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Supplemental Materials

Plasma fucosylated glycans and C-reactive protein as biomarkers of HNF1A-MODY in young adult onset non-autoimmune diabetes

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Supplemental Tables

Table S1. Additional features of the subjects harbouring rare *HNF1A* alleles, resulting in different functional effects

Coding DNA variant	Protein change	Age of diagnosis [years]	BMI [kg/m2]	Parental diabetes	Treatment	HbA1c [mmol/mol (%)]	hsCRP	GP30	GP36	GP38	Functional effect
c.1129delC	L377fs	27	26.79	yes	SU	65 (8.1)	0.21	0.55	1.50	0.22	Damaging
c.871C>A	P291T	15	32.51	yes	INS + MET	80 (9.5)	1.60	1.28	2.97	0.42	VUS
c.1-326del	del exon 1	20	34.29	no	INS	87 (10.1)	5.42	0.38	1.08	0.23	Damaging
c.142G>A	E48K	42	39.82	yes	INS + MET	107 (11.9)	2.00	0.95	2.23	0.47	Benign
c.872delC	P291fs	30	32.15	yes	INS	61 (7.7)	0.11	0.16	0.88	0.14	Damaging
c.139G>C	G47R	37	28.80	yes	INS + MET + SU	60 (7.6)	1.25	n/a	n/a	n/a	Benign
c.1816G>A	G606S	32	24.00	yes	INS	75 (9)	3.98	n/a	n/a	n/a	Benign
c.872delC	P291fs	18	25.73	yes	INS	39 (5.7)	0.02	0.58	1.42	0.17	Damaging
c.1136_1137delCT	P379fs	35	23.53	yes	MET + SU	45 (6.3)	0.06	0.27	0.97	0.16	Damaging
c.872dupC	G292fs	12	25.18	yes	INS	100 (11.3)	0.70	0.96	2.12	0.33	Damaging
c.872dupC	G292fs	17	20.97	no	Diet	44 (6.2)	0.10	0.44	1.22	0.17	Damaging
c.1015G>A	G339S	26	29.68	yes	INS	67 (8.3)	0.84	0.43	1.00	0.22	Benign
c.-4A>G	c.-4A>G	37	28.56	no	MET + SU	83 (9.7)	2.73	0.51	1.02	0.19	Benign
c.586A>G	T196A	42	38.89	yes	INS + TZD + MET	87 (10.1)	0.83	1.79	3.67	0.46	Benign
c.779C>T	T260M	25	30.51	yes	MET + SU	62 (7.8)	0.01	0.34	0.86	0.16	Damaging

c.404delA	D135fs	28	19.29	yes	SU	50 (6.7)	0.01	0.52	1.24	0.14	Damaging
c.1136C>A	P379H	44	30.81	yes	Diet	56 (7.3)	1.57	0.70	2.01	0.25	Damaging
c.1047C>A	H349Q	33	n/a	yes	INS	79 (9.4)	1.01	2.03	3.84	0.42	Benign
c.1165T>G	L389V	37	32.30	no	INS + MET + SU	77 (9.2)	12.07	0.62	1.37	0.25	Benign
c.666G>T	K222N	18	32.01	yes	SU	57 (7.4)	0.20	0.33	0.97	0.16	Damaging
c.451G>A	G151S	35	26.37	yes	MET + SU	45 (6.3)	0.80	0.72	1.62	0.25	Damaging
c.1136C>G	P379R	28	19.94	yes	INS + MET	60 (7.6)	0.60	0.29	1.10	0.17	Damaging
c.1544C>T	T515M	33	27.99	yes	INS	53 (7.0)	4.60	1.11	2.31	0.32	VUS
c.862G>T	G288W	39	38.40	no	Diet	37 (5.5)	15.70	1.24	3.31	0.49	Benign
c.751G>A	A251T	39	27.14	no	Diet	51 (6.8)	0.30	0.64	1.59	0.23	VUS
c.685C>T	R229*	25	19.05	yes	Glinide	56 (7.3)	0.40	0.35	1.12	0.11	Damaging
c.872dupC	G292fs	23	23.95	n/a	INS	57 (7.4)	0.40	0.52	1.23	0.18	Damaging
c.1136_1137delCT	P379fs	16	22.28	n/a	Diet	48 (6.5)	0.10	0.42	1.07	0.12	Damaging
c.8C>G	S3C	37	24.17	yes	INS+ glinide	107 (11.9)	1.40	0.73	1.60	0.26	VUS

INS – insulin; MET – metformin; SU – sulphonylurea derivative; TZD – thiazolidinedione derivative

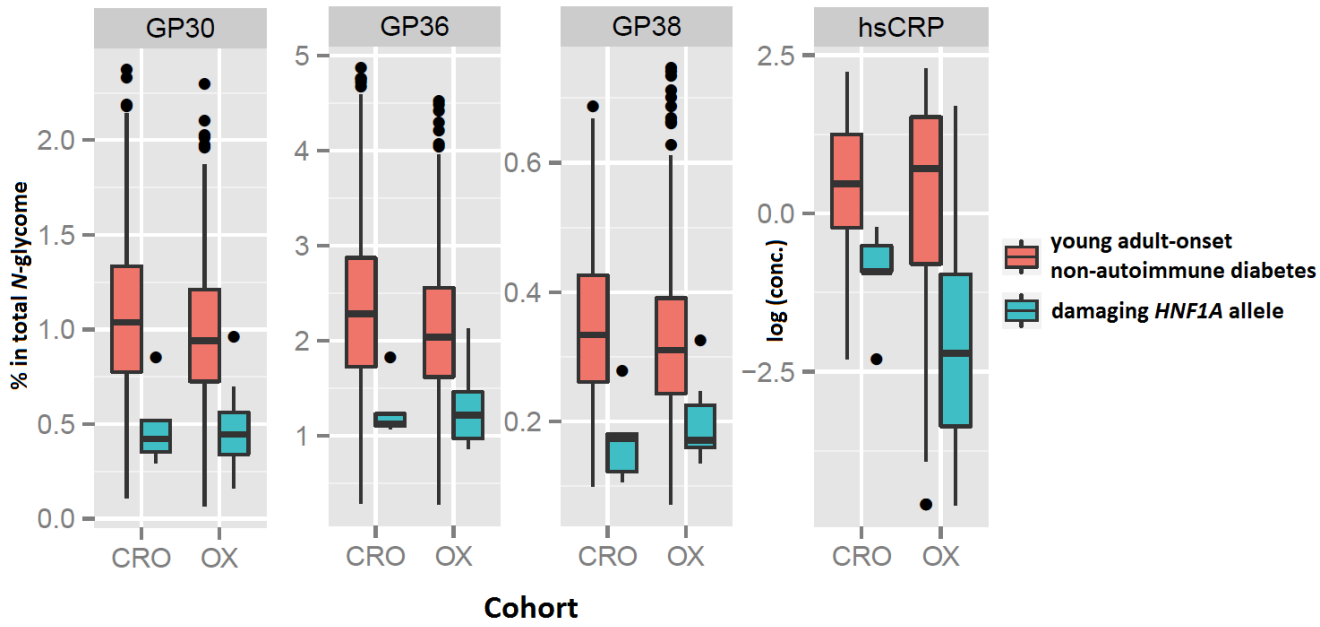
Supplemental Table S2 Comparison of plasma protein *N*-glycome and hsCRP between subjects with likely damaging *HNF1A* alleles and subjects without rare HNF1A alleles, with young adult-onset non-autoimmune diabetes, using general linear model and case control meta-analysis on both, UK and Croatian cohorts. Statistically significant p-values are marked in bold.

	UK cohort			Croatian cohort			Meta-analysis			
marker	effect	SE	p-value	effect	SE	p-value	effect	SE	p-value	adjusted p-value*
GP30	-1.31	0.30	1.23E-05	-1.12	0.44	9.79E-03	-1.25	0.25	4.25E-07	**1.00E-05**
hsCRP	-1.25	0.30	3.90E-05	-1.09	0.45	1.15E-02	-1.20	0.25	1.97E-06	**3.09E-05**
GP38	-1.12	0.31	2.54E-04	-1.17	0.45	8.38E-03	-1.14	0.25	7.10E-06	**7.98E-05**
GP36	-1.14	0.30	1.78E-04	-0.98	0.44	2.34E-02	-1.09	0.25	1.34E-05	**1.05E-04**
GP25	-1.05	0.31	5.65E-04	-0.54	0.46	2.36E-01	-0.90	0.26	4.50E-04	**2.35E-03**
GP42	-0.88	0.31	4.17E-03	-0.80	0.45	7.32E-02	-0.86	0.26	7.98E-04	**3.75E-03**
GP27.28	0.65	0.30	3.18E-02	0.85	0.44	5.29E-02	0.71	0.25	4.49E-03	**1.46E-02**
GP33	0.70	0.30	1.70E-02	0.70	0.45	1.16E-01	0.70	0.25	4.59E-03	**1.46E-02**
GP40	0.71	0.31	1.99E-02	0.74	0.45	9.92E-02	0.72	0.25	4.66E-03	**1.46E-02**
GP31	0.53	0.30	7.87E-02	0.66	0.45	1.34E-01	0.57	0.25	2.29E-02	6.32E-02
GP5	0.84	0.31	6.59E-03	-0.18	0.47	6.96E-01	0.53	0.26	4.06E-02	1.06E-01
GP22	-0.38	0.31	2.15E-01	-0.78	0.46	8.75E-02	-0.50	0.26	4.97E-02	1.23E-01
GP4	0.52	0.31	8.98E-02	0.36	0.47	4.31E-01	0.47	0.26	6.67E-02	1.57E-01
GP14	0.85	0.31	6.35E-03	-0.48	0.47	3.03E-01	0.44	0.26	8.82E-02	1.97E-01
GP10.11	0.17	0.29	5.49E-01	0.85	0.42	4.28E-02	0.39	0.24	1.03E-01	2.21E-01
GP20.21	0.25	0.31	4.13E-01	0.55	0.46	2.31E-01	0.34	0.26	1.82E-01	3.72E-01
GP19	0.29	0.32	3.51E-01	0.45	0.46	3.28E-01	0.34	0.26	1.91E-01	3.73E-01
GP12	0.25	0.32	4.23E-01	0.46	0.45	3.05E-01	0.32	0.26	2.18E-01	4.10E-01
GP24	-0.34	0.31	2.76E-01	-0.23	0.46	6.16E-01	-0.30	0.26	2.41E-01	4.27E-01
GP29	0.35	0.29	2.36E-01	0.15	0.44	7.36E-01	0.29	0.25	2.45E-01	4.27E-01
GP15	-0.29	0.31	3.44E-01	-0.27	0.47	5.57E-01	-0.29	0.26	2.70E-01	4.49E-01
GP6	0.37	0.31	2.26E-01	0.07	0.47	8.78E-01	0.28	0.26	2.77E-01	4.49E-01
GP41	0.28	0.31	3.55E-01	0.17	0.46	7.13E-01	0.25	0.26	3.35E-01	5.20E-01
GP9	0.15	0.31	6.24E-01	0.44	0.45	3.28E-01	0.24	0.26	3.43E-01	5.20E-01
GP23	-0.27	0.32	3.94E-01	-0.18	0.47	6.99E-01	-0.24	0.26	3.61E-01	5.30E-01
GP8	-0.27	0.31	3.88E-01	-0.09	0.47	8.47E-01	-0.21	0.26	4.13E-01	5.81E-01
GP39	0.12	0.31	6.82E-01	0.39	0.46	3.93E-01	0.21	0.26	4.20E-01	5.81E-01
GP2	-0.01	0.28	9.72E-01	-0.47	0.43	2.69E-01	-0.14	0.23	5.36E-01	7.20E-01
GP26	0.18	0.31	5.61E-01	0.09	0.45	8.40E-01	0.15	0.26	5.56E-01	7.27E-01
GP16	0.08	0.31	8.08E-01	0.19	0.45	6.75E-01	0.11	0.26	6.64E-01	8.44E-01
GP32	-0.05	0.32	8.83E-01	0.42	0.47	3.64E-01	0.10	0.26	7.04E-01	8.70E-01
GP35	0.02	0.31	9.38E-01	-0.35	0.46	4.41E-01	-0.09	0.26	7.22E-01	8.70E-01
GP34	-0.14	0.30	6.39E-01	0.10	0.44	8.20E-01	-0.06	0.25	7.96E-01	8.94E-01

GP1	0.32	0.29	2.75E-01	-0.53	0.45	2.34E-01	0.06	0.25	7.97E-01	8.94E-01
GP37	-0.19	0.30	5.13E-01	0.23	0.45	6.09E-01	-0.06	0.25	7.99E-01	8.94E-01
GP13	-0.14	0.30	6.41E-01	0.39	0.46	3.93E-01	0.02	0.25	9.40E-01	9.85E-01
GP3	-0.11	0.29	6.96E-01	0.21	0.45	6.30E-01	-0.02	0.24	9.47E-01	9.85E-01
GP17.18	-0.25	0.30	4.09E-01	0.54	0.45	2.30E-01	-0.01	0.25	9.81E-01	9.85E-01
GP7	0.03	0.31	9.25E-01	-0.05	0.47	9.22E-01	0.01	0.26	9.82E-01	9.85E-01

* p-value corrected for multiple measures using Benjamini-Hochberg test.

Supplemental Figures



Supplemental Figure S1 Marked differences in abundances of individual glycan groups (GP30, GP36, GP38) and hsCRP in subjects with young adult-onset non-autoimmune diabetes, without rare *HNF1A* alleles and subjects with likely damaging *HNF1A* alleles. Differences in plasma *N*-glycans and hsCRP are shown as box plots. Each box represents the 25th to 75th percentile. Lines inside the boxes represent the median. The upper whisker extends from the hinge to the highest value that is within 1.5 x IQR of the hinge, where IQR is the inter-quartile range, or distance between the first and third quartiles. The lower whisker extends from the hinge to the lowest value within 1.5 x IQR of the hinge. Circles indicate outliers. GP – glycan peak; CRO – Croatian cohort; OX – UK (Oxford) cohort.