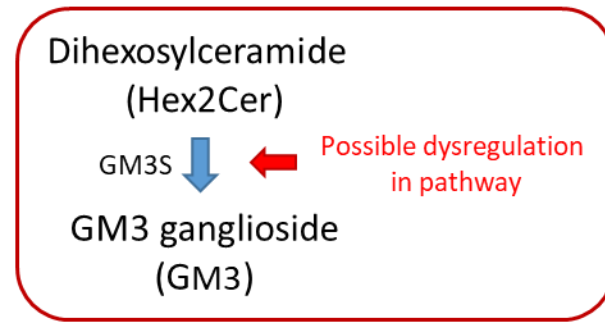
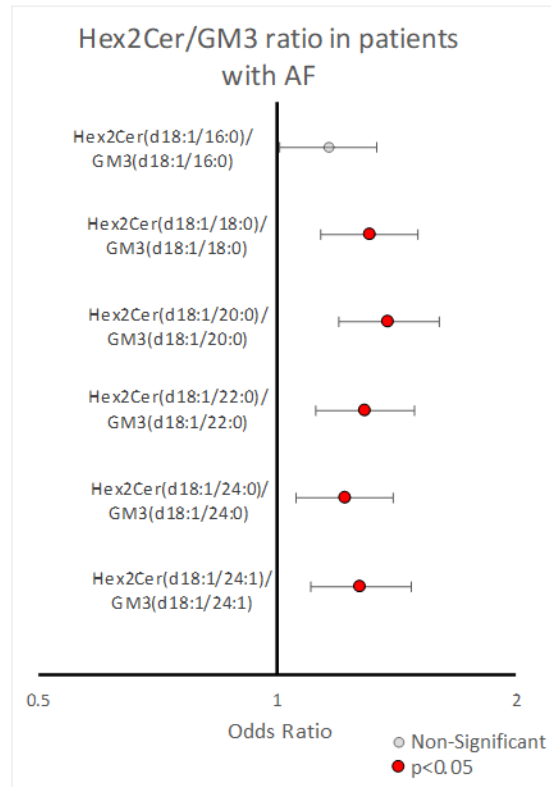


Supplementary Figure 1

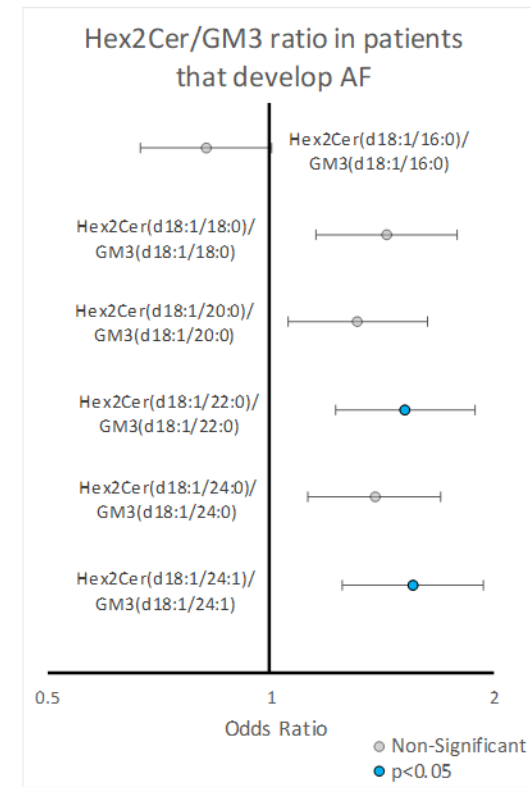
a



b

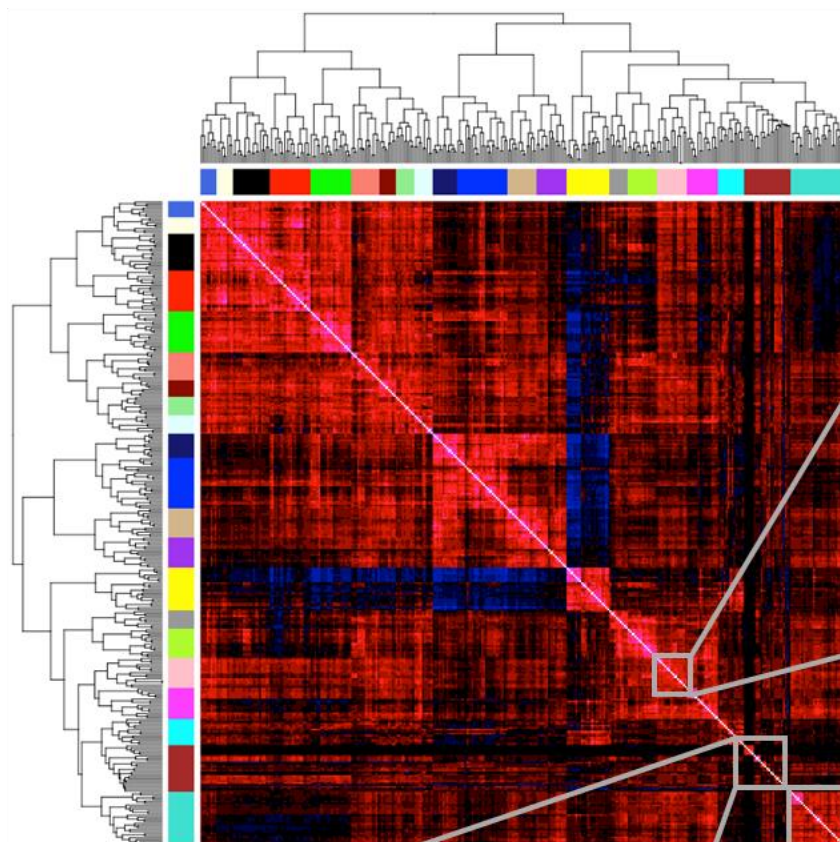


c

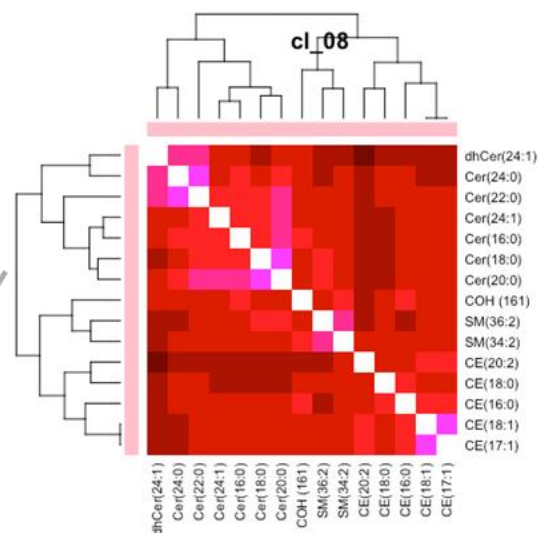


Supplementary Figure 1. (a) Simplified schematic of the sphingolipid pathway depicting dihexosylceramide and GM3. Association of Hex2Cer/GM3 lipid ratios to (b) patients with AF, and (c) development of AF in the future. Logistic regression model of Hex2Cer/GM3 lipid ratios against prevalence of AF at baseline (subset 1, AF Baseline) and future incidence of AF (subset 2, AF Future) adjusting for 12 covariates (age, weight, height, systolic blood pressure, diastolic blood pressure, total cholesterol, HDL cholesterol, triglycerides, myocardial infarction, antihypertensive medication used, current smoking status and hospital admission for heart failure). Odds ratios and 95% confidence intervals are shown. Lipids in (b) red and (c) blue were significant ($P < 0.05$) after applying the BH correction. Hex2Cer, dihexosylceramide; GM3, GM3 ganglioside; GM3S, GM3 Synthase

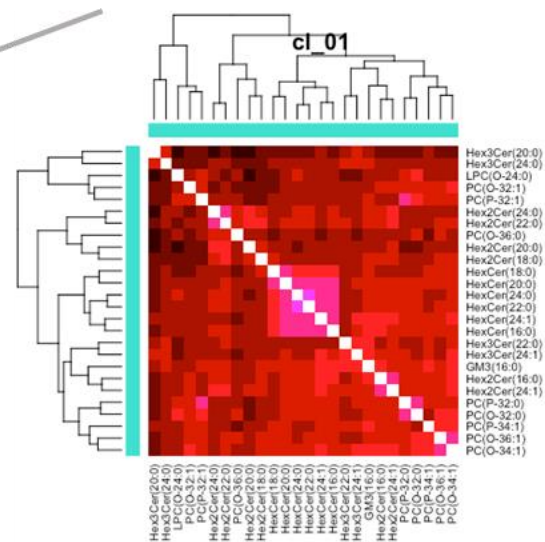
Supplementary Figure 2



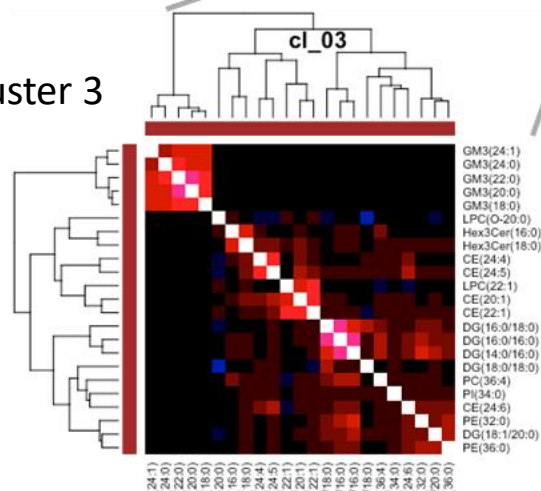
Cluster 8



Cluster 1



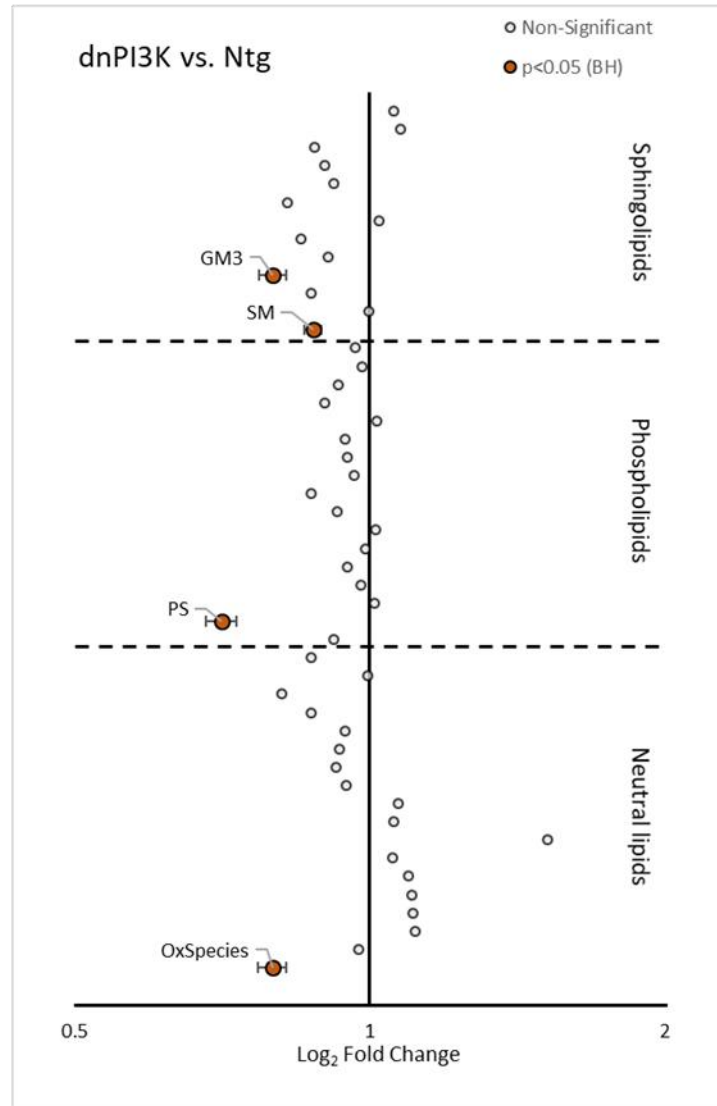
Cluster 3



Supplementary Figure 2. Correlation heatmaps ordered by clusters including all 316 lipids. Cluster 1 (relevant to AF at baseline, Figure 2a) contains significant HexCer, Hex2Cer and Hex3Cer lipid species and closest related lipid species. Cluster 8 (relevant to AF at baseline, Figure 2a) contains CE(16:0), CE(17:1) and CE(18:1) and closest related lipid species. Cluster 3 (relevant to prediction of future AF, Figure 2b) contains GM3(d18:1/24:1) and closest related lipid species. Lipids were organised into a dendrogram using Ward's algorithm applied to a distance of $(1-\rho^2)$, where ρ is the Pearson correlation coefficient between lipids. The dendrogram was then cut into clusters of size 8 or more using the hybrid cutreeDynamic algorithm. Colour scale: cyan ($\text{corr}=-1$) to blue to black ($\text{corr}=0$) to red to magenta ($\text{corr}=1$); diagonal (self correlations=1) shown in white. Different colour bars correspond to different clusters.

Supplementary Figure 3

Total lipids



Supplementary Figure 3. Changes to total lipid classes in the plasma of dnPI3K mice. Data points are represented as mean \pm SEM. Lipids in brown were significant ($P < 0.05$) after applying the BH correction. Male-Ntg $n=25$, dnPI3K $n=21$, Female-Ntg $n=17$, dnPI3K $n=18$. GM3, GM3 ganglioside; PS, Phosphatidylserine; OxSpecies, Oxidized Species