

A type 1 diabetes genetic risk score can discriminate monogenic autoimmunity with diabetes from early-onset clustering of polygenic autoimmunity with diabetes

Matthew B Johnson¹, Kashyap E Patel¹, Elisa De Franco¹, Jayne A L Houghton², Sian Ellard¹, Sarah E Flanagan¹, & Andrew T Hattersley¹

¹Institute of Biomedical and Clinical Science, University of Exeter Medical School, Exeter, EX2 5AD, UK

²Molecular Genetics, Royal Devon and Exeter Hospital, UK

Supplementary table S1: SNPs used for the T1-GRS calculation. Disease associations taken from www.gwascatalog.com.

SNP(s)	Gene	Odds Ratio	Weight	Autoimmune disease associations
rs2187668, rs7454108	DR3/DR4-DQ8	48.18	3.87	Type 1 diabetes, Coeliac disease, Autoimmune thyroid disease, Autoimmune hepatitis
	DR3/DR3	21.12	3.05	
	DR4- DQ8/DR4- DQ8	21.98	3.09	
	DR4-DQ8/X	7.03	1.95	
	DR3/X	4.53	1.51	
rs1264813	HLA_A_24	1.54	0.43	Type 1 diabetes, Myasthenia gravis
rs2395029	HLA_B_5701	2.5	0.92	Type 1 diabetes, Psoriasis
rs3129889	HLA_DRB1_15	14.88	2.7	Type 1 diabetes (protective), Multiple sclerosis
rs2476601	<i>PTPN22</i>	1.96	0.67	Type 1 diabetes, Autoimmune thyroid disease Crohn's disease, Myasthenia gravis, Systemic lupus erythematosus, Rheumatoid arthritis
rs689	<i>INS</i>	1.75	0.56	Type 1 diabetes
rs12722495	<i>IL2RA</i>	1.58	0.46	Type 1 diabetes, coeliac disease, Systemic sclerosis
rs2292239	<i>ERBB3</i>	1.35	0.3	Type 1 diabetes
rs10509540	C10orf59	1.33	0.29	Type 1 diabetes

Supplementary table S2: HLA DR3 status of patients with coeliac disease and autoimmune thyroid disease in those with confirmed monogenic autoimmunity and unknown aetiology. X = any HLA allele other than DR3.

	Monogenic autoimmunity (n=37)			Unknown aetiology (n=42)		
	Coeliac disease (n=2)	Autoimmune thyroid disease (n=6)	Either/both (n=8)	Coeliac disease (n=12)	Autoimmune thyroid disease (n=17)	Either/both (n=29)
DR3/DR3	0	0	0	4	2	6
DR3/X	1	2	3	7	9	16
X/X	1	4	5	1	6	7