RESEARCH ARTICLE

Figures and figure supplements

Genetic and environmental determinants of variation in the plasma lipidome of older Australian twins

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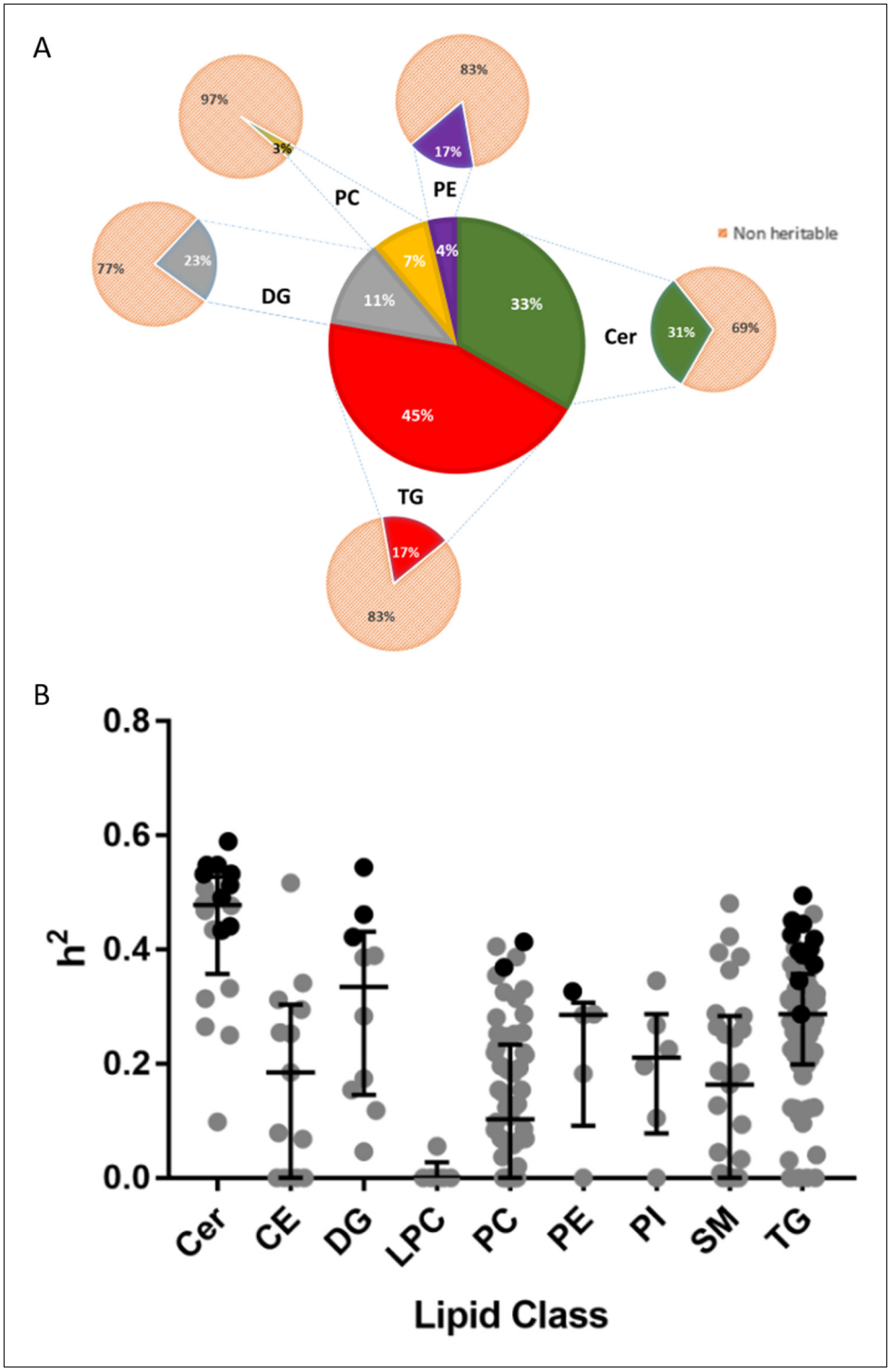

Figure 1. Heritability of lipids. (**A**) Percentage distribution of heritable lipids. The central wheel represents significantly heritable lipids and their percentage distribution by lipid class. Smaller wheels emanating from each sector represent proportions of these heritable lipids compared to total measured lipids of that class, such that the sum of these smaller wheels equals the total pool of 207 individual lipids measured. For example, 45% of significantly heritable lipids belonged to the TG lipid class, and these heritable lipids represented 17% of total measured plasma TG. Orange sectors represent non-heritable percentage of each lipid class. (**B**) The distribution of heritability (h^2), estimated from the ACE model, for each individual lipid species grouped according to class.

Figure 1 continued on next page

Figure 1 continued

Boxplots show median with interquartile range for each class. Dark circles represent heritable lipids, as opposed to grey circles, which represent lipids that were not significantly heritable. Minimum (significant) heritability is h^2 >0.287.

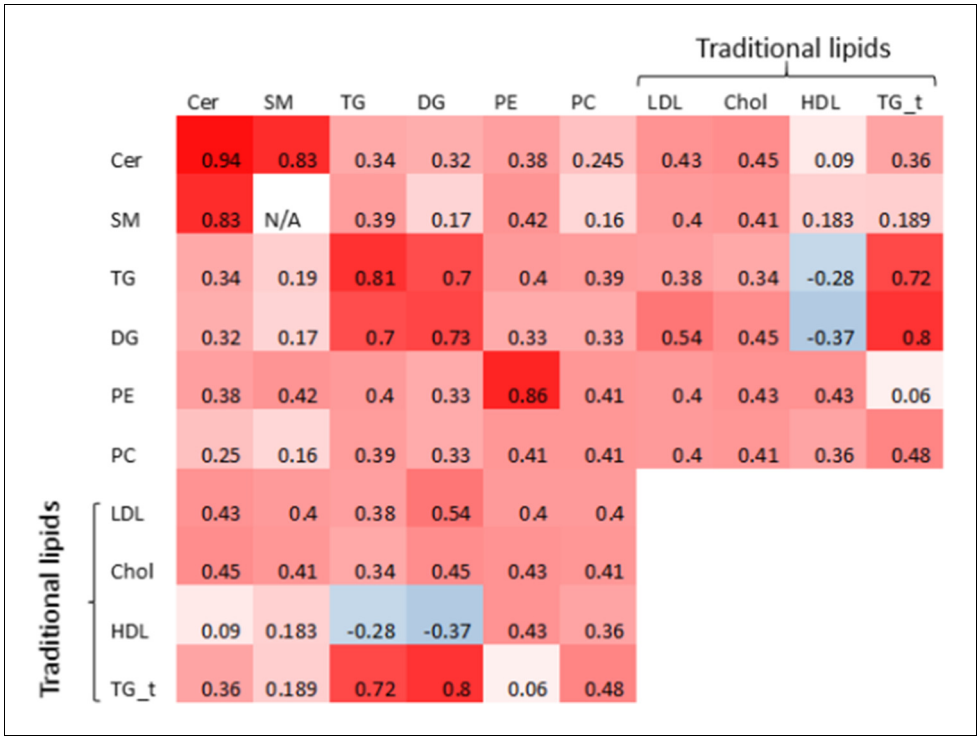

Figure 1—figure supplement 1. Genetic correlation heatmap. Genetic correlation matrix heatmap. Values represent the median of genetic correlations taken between combinations of heritable lipid species of one lipid class with lipid species of another class (or the same class). Note SM represents the sum of SM with a single double bond, thus no correlation could be computed for SM with itself. TG_t represents triglycerides referred to as a traditional lipid measure (as opposed to individual species measured by mass spectrometry).

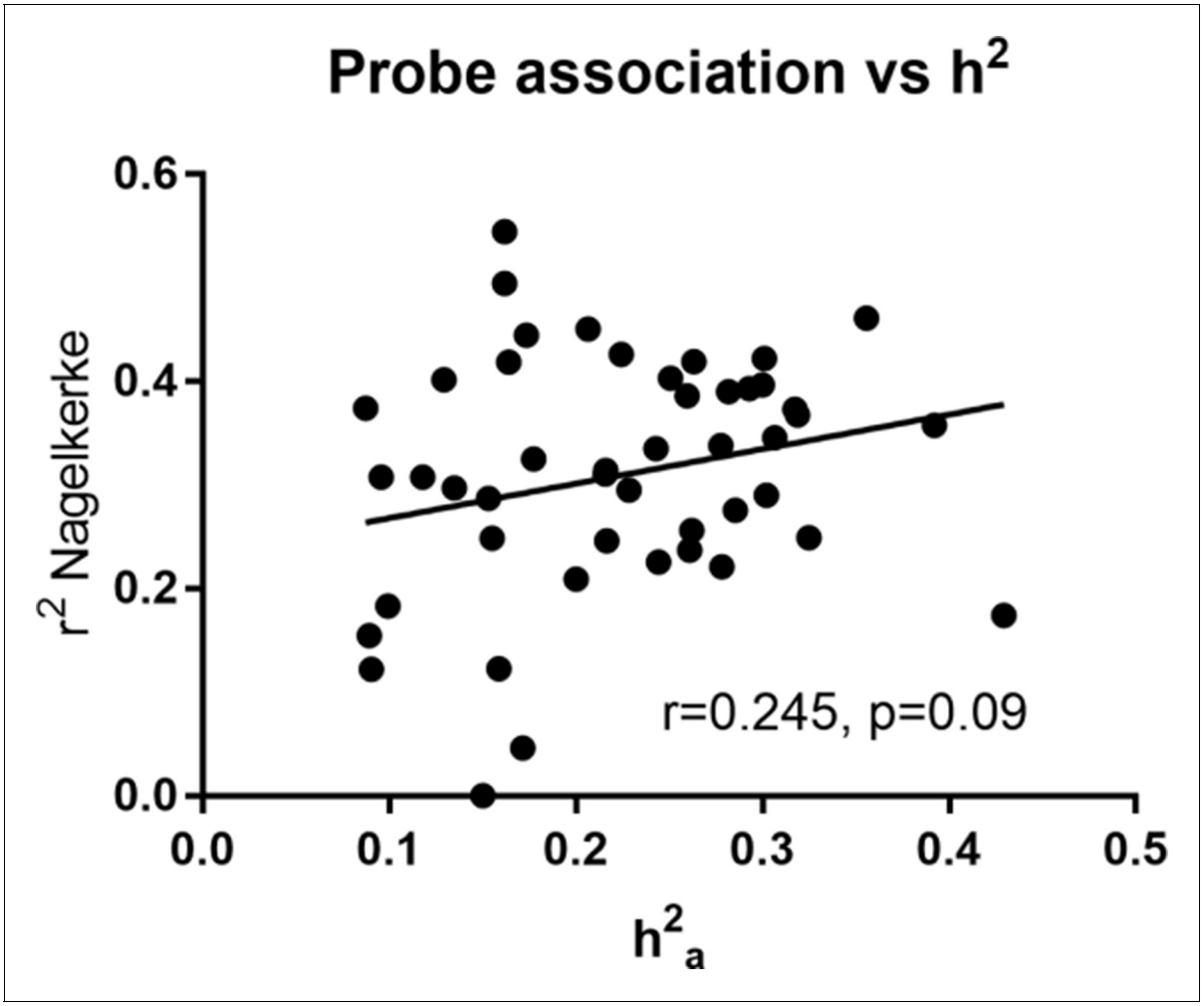

Figure 2. Heritability estimate (h^2_a) vs total variance explained (Nagelkerke r^2) by gene expression probe transcripts for heritable lipids. Pearson correlation was calculated.

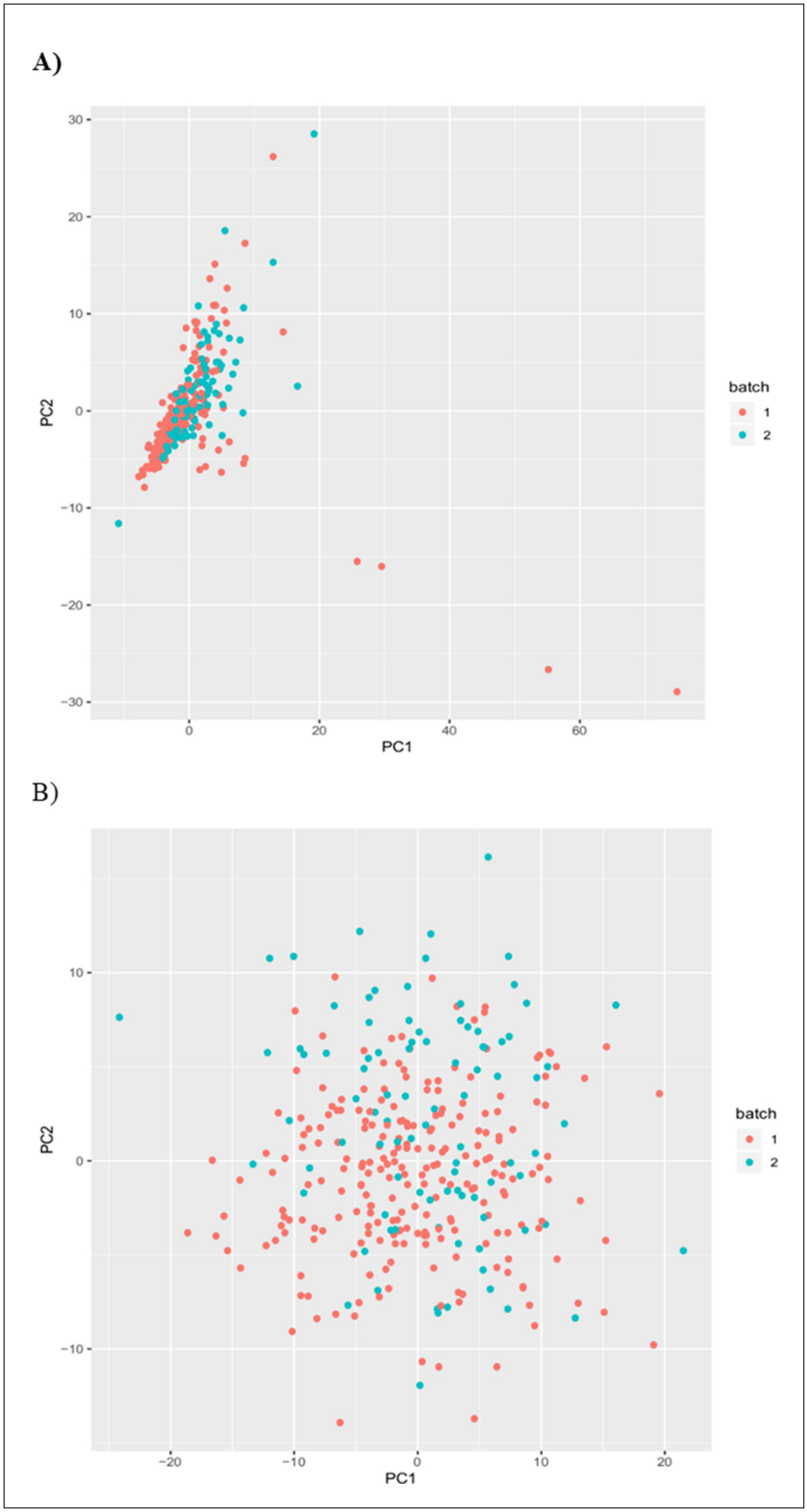
A)
PC2
PC1
batch
1
2
B)
PC2
PC1
batch
1
2

Figure 2—figure supplement 1. Batch correction using inverse rank normal transform of residuals. PCA plots showing good overlap of experimental batch lipids after (**A**) residuals were taken and (**B**) after inverse rank normal transformation was applied to these residuals.

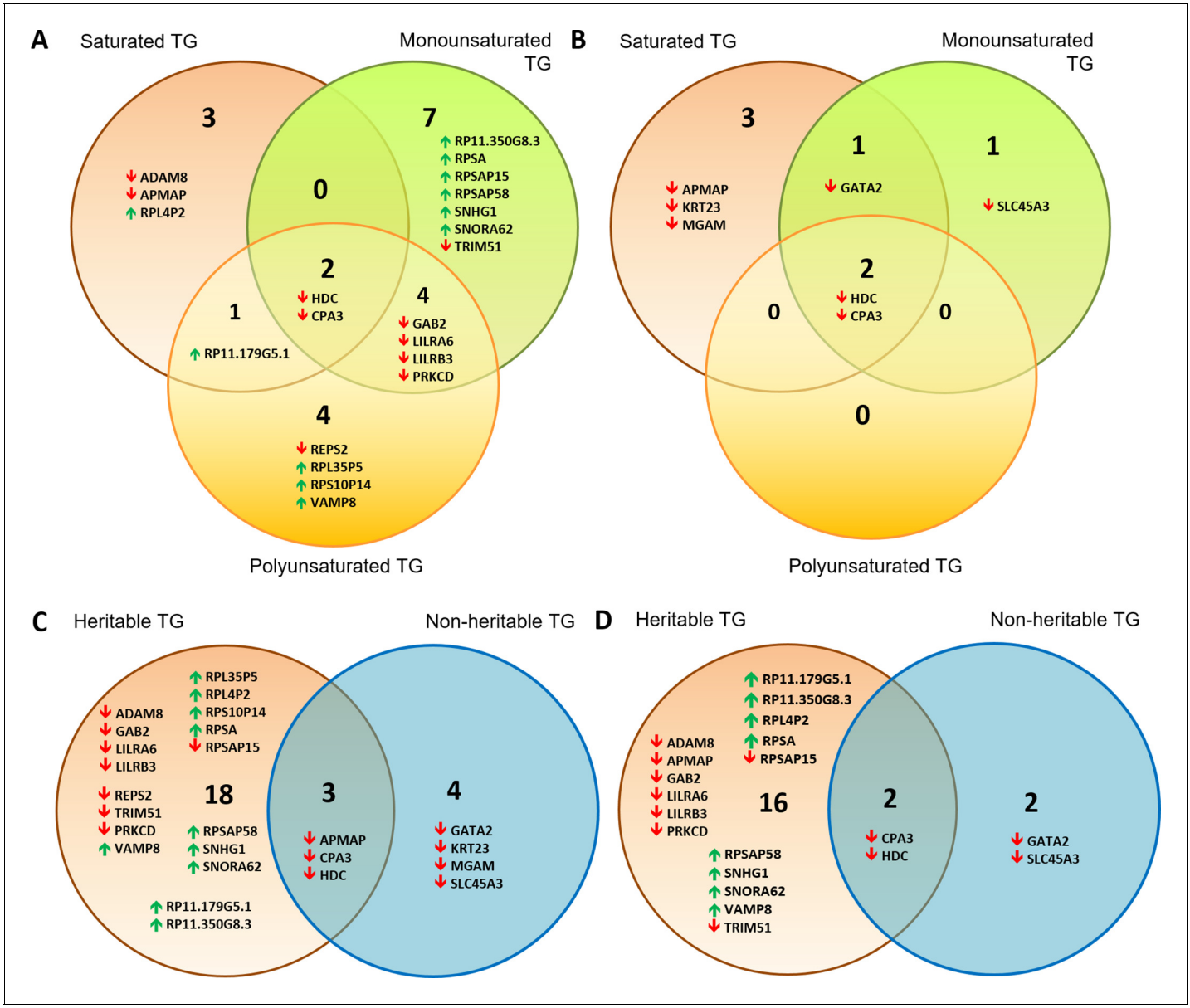

Figure 3. Venn diagrams showing distribution of gene transcripts associated with a majority of TG lipids. These were subdivided into those associated with saturated vs monounsaturated vs polyunsaturated lipids for (**A**) significantly heritable TGs and (**B**) non-heritable TGs. Also shown are heritable vs non-heritable set of significant gene expression associations of TG lipids that were first subdivided based on (**C**) double bond group/saturation (***Supplementary file 2G***) and (**D**) total number of carbons (<49 carbons, 49–55 carbons and 56+ carbons, ***Supplementary file 2H***). Gene transcripts included in these Venn diagrams were those significantly associated with the highest and second highest number of lipids of a particular saturation class (**A and B**), or among heritable and non-heritable lipids (**C and D**). Upwards and downwards arrows indicate positive and inverse gene expression associations with lipid levels respectively.

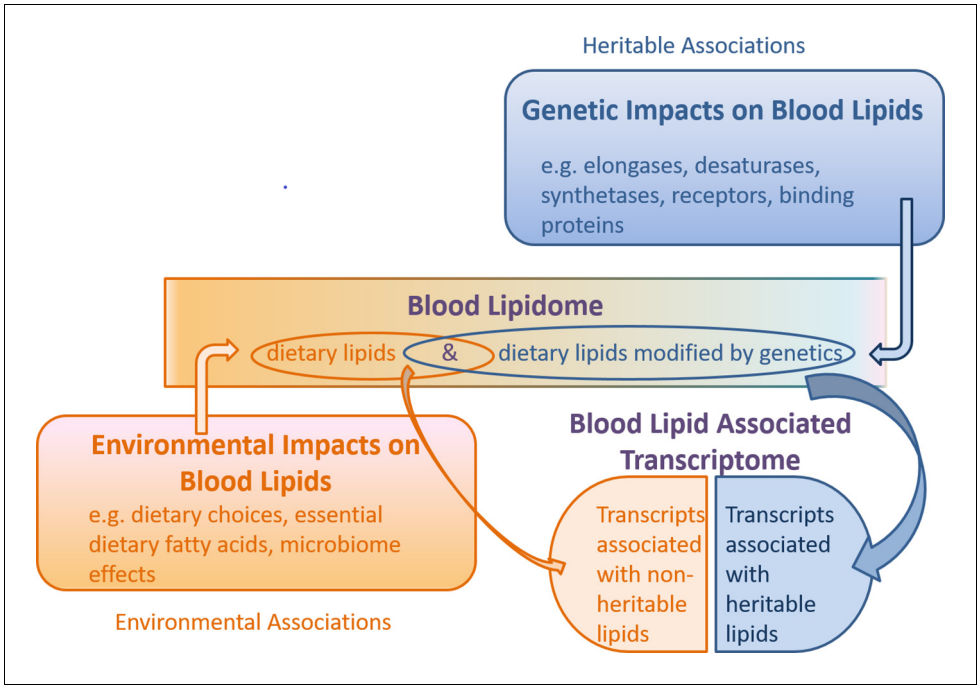

Figure 4. Schematic of the combined genetic and environmental influences on the blood lipidome, and the association of this lipidome with the blood transcriptome. Under this model, non-heritable lipids could affect gene transcription, while heritable lipids could also affect gene transcription (collectively 'blood lipid associated transcriptome'), but are possibly modified upstream by genetic machinery such as elongases, desaturases, synthetases, receptors and binding proteins. Gene transcripts encoding these enzymes and proteins may be independent of the 'blood lipid associated transcriptome' noted in this study.