

Supplementary material

Supplementary Tables:

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Supplementary Tables:

Blood test result	Mean	Standard deviation
HbA1c* (%), (mmol / mol)	7.3, 56.3	1.0, 10.9
Glucose (mg/dl), (mmol/L)	143.3, 8.0	48.7, 2.7
Creatinine (mg/dl)	0.8	0.1
Sodium (meq/l)	138.2	2.6
Potassium (meq/l)	4.3	0.4
Chloride (meq/l)	103.9	2.4
Calcium (mg/dl)	9.4	0.4
Total bilirubin (mg/dl)	0.7	0.4
Uric acid (mg/dl)	4.2	1.1
ALT (IU/l)	19.4	12.3
AST (IU/l)	23.1	7.8
Alkaline Phosphatase (IU/l)	76.9	20.7
Protein, total (g/dl)	7.1	0.4
Albumin (g/dl)	4.3	0.3
Cholesterol, total (mg/dl)	169.7	31.5
HDL Cholesterol (mg/dl)	61.1	13.9
LDL Cholesterol (mg/dl)	99.0	28.4
Triglycerides (mg/dl)	73.3	36.9
TSH (mIU/l)	2.0	1.1

Table S1: Blood test results. Mean values of blood test results at study initiation are presented. AST- aspartate transaminase, ALT- alanine transaminase, HbA1c - Hemoglobin A1C, TSH- thyroid stimulating hormone.

Medical diagnosis	N	%
Hypothyroidism	12	16.22%
Hyperlipidemia	10	13.51%
Anemia	3	4.05%
Helicobacter pylori carrier	2	2.70%
Asthma	2	2.70%
Gastro-Esophageal reflux	2	2.70%
PCOS	2	2.70%
Osteoporosis	2	2.70%
Allergy	1	1.35%
Endometriosis	1	1.35%
Hypertension	1	1.35%
Fibromyalgia	1	1.35%
Alopecia areata	1	1.35%
Graves' disease	1	1.35%
Osteoarthritis	1	1.35%
Vitamin B12 and Folic acid deficiency	1	1.35%
S/P Acute coronary syndrome	3	4.05%
s/p Appendectomy	2	2.70%
S/P Malignancy	2	2.70%
Medication class		%
Levothyroxine	12	16.22%
Oral contraceptives	8	10.81%
Antilipidemic drug	8	10.81%
Antihypertensive drug	7	9.46%
Anti-anxiety or antidepressants drugs	5	6.76%
Aspirin	4	5.41%

Metformin	4	5.41%
Methylphenidate	4	5.41%
GLP-1 agonist	2	2.70%
Antihistamine	2	2.70%
Proton pump inhibitor	2	2.70%
Atomoxetine	1	1.35%
Ticagrelor	1	1.35%

Table S2: Medical conditions and medications consumed by study participants. Number and percentage of individuals reported as suffering from a medical condition or consuming drugs apart from insulin on a daily basis are presented. Medical conditions and medication were reported in the survey and medications were also logged in the smartphone application. GLP-1 -Glucagon-like peptide-1, PCOS- Polycystic ovary syndrome, SSRI - Selective Serotonin Reuptake Inhibitor, S/P - status post

	T1D	Healthy	p-value
Diversity	5.15	5.24	0.88
Richness	200.18	191.33	0.37
F/B Ratio	1.46	1.41	0.93

Table S3: Microbiome of individuals with T1D compared to healthy controls Mean values of microbiome diversity calculated by Shannon index, richness, *Firmicutes* to *Bacteroidetes* (F/B) ratio. p-values were calculated by Mann-Whitney U test.

Bacterial taxa	Group	LDA score	p-value (FDR corrected)
<i>k_Bacteria.p_Bacteroidetes.c_Bacteroidia.o_Bacteroidales.f_Prevotellaceae</i>	T1D	4.04	7.92E-04
<i>k_Bacteria.p_Bacteroidetes.c_Bacteroidia.o_Bacteroidales.f_Prevotellaceae.g_Prevotella.s_Prevotella_copri</i>	T1D	3.90	4.62E-07
<i>k_Bacteria.p_Bacteroidetes.c_Bacteroidia.o_Bacteroidales.f_Prevotellaceae.g_Prevotella</i>	T1D	3.89	1.19E-06
<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Ruminococcaceae.g_Ruminiclostridium</i>	T1D	3.05	8.20E-03
<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Ruminococcaceae.g_Ruminiclostridium.s_Eubacterium_siraeum</i>	T1D	3.03	6.44E-03
<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Clostridiaceae.g_Clostridium.s_Clostridium_sp_CAG_127</i>	T1D	2.90	1.04E-02

<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Oscillospiraceae.g_Oscillibacter.s_Oscillibacter_sp_CAG_241</i>	T1D	2.76	3.68E-03
<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Clostridiales_unclassified</i>	T1D	2.59	5.51E-04
<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Clostridiales_unclassified.g_Clostridiales_unclassified</i>	T1D	2.59	5.51E-04
<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Clostridiales_unclassified.g_Clostridiales_unclassified.s_Clostridiales_bacterium_KLE1615</i>	T1D	2.59	5.51E-04
<i>k_Bacteria.p_Bacteroidetes.c_Bacteroidia.o_Bacteroidales.f_Rikenellaceae.g_Alistipes.s_Alistipes_inops</i>	T1D	2.58	2.22E-02
<i>k_Bacteria.p_Bacteroidetes.c_Bacteroidia.o_Bacteroidales.f_Rikenellaceae</i>	T1D	2.58	2.22E-02
<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Clostridiaceae.g_Clostridium.s_Clostridium_sp_CAG_167</i>	T1D	2.44	3.86E-02
<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Lachnospiraceae.g_Anaoerostipes.s_Anaoerostipes_hadrus</i>	T1D	2.42	1.95E-02
<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Lachnospiraceae.g_Anaoerostipes</i>	T1D	2.42	1.95E-02
<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Lachnospiraceae.g_Blautia.s_Blautia_sp_CAG_237</i>	T1D	2.35	4.08E-02
<i>k_Bacteria.p_Firmicutes.c_Firmicutes_unclassified.o_Firmicutes_unclassified.f_Firmicutes_unclassified.g_Firmicutes_unclassified.s_Firmicutes_bacterium_CAG_95</i>	T1D	2.04	3.08E-02
<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Ruminococcaceae.g_Faecalibacterium</i>	HC	3.57	1.47E-03
<i>k_Bacteria.p_Bacteroidetes.c_Bacteroidia.o_Bacteroidales.f_Rikenellaceae.g_Alistipes</i>	HC	3.52	3.68E-02
<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Ruminococcaceae</i>	HC	3.50	1.26E-02
<i>k_Bacteria.p_Bacteroidetes.c_Bacteroidia.o_Bacteroidales.f_Rikenellaceae.g_Alistipes.s_Alistipes_putredinis</i>	HC	3.42	1.09E-02
<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Ruminococcaceae.g_Faecalibacterium.s_Faecalibacterium_prausnitzii</i>	HC	3.41	8.06E-04
<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Ruminococcaceae.g_Ruminococcus</i>	HC	3.22	2.97E-02
<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Eubacteriaceae.g_Eubacterium.s_Eubacterium_sp_CAG_180</i>	HC	2.94	4.28E-03

<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Eubacteriaceae.g_Eubacterium.s_Eubacterium_hallii</i>	HC	2.83	4.07E-06
<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Eubacteriaceae.g_Eubacterium.s_Eubacterium_eligens</i>	HC	2.63	3.34E-02
<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Clostridiales_unclassified.g_Flavonifractor.s_Flavonifractor_sp</i>	HC	2.61	4.94E-02
<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Eubacteriaceae.g_Eubacterium.s_Eubacterium_sp_CAG_38</i>	HC	2.57	1.16E-03
<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Lachnospiraceae.g_Blautia.s_Ruminococcus_gnavus</i>	HC	2.53	2.50E-02
<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Peptostreptococcaceae</i>	HC	2.40	2.53E-02
<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Clostridiaceae.g_Clostridium.s_Clostridium_sp_CAG_58</i>	HC	2.34	1.21E-02
<i>k_Bacteria.p_Firmicutes.c_Clostridia.o_Clostridiales.f_Oscillospiraceae.g_Oscillibacter.s_Oscillibacter_sp</i>	HC	2.31	1.28E-02

Table S4: Bacterial taxa with a significantly different LDA score in adults with T1D compared to healthy controls (HC) p-values were calculated by Mann Whitney (MW) test and are FDR corrected. k- kingdom, p- phylum, c- class, o -order, f- family, g- genus, s- species. For each microbial taxon, the LDA score and the group of individuals in which a significantly higher LDA scores was obtained (individuals with T1D or healthy adults is indicated.

Metabolic pathway	T1D	Healthy controls	p value	p value (FDR corrected)
PWY-5505: L-glutamate and L-glutamine biosynthesis	-6.68596	-6.52453	5.82E-06	1.86E-03
ARGININE-SYN4-PWY: L-ornithine de novo biosynthesis	-6.89089	-6.70545	5.18E-05	8.28E-03
GALACT-GLUCUROCAT-PWY: superpathway of hexuronide and hexuronate degradation	-6.01673	-5.88939	0.000555	5.92E-02

Table S5: Metabolic pathways significantly different in adults with T1D compared to healthy controls. Values are presented in a log scale. p-values were calculated by Mann Whitney (MW) test.

Supplementary Figures

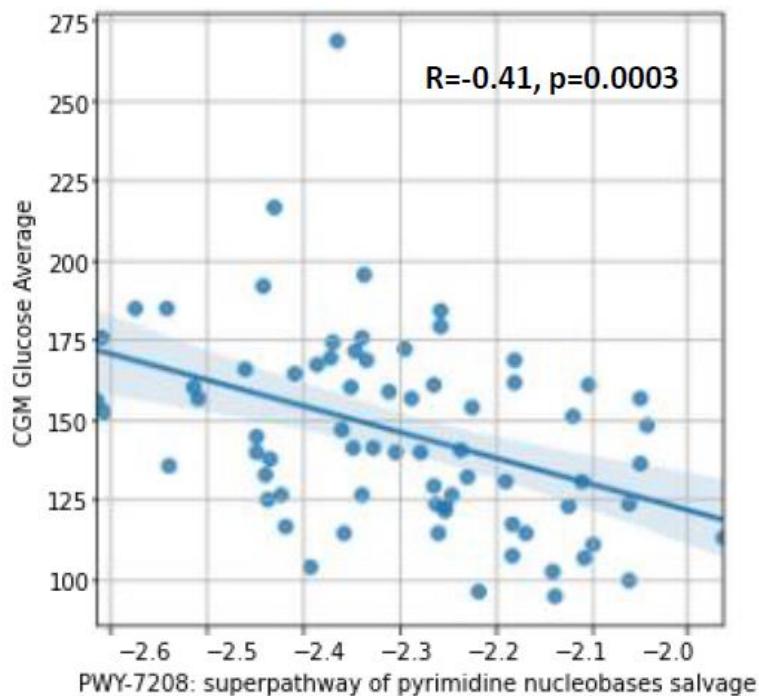


Figure S1: Inverse correlation between PWY-7208: superpathway of pyrimidine nucleobases salvage and glucose average

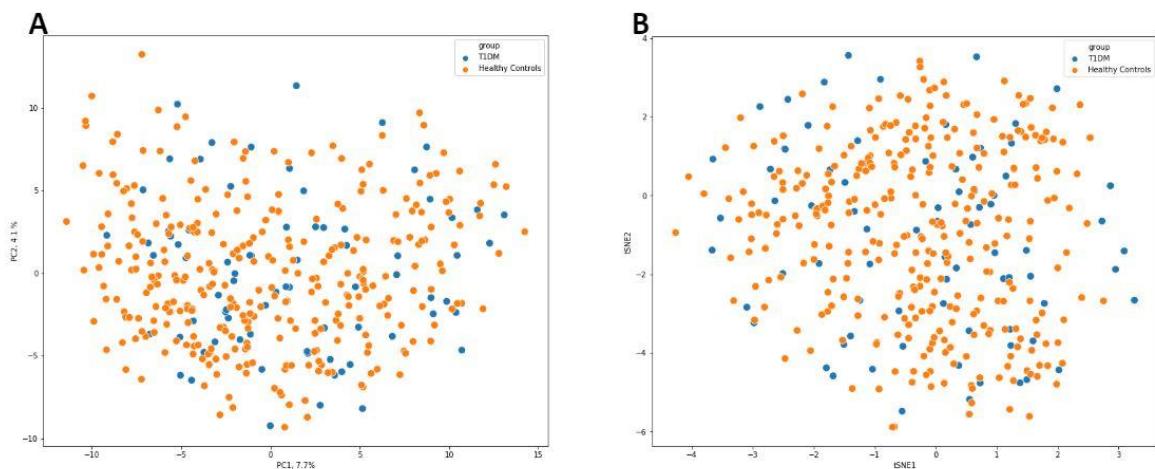


Figure S2: Differences in gut microbiota between control and individuals with T1DM by T-distributed Stochastic Neighbor Embedding (t-SNE) analysis, and Principal Component Analysis (PCA) analysis

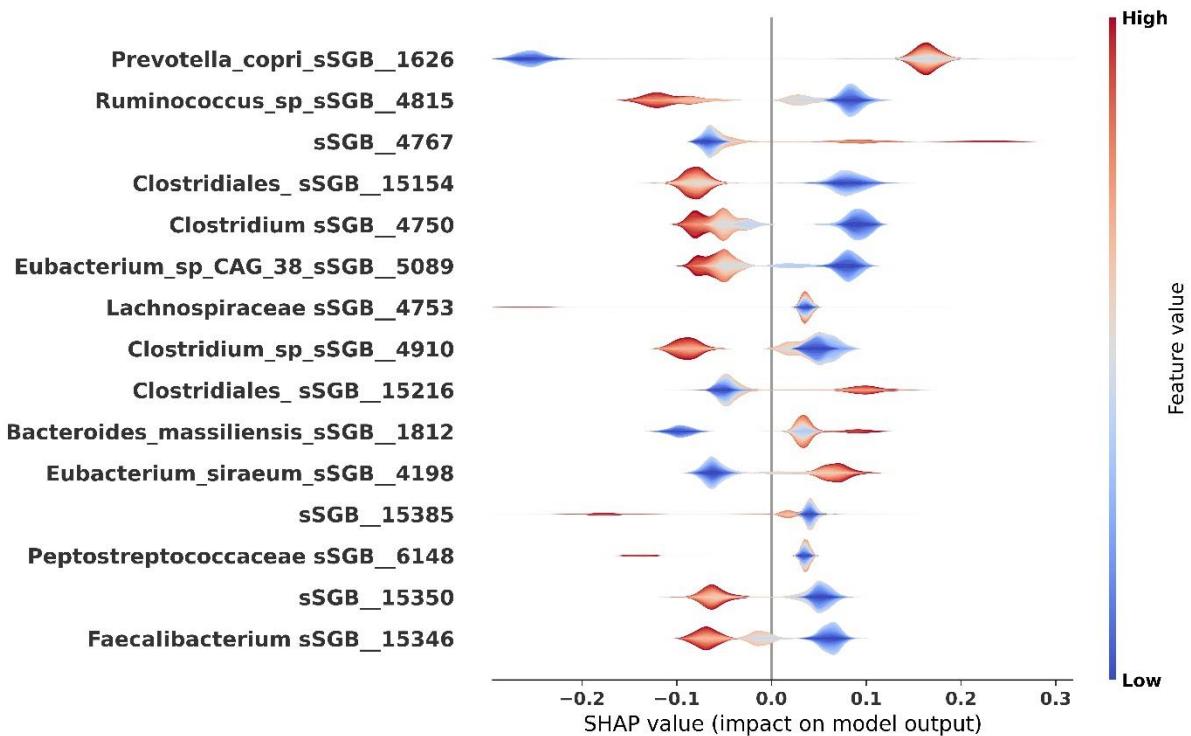


Figure S3: Interpretation of a prediction model for distinguishing individuals with T1D from healthy controls. SHAP values (in absolute log-odds scale) of different microbial strains and their impact on prediction of T1D status in adults. For bacterial strains which are not classified yet, the species-level genome bin (SGB) is indicated.