Analyze omics from SLIMM-T2D trial

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# Read data and take the difference from baseline per person

Clinical metadata at [clin\_metadata.csv](./data/clin_metadata.csv). This file also used for uploads to GEO. Here, change colnames in workflow, so can use them more easily in ggplot2. After taking differences of phenotypes, we remove individual points from R object *diff.pheno*, such as Topaz\_3, who have NA in every measure.

The original SOMAscan dataset was parsed to write [soma\_annot.csv](./data/soma_annot.csv) and log2-transformed to write [soma\_mat.csv](./data/soma_mat.csv).

The original metabolomics dataset was parsed, filtered, and log2-transformed to write [met\_mat\_norm.csv](./data/met_mat_norm.csv). Annotations for metabolites had CHEBI annotations added using CTSgetR to write [met\_annot\_with\_chebi.csv](./data/met_annot_with_chebi.csv).

Samples in 12mo metabolomics and proteomics are identical, so create diff\_mats at 1 year. Also, create a combined annotation.

Calculate metadata differences from baseline and remove samples with too many NAs, who shouldn’t be used in Hitman.

Check consistency of some values

# Differential abundance between groups

Analyze differences between groups at each time point, and these differences after taking each person’s difference from baseline, with and without adjusting for each person’s change in BMI.

## Proteome

The Soma supp table with means per group per time point and statistics on differences between groups on differences from baseline is at [soma\_supp\_table.csv](./output/soma_supp_table.csv).

A table representing a Venn diagram of proteomics using FDR = 0.05 is at [soma\_FDR05\_venn.csv](./output/soma_FDR05_venn.csv). A table representing a heatmap of the logFC of each of the proteins that ever has FDR < 0.05 without BMI adjustment over time is at [soma\_heat.csv](./output/soma_heat.csv).

## Metabolome

Analyze differences between groups at each time point, and these differences after taking each person’s difference from baseline. The met supp table with means per group per time point and statistics on differences between groups on differences from baseline is at [met\_supp\_table.csv](./output/met_supp_table.csv).

A table representing a Venn diagram of metabolomics using FDR = 0.05 is at [met\_FDR05\_venn.csv](./output/met_FDR05_venn.csv). A table representing a heatmap of the logFC of each of the metabolites that ever has FDR < 0.05 without BMI adjustment over time is at [met\_heat.csv](./output/met_heat.csv).

# Hitman

We apply Hitman to 12mo outcome change from baseline using change at 3mo from baseline as mediators and arm as exposure. The results of these mediation tests are written as CSVs to [output](./output/) folder using the naming convention outcome-timepoint\_vs\_mediator-timepoint\_hitman, such as “HbA1c12\_vs\_soma3\_hitman.csv,” whose *EMY* columns hold the overall p-values and FDRs.

## HbA1c

We apply Hitman to 12mo HbA1c change using change at 3mo from baseline in analytes and clinical parameters as mediators.

## HOMA-IR

We apply Hitman to 12mo HOMA-IR change using 3mo analyte change as mediators.

## dins030

We apply Hitman to dins030 [change in insulin from 0 to 30 min in mixed-meal tolerance test (mcU/ml)] change at 12mo from baseline using 3mo analyte change from baseline as mediators.