The circulating metabolites in the progression to **islet autoimmunity** and **type 1 diabetes**

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Objective

- To identify metabolic signature associated with the rate of progression to islet autoimmunity and to overt type 1 diabetes by analysing circulating metabolites in a prospective series of plasma and stool samples.

Study design

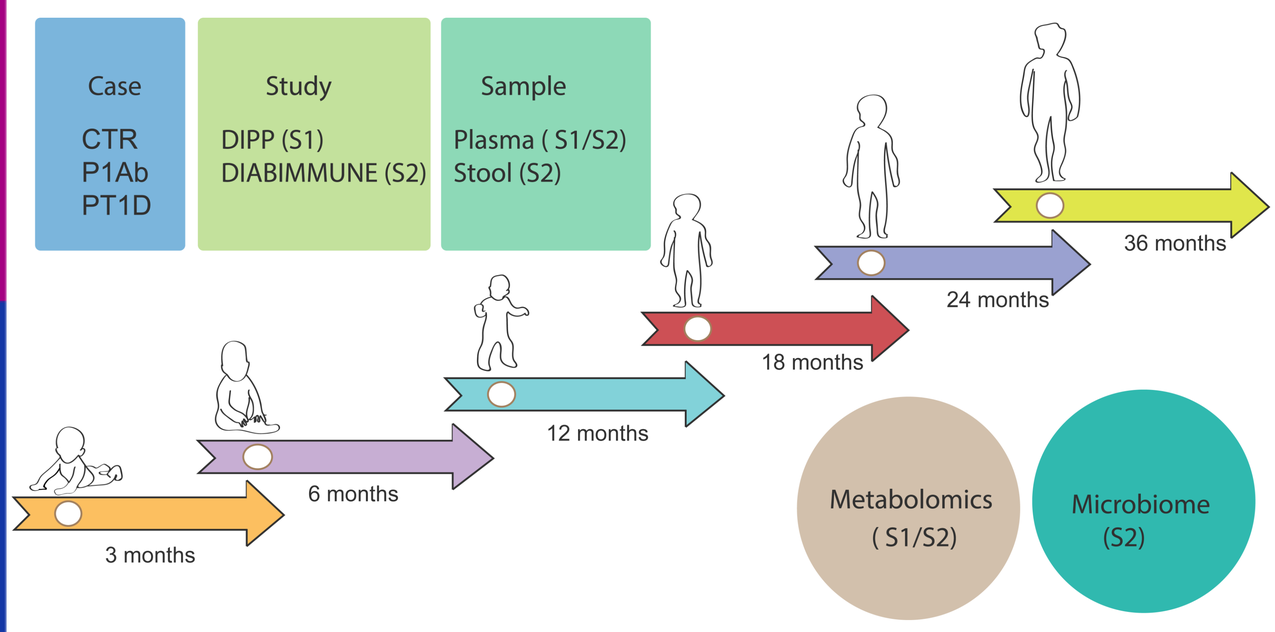

Figure 1. An overview of sample and the study design. The study cohort comprises the samples from children, who progressed to T1D (PT1D,), who developed islet auto-antibody (Ab) but not T1D during the follow-up (P1Ab), and age matched control (CTR).

Results

- Sphingomyelins were found to be persistently downregulated in PT1D when compared to the P1Ab and CTR groups.

- Amino acids including glutamic acid, aspartic acid were downregulated in PT1D as compared to CTR at the early age.

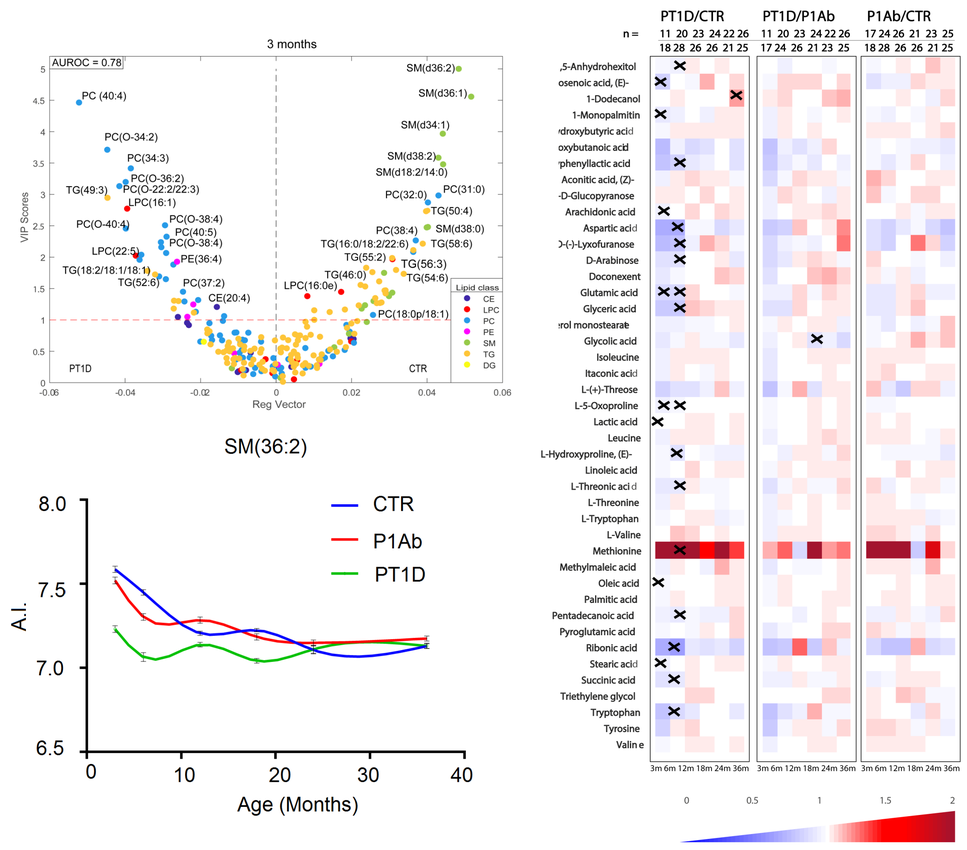

Figure 2. The differences in global plasma metabolites between the three study groups (in study S1).

- Shotgun metagenomics data showed differences in microbial metabolic pathways such as fatty acids, methionine, bile acids and amino acid biosynthesis among the cases. Key metabolites of these pathways as measured by plasma and stool metabolomics showed significant differences between the study groups (S2).

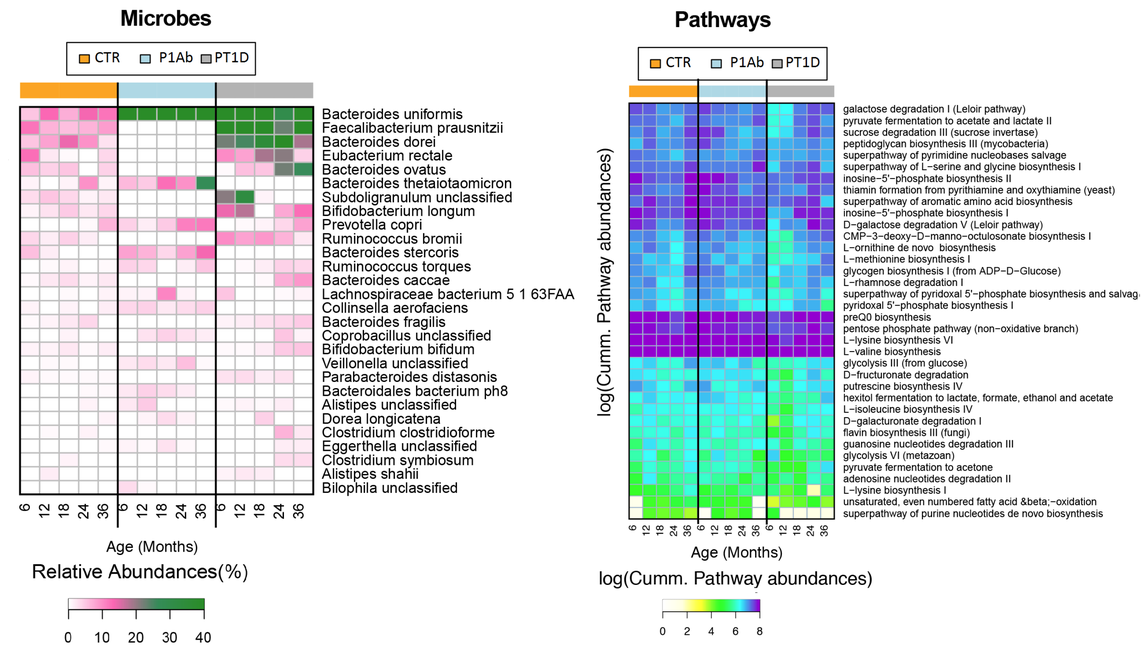

Figure 3. Differences in the microbial abundances and metabolic pathways among study cases (in study S2).

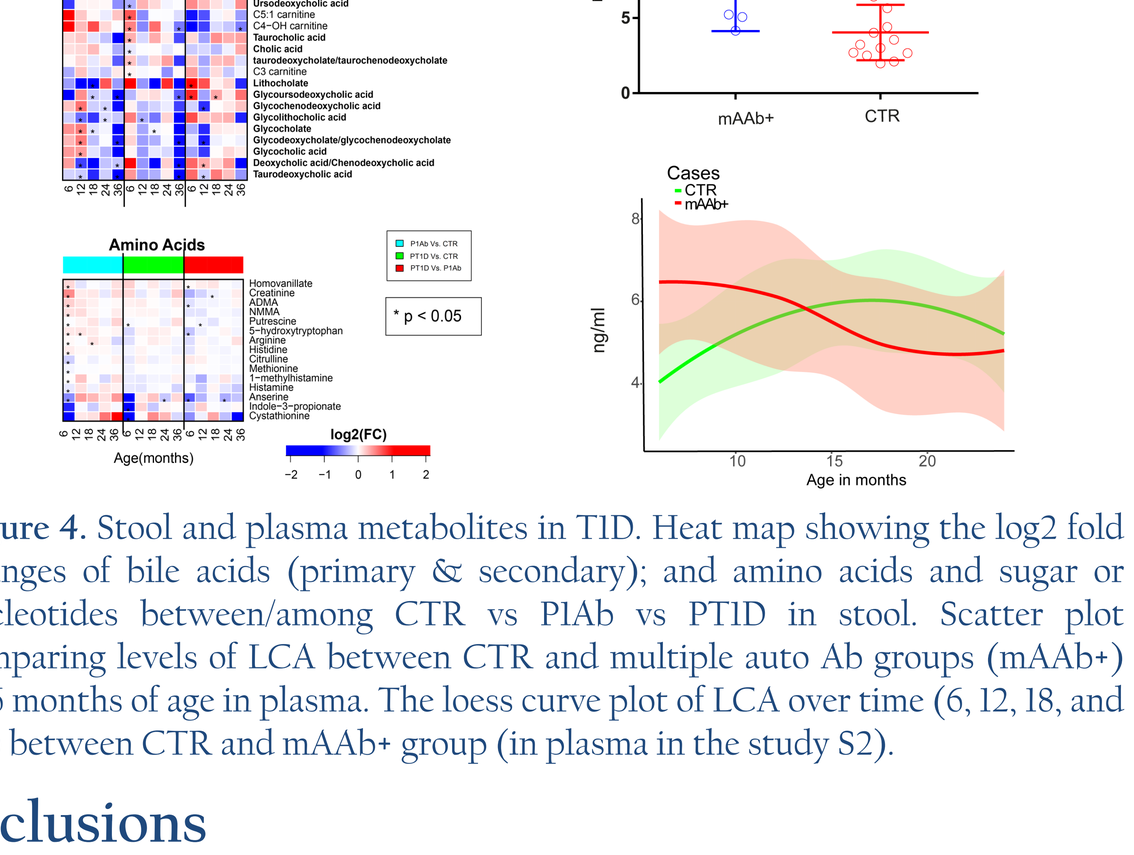

Figure 4. Stool and plasma metabolites in T1D. Heat map showing the log2 fold changes of bile acids (primary & secondary); and amino acids and sugar or nucleotides between/among CTR vs P1Ab vs PT1D in stool. Scatter plot comparing levels of LCA between CTR and multiple auto Ab groups (mAAb+) at 6 months of age in plasma. The loess curve plot of LCA over time (6, 12, 18, and 24) between CTR and mAAb+ group (in plasma in the study S2).

Conclusions

Our study support findings from earlier studies and suggests novel metabolic signatures , including microbial metabolites that specifically characterize children who progressed to islet autoimmunity or overt T1D, respectively, which may be helpful in the identification of at risk children before the initiation of autoimmunity.

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