

Electronic Supplementary Materials

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Family history of type 2 diabetes delays development of type 1 diabetes in TEDDY children with islet autoimmunity

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Abbreviations

BMI	Body mass index
IA	Islet autoimmunity
T1D	Type 1 diabetes
T2D	Type 2 diabetes

ESM Methods

TEDDY families were asked to fill out a questionnaire that collected information about the presence of the following autoimmune diseases in the family, among the FDRs and SDRs.

- 1) Graves disease (Hyperthyroid-High)
- 2) Hyperthyroid, not confirmed Graves
- 3) Hashimoto's disease (Hypothyroid-Low)
- 4) Rheumatoid arthritis
- 5) Juvenile rheumatoid arthritis
- 6) Coeliac disease
- 7) Myasthenia gravis
- 8) Addison's disease
- 9) Pernicious anaemia
- 10) Lupus
- 11) Ulcerative colitis
- 12) Crohn's disease
- 13) Multiple sclerosis
- 14) Ankylosing spondylitis
- 15) Juvenile ankylosing spondylitis
- 16) Psoriasis
- 17) Vitiligo
- 18) Wegener's granulomatosis or syndrome
- 19) Scleroderma
- 20) Alopecia areata (patchy hair loss)
- 21) Alopecia totalis (entire scalp hair loss)
- 22) Alopecia universalis (loss of all body hair)
- 23) Sjögren's syndrome
- 24) Other, specify

ESM Table 1

Characteristics of the TEDDY participants with or without a second-degree relative (SDR) with type 2 diabetes (T2D)

Characteristic	No SDR with T2D (N=5059)	SDR with T2D (N=2420)	Total (N=7479)	P value
IA persistent positive				0.410
Yes	441 (8.7%)	225 (9.3%)	666 (8.9%)	
No	4618 (91.3%)	2195 (90.7%)	6813 (91.1%)	
Country				< 0.001
USA	1966 (38.9%)	1093 (45.2%)	3059 (40.9%)	
Finland	1090 (21.5%)	559 (23.1%)	1649 (22.0%)	
Germany	342 (6.8%)	143 (5.9%)	485 (6.5%)	
Sweden	1661 (32.8%)	625 (25.8%)	2286 (30.6%)	
Sex				0.573
Female	2465 (48.7%)	1196 (49.4%)	3661 (49.0%)	
Male	2594 (51.3%)	1224 (50.6%)	3818 (51.0%)	
HLA				0.674
DR3/4	1965 (38.8%)	953 (39.4%)	2918 (39.0%)	
DR4/4	987 (19.5%)	483 (20.0%)	1470 (19.7%)	
FDR-specific	176 (3.5%)	75 (3.1%)	251 (3.4%)	
DR4/8	867 (17.1%)	428 (17.7%)	1295 (17.3%)	
DR3/3	1064 (21.0%)	481 (19.9%)	1545 (20.7%)	
Probiotic use prior to 3 months of age				0.115
No	3310 (65.4%)	1628 (67.3%)	4938 (66.0%)	
Yes	1749 (34.6%)	792 (32.7%)	2541 (34.0%)	
rs1004446_a ¹				0.171
0	1794 (39.6%)	889 (40.7%)	2683 (39.9%)	
1	2091 (46.1%)	1017 (46.6%)	3108 (46.3%)	
2	651 (14.4%)	277 (12.7%)	928 (13.8%)	
rs10517086_a				0.427
0	2291 (50.5%)	1135 (52.0%)	3426 (51.0%)	
1	1874 (41.3%)	884 (40.5%)	2758 (41.0%)	
2	371 (8.2%)	164 (7.5%)	535 (8.0%)	
rs12708716_g				0.703
0	2020 (44.5%)	951 (43.6%)	2971 (44.2%)	
1	1990 (43.9%)	981 (44.9%)	2971 (44.2%)	
2	526 (11.6%)	251 (11.5%)	777 (11.6%)	

Characteristic	No SDR with T2D (N=5059)	SDR with T2D (N=2420)	Total (N=7479)	P value
rs2292239_a				0.078
0	2023 (44.6%)	1036 (47.5%)	3059 (45.5%)	
1	2051 (45.2%)	928 (42.5%)	2979 (44.3%)	
2	462 (10.2%)	219 (10.0%)	681 (10.1%)	
rs2476601_a				0.821
0	3595 (79.3%)	1734 (79.4%)	5329 (79.3%)	
1	884 (19.5%)	418 (19.1%)	1302 (19.4%)	
2	57 (1.3%)	31 (1.4%)	88 (1.3%)	
rs2816316_c				0.932
0	3041 (67.0%)	1458 (66.8%)	4499 (67.0%)	
1	1338 (29.5%)	652 (29.9%)	1990 (29.6%)	
2	157 (3.5%)	73 (3.3%)	230 (3.4%)	
rs3184504_a				0.961
0	1397 (30.8%)	679 (31.1%)	2076 (30.9%)	
1	2230 (49.2%)	1071 (49.1%)	3301 (49.1%)	
2	909 (20.0%)	433 (19.8%)	1342 (20.0%)	
rs4948088_a				0.657
0	4124 (90.9%)	1999 (91.6%)	6123 (91.1%)	
1	398 (8.8%)	177 (8.1%)	575 (8.6%)	
2	14 (0.3%)	7 (0.3%)	21 (0.3%)	

¹N = 6719 children not missing SNP data

ESM Table 2

Characteristics of the TEDDY participants who had persistent confirmed islet autoimmunity (IA). Children with or without second-degree relative (SDR) with type 2 diabetes (T2D) shown separately.

Characteristic	No SDR with T2D (N=441)	SDR with T2D (N=225)	Total (N=666)	P value
T1D				0.008
No	289 (65.5%)	170 (75.6%)	459 (68.9%)	
Yes	152 (34.5%)	55 (24.4%)	207 (31.1%)	
First appearing islet autoantibody				0.593
IA-2A only	11 (2.5%)	4 (1.8%)	15 (2.3%)	
GADA only	179 (40.6%)	96 (42.7%)	275 (41.3%)	
GADA and IA-2A	3 (0.7%)	2 (0.9%)	5 (0.8%)	
IAA only	173 (39.2%)	88 (39.1%)	261 (39.2%)	
IAA and IA-2A	7 (1.6%)	0 (0.0%)	7 (1.1%)	
IAA and GADA	58 (13.2%)	28 (12.4%)	86 (12.9%)	
IAA, GADA and IA-2A	10 (2.3%)	7 (3.1%)	17 (2.6%)	
IA seroconversion age (years)				0.188
Median	2.4	2.8	2.5	
IQR	3.2	3.7	3.3	
Time from IA seroconversion to T1D diagnosis (years)				0.727
Median	2.2	2.8	2.4	
IQR	3.0	3.5	3.1	
T1D diagnosis age (years)				0.452
Median	4.3	4.6	4.3	
IQR	3.5	4.8	3.6	
Country				0.003
USA	134 (30.4%)	93 (41.3%)	227 (34.1%)	
Finland	106 (24.0%)	62 (27.6%)	168 (25.2%)	
Germany	33 (7.5%)	14 (6.2%)	47 (7.1%)	
Sweden	168 (38.1%)	56 (24.9%)	224 (33.6%)	
Sex				0.440
Female	204 (46.3%)	97 (43.1%)	301 (45.2%)	
Male	237 (53.7%)	128 (56.9%)	365 (54.8%)	
HLA				0.607
DR3/4	213 (48.3%)	119 (52.9%)	332 (49.8%)	
DR4/4	83 (18.8%)	37 (16.4%)	120 (18.0%)	
FDR-specific	19 (4.3%)	6 (2.7%)	25 (3.8%)	
DR4/8	75 (17.0%)	34 (15.1%)	109 (16.4%)	
DR3/3	51 (11.6%)	29 (12.9%)	80 (12.0%)	

Characteristic	No SDR with T2D (N=441)	SDR with T2D (N=225)	Total (N=666)	P value
BMI at IA seroconversion				0.370
Median	16.6	16.5	16.5	
IQR	1.9	2.1	2.0	
Coeliac disease				0.481
No	414 (93.9%)	208 (92.4%)	622 (93.4%)	
Yes	27 (6.1%)	17 (7.6%)	44 (6.6%)	
rs1004446_a ¹				0.291
0	186 (45.0%)	88 (43.1%)	274 (44.4%)	
1	183 (44.3%)	101 (49.5%)	284 (46.0%)	
2	44 (10.7%)	15 (7.4%)	59 (9.6%)	
rs2292239_a				0.990
0	160 (38.7%)	78 (38.2%)	238 (38.6%)	
1	202 (48.9%)	101 (49.5%)	303 (49.1%)	
2	51 (12.3%)	25 (12.3%)	76 (12.3%)	
rs2476601_a				0.963
0	288 (69.7%)	143 (70.1%)	431 (69.9%)	
1	118 (28.6%)	57 (27.9%)	175 (28.4%)	
2	7 (1.7%)	4 (2.0%)	11 (1.8%)	
rs3184504_a				0.486
0	95 (23.0%)	50 (24.5%)	145 (23.5%)	
1	209 (50.6%)	93 (45.6%)	302 (48.9%)	
2	109 (26.4%)	61 (29.9%)	170 (27.6%)	
rs7111341_a				0.608
0	235 (56.9%)	114 (55.9%)	349 (56.6%)	
1	156 (37.8%)	75 (36.8%)	231 (37.4%)	
2	22 (5.3%)	15 (7.4%)	37 (6.0%)	
rs11711054_g				0.806
0	197 (47.7%)	99 (48.5%)	296 (48.0%)	
1	177 (42.9%)	89 (43.6%)	266 (43.1%)	
2	39 (9.4%)	16 (7.8%)	55 (8.9%)	
rs3825932_a				0.146
0	197 (47.7%)	81 (39.7%)	278 (45.1%)	
1	161 (39.0%)	95 (46.6%)	256 (41.5%)	
2	55 (13.3%)	28 (13.7%)	83 (13.5%)	

¹N = 616 children not missing SNP data

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