

Supplementary Table S1. Clinical, immunological and genetic characteristics of polyendocrine patients (3) screened for the identified *TIM-3* variants

Patient N°	Gender	Age (actual, yrs)	Age at referral	APS	Clinical manifestations	Auto Abs	TIM-3 c.331C>T c.302C>T	AIRE pattern	AIRE promoter SNP	C1858T PTPN22	Therapy
1	F	29.9	8.7	IIIA IIIB	T1D, celiac disease, HT	TgAb, TPOAb, GADA, IA2Ab, APCA pos	WT	het IVS9 delC +78	-230Y (C/T het)	WT	Insulin
2	F	30.1	9.2	IIIA IIIC	T1D, vitiligo	ANA, ASMA, TgAb, GADA, IA2Ab, pos AMA, CAAb, TPOAb, APCA, TRGAb, Adrenal Ab, anti-21-hydroxylase Ab neg	WT	het IVS9+78delC	WT	WT	Insulin aspart
3	F	24.2	2.8	IV	T1D, celiac disease	IAA, GADA pos TgAb, TPOAb, IA2Ab, TRGAb, Adrenal Ab neg	WT	hom IVS9+78delC	WT	WT	Insulin aspart Insulin degludec
4	M	NA	NA	IV	T1D, celiac disease	NA	WT	het IVS9 +6 G>A	WT	het	NA
5	F	29	11.2	IV	T1D, celiac disease	GADA pos TgAb, TPOAb, IAA, IA2Ab, TRGAb neg	WT	het IVS9+78delC	-230Y (C/T het)	het	none
6	F	19.6	6.1	IIIC IIID	HT, alopecia universalis, onicodystrophy, allergic rhinitis, arthralgias, Raynaud phenomenon, recurrent infections in pediatric age, celiac disease	ANA, TgAb, TPOAb, CAAb, Dense Fine Speckled 70kDa (DFS70) Ab pos ASMA, ANCA, ARA, RbAb dsDNA, DNA/ENA/pRIBAb, phospholipid Ab, beta2 glycoprotein Ab, IAA, GADA, IA2Ab, LKMab, LC1Ab, APCA, TRGA, Adrenal Ab neg	WT	het IVS9+6 G>A	WT	WT	Levothyroxine (LT4) Vitamin D
7	F	33.6	8.9	IIIA IV	T1D, hypertension, Basedow's disease, POF	ANA, TgAb, TPOAb, GADA, IA2Ab, APCA pos AMA, ASMA, ARA, RbAb, CAAb, LKMab, LC1Ab, IFIgG, TRGAb, DGP IgG, Adrenal Ab neg	WT	WT	WT	WT	Insulin aspart Cholecalciferol methimazole propanolol hydrochloride Folic acid
8	F	39.1	14.8	IIIA IIIB	T1D, celiac disease, HT	TgAbs, TPOAb, TRGAb neg	WT	WT	WT	het	LT4 Insulin
9	F	32.5	5	IIIA	T1D, HT	TPOAb, IAA pos	WT	WT	-380S (C/G het)	WT	Insulin aspart LT4

						ANA, AMA, ASMA, ARA, RAb, CAb, TgAb, GADA, IA2Ab, LKMab, LC1Ab APCA, TRAb, TRGAb, Adrenal Ab, anti-21-hydroxylase Ab neg			-230Y (C/T het)		
10	F	30.4	0.6	IV	T1D, celiac disease, Turner syndrome	IAA GADA IA2Ab pos ANA, AMA, ASMA, ARA, RAb, CAb, TgAb, TPOAb, LKMab, LC1Ab, APCA, TRGAb, DGPIgG, Adrenal Ab neg	WT	het IVS9+78delC	WT	het	Insulin lispro Insulin degludec
11	M	33.4	13.8	IIIA IIIB	T1D, HT, autoimmune atrophic gastritis	TPOAb, APCA pos ANA, AMA, ASMA, ARA, RAb, CAb, TgAb, GADA, IA2Ab, LKMab, LC1Ab, IFIgG, TRAb, TRGAb, Adrenal Ab neg	WT	het c.834 C>G (S278R) het IVS9+6 G>A het IVS9+78delC	-230Y (C/T het)	WT	LT4 Insulin aspart, Insulin degludec
12	F	30.2	6	IIIA	T1D, HT	ASMA, TgAb, TPOAb, IAA pos ANA, AMA, ARA RAb, CAb, GADA, IA2Ab, LKMab, LC1Ab, IFIgG, APCA, TRGAb, Adrenal Ab, snti-21-hydroxylase Ab neg	WT	het IVS9+78delC	WT	WT	LT4 Insulin aspart Insulin glargine
13	F	34.1	10.5	IIIA IIIB IIIC	T1D, HT, vitiligo, chronic gastritis	ANA, CAb, TgAb, TPOAb, GADA IA2Ab, APCA pos AMA, ASMA, ARA, RAb, anti-beta2 glycoprotein Ab, LKMab, LC1Ab, IFIgG, TRGAb. Adrenal Ab neg	WT	hom IVS9+78delC	WT	WT	LT4 Insulin aspart Insulin glargine
14	M	36.9	12.6	IV	T1D, celiac disease	TPO, IAA pos GADA, IA2Ab, TgAb, TRGAb, anti-21-hydroxylase Ab neg	WT	het IVS9+78delC	-230Y (C/T het)	WT	Insulin aspart
15	M	38.8	16.6	IIIA	T1D, HT	TPOAb, IAA, IA2Ab pos ANA, AMA, ASMA, ARA, RAb, CAb, TgAb, GADA, LKMab, LC1Ab, APCA,	WT	het c.834 C>G (S278R)	-230Y (C/T het)	WT	Human insulin Insulin detemir LT4

						TRGAb, Adrenal Ab neg					
16	M	26.1	5.1	IV	T1D, celiac disease	IAA, IA2Ab pos ANA, AMA, ASMA, ARA, RAb, CAb, TgAb TPOAb GADA LKMAb, LC1Ab, APCA, TRGAb DGPIgG Adrenal Ab neg	WT	het IVS9+78delC	-230Y (C/T het)	het	Human insulin, Insulin glargine
17	M	30.2	8.3	IV	T1D, celiac disease	IAA, GADA, IA2Ab, IFIgG, APCA pos ANA, AMA, ASMA, ARA, RAb, CAb, TgAb, TPOAb, LKMAb, LC1Ab, TRAb, TRGAb, DGPIgG, Adrenal Ab, anti-21-hydroxylase Ab neg	WT	WT	-230Y (C/T het)	WT	Human insulin, Insulin detemir, Insulin glulisine
18	M	19.6	11.4	IIIC	HT, alopecia areata	TPOAb, IAA, GADA pos ANA, AMA, ASMA, ARA, Rb Ab, Cab, TgA,b, IA2Ab, LKMAb, LC1Ab, TRGAb, APCA, Adrenal Ab, neg	WT	het IVS9+6G>A hom IVS9+78delC	WT	WT	
19	M	25.5	2.8	IIIA IIIB	T1D, celiac disease, HT	TgAb, TPOAb, IAA, GADA, IFIgG, APCA pos ANA, AMA, ASMA, ARA, RbAb, CAb, IA2Ab, LKMAb, LC1Ab, TRGAb, DGPIgG, Adrenal Ab neg	WT	het IVS9 delC +78	-230Y (C/T het)	hom	Insulin
20	F	25.5	3.8	IV	T1D, celiac disease, vitiligo	IAA, GADA, IA2Ab pos ANA, AMA, ASMA, ARA, RAb, CAb, Beta2 Glycoprotein Ab, TgAb, TPOAb, LKMAb, LC1Ab, APCA, TRGAb,	WT	het IVS9 +6 G>A het IVS9 delC +78	-230Y (C/T het)	WT	Insulin aspart

						DGPIgG, anti-21-hydroxylase Ab neg					
21	F	26.6	4.4	IIIA IIIC	T1D, vitiligo, HT, scoliosis	APCA, Adrenal Abs pos TgAb, TPOAb neg	WT	WT	WT	WT	Insulin aspart Insulin degludec
22	F	22.9	8.1	II IIIB	Addison's disease, celiac disease, HT	ANA, TgAb, TPOAb, Adrenal Ab pos AMA, ASMA, ANCA, ARA, RAb, IAA, GADA, IA2Ab, LKMab, LC1Ab, IFIgG, APCA, TRAb, TRGAb, DGPIgG neg	WT	WT	WT	WT	Hydrocortisone Fludrocortisone LT4
23	M	14.6	12.8	IIIB	autoimmune hepatitis, HT	ANA, ASMA, ANCA RAb, LKMab, SLAIgG, LC1Ab neg	WT	WT	-655R (A/G het), -230Y (C/T het)	WT	Cyclosporine Azathioprine Ursodeoxycholic Acid LT4
24	M	30.2	13.5	IIIA	T1D, HT	IAA, IA2Ab pos ANA, AMA, ASMA, ANCA, ARA, RAb, CAB, TgAb, TPOAb, GADA, LKMab, LC1Ab, APCA, TRGAb, Adrenal Ab, anti-21-hydroxylase Ab neg	WT	NT	WT	WT	Insulin aspart, Insulin degludec
25	M	40.6	14.2	IIIA	T1D, HT	ANA, TPOAb, GADA, IA2Ab, pos AMA, ASMA, ARA, RAb, ACA, TgAb, LKMab, LC1Ab, APCA, TRGAb neg	WT	het IVS9+78delC	WT	WT	Insulin, Bisopropol fumarate
26	F	35.4	15	IIIA	T1D, HT	TgAb, TPO Ab, IAA, GADA, IA2Ab pos ANA, AMA, ASMA, ARA, RAb, CAB, LKMab, LC1Ab, APCA, TRGAb, Adrenal Ab neg	WT	het c.834 C>G (S278R) het IVS9+6G>A het IVS9+78delC	WT	het	LT4, Insulin aspart, Insulin degludec
27	F	25.8	4.7	IIIA IV	T1D, HT	TPOAb, IAA, IA2Ab, TRGAb pos ANA, AMA, ASMA, CAB,	WT	het IVS9+78delC	WT	WT	None

						TgAb, GADA, APCA, TRA, DGPIgG, Adrenal Ab, anti- 21-hydroxylase Ab neg					
28	F	22.9	0.9	IIIA	T1D, HT	TPOAb, IAA, GADA pos ANA, AMA, ASMA, ARA, RAb, CAb, TgAb, IA2Ab, LKMAb, LC1Ab, APCA, TRGAb, DGPIgG, Adrenal Ab, anti-21- hydroxylase Ab neg	WT	het c.834 C>G (S278R) het IVS9+78delC	WT	WT	Insulin aspart, Insulin glargine
29	M	35.7	3.9	IIIA	T1D, HT	ANA, TgAb, TPOAb, IAA, GADA, IA2Ab pos AMA, ASMA, ARA, RAb, anti-dsDNA Ab, CAb, LKMAb, LC1Ab, APCA, TRGAb, Adrenal Ab neg	WT	het IVS9+78delC	WT	het	Insulin aspart
30	F	18.4	3.8	IIIB IIIC	alopecia universalis, HT, celiac disease, allergic rhinitis, family history for myasthenia gravis	TPOAb pos ANA, AMA, ASMA, ARA ANCA, RbAb, TgAb, IAA, GADA, IA2Ab, LKMAb, LC1Ab, APCA, TRGAb, DGPIgG, , Adrenal Ab neg	WT	het IVS9 delC +78	-230Y (C/T het)	WT	None

NA= not available; HT= Hashimoto's thyroiditis; POF= primary ovarian failure