.Ser138Cys	rs200382562	2/0	0.3	0/0	0	0.1	0.2
2	c.428C>T	p.Thr143Met	rs375529211	1/0	0.1	0/0	0	0.0	0.0
3	c.514G>A	p.Gly172Arg	rs201406396	0/1	0.3	0/0	0	0.0	0.0
4	c.515-7G>A		NA	1/0	0.1	0/0	0	NA	NA
4	c.540G>A	p.Thr180Thr	rs2277892	88/6	12.2	35/0	12.2	9.2	11.1
4	c.543G>A	p.Gly181Gly	rs2277893	150/15	21.4	57/2	21.2	17.7	17.8
4	c.552G>C	p.Gly184Gly	rs199702457	2/0	0.3	1/0	0.3	0.1	0.1
5	c.683G>T	p.Gly228Val	NA	1/0	0.1	0/0	0	NA	NA
5	c.729+18C>G		rs11864203	229/56	37.0	67/16	34.4	27.9	31.3
6	c.730-49C>T		rs201996962	1/0	0.1	0/0	0	0.2	0.4
6	c.756G>A	p.Ala252Ala	rs2076425	92/3	12.3	36/1	13.2	11.1	15.8
6	c.837C>A	p.Phe279Leu	rs61745065	1/0	0.1	1/0	0.3	0.0	0.0
6	c.861G>A	p.Ala287Ala	rs61740409	9/0	1.2	4/0	1.4	0.2	0.1
6	c.897+27C>T		rs76200860	1/0	0.1	0/0	0	0.0	0.0

6	c.897+28G>A		rs184361133	7/0	0.9	0/0	0	0.7	0.8
7	c.898-14C>G		rs556303155	2/0	0.3	0/0	0	0.0	0.0
7	c.1001C>G	p.Ser334Cys	rs765992133	1/0	0.1	0/0	0	NA	0.0
7	c.1052G>A	p.Arg351Gly	rs192520307	7/0	0.9	2/0	0.7	0.2	0.2
7	c.1060C>T	p.Arg354Trp	rs143076454	9/0	1.2	6/0	2.1	2.5	3.0
7	c.1078+17G>T		rs74001087	7/0	0.9	2/0	0.7	0.1	0.1
8	c.1091G>A	p.Arg364Gln	rs35168378	15/0	1.9	7/0	2.4	3.0	3.6
8	c.1228G>A	p.Gly410Arg	rs199713950	1/0	0.1	0/0	0	0.1	0.0
8	c.1232+20G>A		rs149871283	3/0	0.4	1/0	0.3	0.0	0.6
9	c.1233-5G>A		rs200343204	2/0	0.3	0/0	0	0.0	0.0
9	c.1290C>T	p.Ser430Ser	rs148734358	1/0	0.1	0/0	0	0.2	0.1
9	c.1292C>A	p.Ala431Asp	rs115416993	1/0	0.1	0/0	0	0.0	0.1
9	c.1351C>T	p.Arg451Trp	rs138205062	5/0	0.6	0/0	0	0.4	0.5
9	c.1382G>A	p.Arg461His	rs557053661	1/0	0.1	0/0	0	0.0	0.0
9	c.1391G>A	p.Trp464Ter	rs587777626	1/0	0.1	0/0	0	NA	NA
9	c.1405G>A	p.Ala469Thr	rs181731943	1/0	0.1	2/0	0.7	0.2	0.1
9	c.1416+13C>T		rs114354808	1/0	0.1	0/0	0	0.0	0.0
9	c.1416+20G>A		rs367631358	1/0	0.1	1/0	0.3	0.0	0.0
9	c.1416+24G>A		rs138911395	1/0	0.1	1/0	0.3	0.3	0.1
10	c.1473C>T	p.Asp491Asp	rs62012416	1/0	0.1	0/0	0	0.4	0.2
10	c.1476C>T	p.Ala492Ala	rs142258761	1/0	0.1	1/0	0.3	0.1	0.0
10	c.1529+20G>A		rs149923445	3/0	0.4	0/0	0	0.0	0.0
10	c.1529+39del		rs376645804	1/0	0.1	0/0	0	0.0	0.0
11	c.1530-15T>C		rs367769866	1/0	0.1	0/0	0	0.0	0.0
11	c.1590C>T	p.Ala530Ala	NA	1/0	0.1	0/0	0	NA	NA
11	c.1609C>T	p.Arg537Trp	rs555435528	1/0	0.1	0/0	0	NA	0.0
11	c.1685C>G	p.Pro562Arg	rs4984948	11/0	1.4	1/0	0.3	0.8	0.9