Circulating triacylglycerol signatures and insulin sensitivity in NAFLD associated with the E167K variant in TM6SF2

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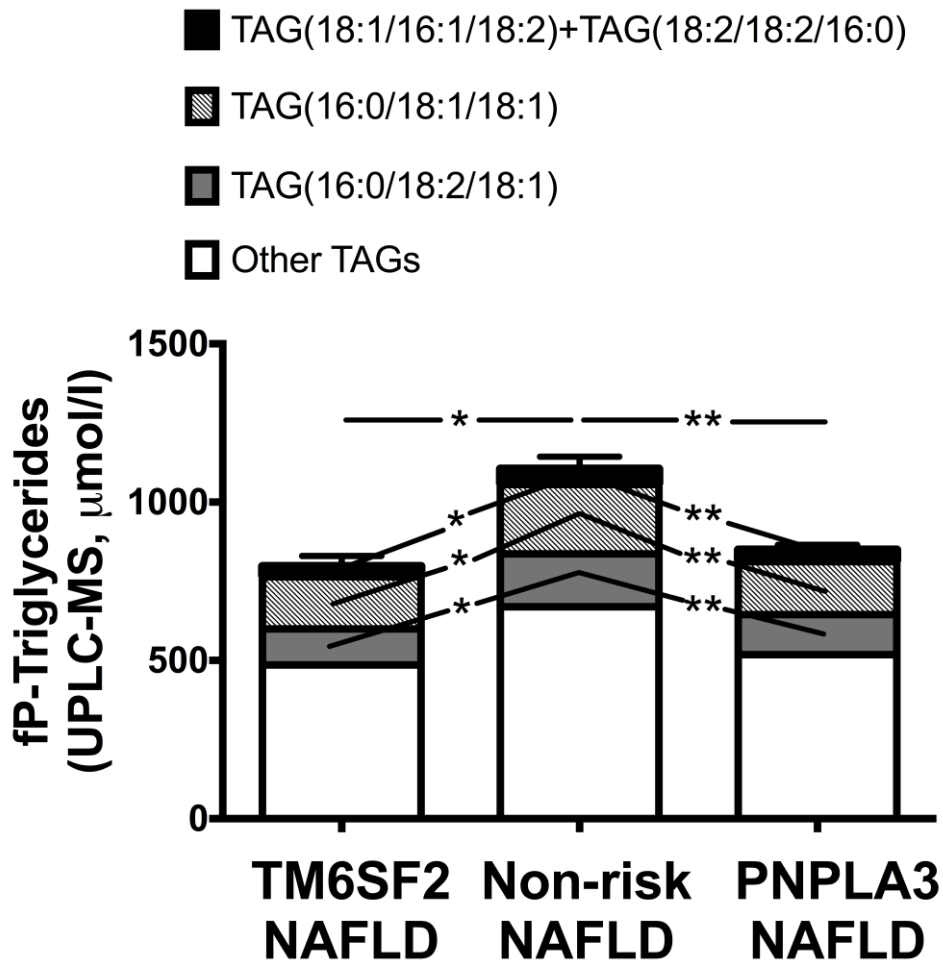
Supplementary Methods

Lipidomic analysis with UPLC-MS

For further identification of unknown lipids, fractions collected from UPLC run were infused to a LTQ-Orbitrap (Thermo Fischer Scientific, San Jose, CA) mass spectrometer by a TriVersa Nanomate (Advion Biosciences, Ithaca, NY) using chip-based nanoelectrospray in positive and negative ionization mode. Identifications were based on the exact mass and MS^n spectra. The instrument was calibrated externally according to the instructions of manufacturer. MS^2 and MS^3 were acquired using either low resolution or high resolution up to target mass resolution R = 60 000 at m/z 400. The normalized collision energies of 30-40% were applied in MS^n experiments.



Supplementary Fig. 1. Distribution of plasma TAG species in the 'TM6SF2 NAFLD', PNPLA3 NAFLD' and 'Non-risk NAFLD' groups. Total TAGs are shown as mean ± SEM. The significant differences in concentrations of total TAGs, TAG(16:0/18:2/18:1), TAG(16:0/18:1/18:1), TAG(18:1/16:1/18:2)+TAG(18:2/18:2/16:0) are indicated (*$p < 0.05$, **$p < 0.01$).

Supplementary Table 1. Composition of circulating lipid clusters

Cluster name	Size	Representative members
LC1	19	TAG(16:0/18:2/18:1); TAG(16:0/18:1/18:1); TAG(18:1/16:1/18:2)+TAG(18:2/18:2/16:0); TAG(18:1/18:2/18:1); TAG(18:1/18:1/18:1); TAG(14:0/18:1/18:1)+TAG(16:0/16:1/18:1); TAG(16:0/18:1/16:0); TAG(50:3); TAG(54:5); TAG(56:4); TAG(18:1/18:1/20:1)
LC2	22	PC(34:2); PC(36:2); PC(34:1); PC(36:3); PC(38:3); PC(36:1); PC(32:1); PC(38:6); PC(32:0); PC(40:6); PC(34:3); PE(38:1); PC(32:1); PC(38:4)
LC3	19	PC(36:4); PC(38:4); PC(38:6); TAG(56:7); TAG(56:6); PC(40:7); TAG(56:8); 68_TAG(58:8); TAG(58:9); TAG(56:5); PE(38:4)+PC(35:4); PC(38:4).TAG(54:6)
LC4	13	LysoPC(16:0); LysoPC(18:2); LysoPC(18:0); LysoPC(18:1); LysoPC(18:3); LysoPC(20:3); LysoPC(20:4); LysoPC(20:4); LysoPC(22:6); LysoPC(20:3); LysoPC(16:1)
LC5	24	SM(d18:1/24:1); SM(d18:1/16:0); SM(d18:1/22:0); SM(d18:1/24:0); SM(d18:1/22:1); 29_SM(d18:1/18:0); SM(d18:1/20:0); SM(d18:1/23:0); SM(d18:1/16:1); 56_PA(34:0); SM(d18:1/20:1); SM(d18:0/18:0)
LC6	19	TAG(16:0/18:0/18:1); TAG(14:0/16:0/18:1); TAG(46:1);

		TAG(49:1); TAG(16:0/16:0/18:0); TAG(14:0/16:0/16:0)+TAG(16:0/18:0/12:0); TAG(54:1); TAG(44:0); TAG(16:0/18:0/18:0); TAG(44:1); TAG(49:0)*; TAG(42:0); TAG(14:0/16:0/18:0)+TAG(16:0/16:0/16:0)
LC7	8	PC(38:7); PE(38:4); Cer(d18:1/22:6); PC(40:8); PE(40:7); PE(40:4); PC(38:5); PC(40:8)
LC8	16	PC(37:4)/PE(40:4); PC(35:2); PC(p16:0/18:2)+PC(34:3e); PC(34:1e)+PE(37:1e); PE(34:4e); PC(33:2)+PE(36:2); PC(31:1)+PE(34:1); PG(34:0e); PC(33:1)+PE(36:1); TAG(50:2)
LC9	19	PC(38:5e); PC(36:5e)+PE(38:5e); PC(40:7); PC(38:5e); PC(O-24:1/20:4)+PC(44:5e); PE(38:5e); PE(38:3); PE(38:2); PE(38:3).1; PC(40:5e); PS(38:2); PE(40:6)