

Supplementary Data, Table S1: Patient and Family Histories and Medical Data

Subject ID	family ID	recent antibiotic treatment	recent infections	year of birth	gender	autoantibody status	T1D status	*A1c	date of diagnosis	# Biological mother's T1D history	# Biological father's T1D history	GAD65 status
SABO1	FABO	NO	no	2000	FEMALE	Unknown	T1D	7.6	10/1/2003	No history	Unknown	
SABO2	FABO	NO	no	2003	MALE	Unknown	Control			No history	Unknown	
SACI1	FACI	NO	no	1997	MALE	AA-	T1D	7	7/1/2013	No history	No history	negative
SACI2	FACI	NO	no	2000	FEMALE	Unknown	Control			No history	No history	
SACU1	FACU	NO	no	2002	MALE	AA+	T1D	7.3	3/1/2011	No history	No history	positive
SACU2	FACU	NO	no	2005	FEMALE	Unknown	Control			No history	No history	
SAHO1	FAHO	NO	no	1999	MALE	AA+	T1D	11.5	2/1/2009	No history	No history	negative
SAHO2	FAHO	NO	no	2001	MALE	AA-	Control			No history	No history	
SAHU1	FAHU	NO	no	1998	MALE	Unknown	T1D	5.8	9/1/2013	T1D	No history	
SAHU2	FAHU	NO	no	2000	FEMALE	AA-	T1D	6.6	2/1/2008	T1D	No history	negative
SAHU3	FAHU	NO	no	2003	FEMALE	Unknown	Control			T1D	No history	
SALU1	FALU	NO	no	2000	FEMALE	AA+	T1D	8	5/1/2004	No history	No history	
SALU2	FALU	NO	no	2003	MALE	Unknown	Control			No history	No history	
SALY1	FALY	NO	no	1998	MALE	AA+	T1D	8.2	2/1/2005	No history	No history	negative
SALY2	FALY	NO	no	2000	FEMALE	Unknown	Control			No history	No history	
SAME1	FAME	NO	no	1997	FEMALE	Unknown	T1D	11.3	9/1/2005	Unknown	No history	
SAME2	FAME	NO	no	2000	FEMALE	Unknown	Control			Unknown	No history	
SANY1	FANY	NO	no	2004	MALE	Unknown	T1D	7.1	7/1/2007	No history	No history	
SANY2	FANY	NO	no	1997	MALE	Unknown	Control			No history	No history	
SANY3	FANY	NO	no	2000	MALE	Unknown	Control			No history	No history	
SAPA1	FAPA	NO	no	2003	MALE	AA+	T1D	8.8	8/1/2008	No history	No history	positive
SAPA2	FAPA	NO	no	1997	FEMALE	Unknown	Control			No history	No history	
SARU1	FARU	NO	no	2001	MALE	AA+	T1D	9.3	3/1/2010	No history	No history	positive
SARU2	FARU	NO	no	1998	FEMALE	Unknown	Control			No history	No history	
SATY1	FATY	NO	unknown	1999	FEMALE	Unknown	T1D	9.2	1/1/2007	No history	No history	
SATY2	FATY	NO	no	1996	FEMALE	Unknown	Control			No history	No history	
SAVA1	FAVA	NO	no	2005	MALE	AA+	T1D	9.4	1/1/2012	AA-	AA-	positive

SAVA2	FAVA	NO	no	2002	FEMALE	AA-	Control			AA-	AA-	
SAVU1	FAVU	NO	no	2004	MALE	AA+	T1D	10.5	2/1/2005	No history	Unknown	
SAVU2	FAVU	NO	no	1996	FEMALE	Unknown	Control			No history	Unknown	
SAWE1	FAWE	NO	no	1997	FEMALE	AA-	Control			No history	T1D	
SAWE2	FAWE	NO	no	1997	FEMALE	AA-	Control			No history	T1D	
SAWE3	FAWE	NO	no	1999	MALE	AA-	Control			No history	T1D	
SAXU1	FAXU	NO	no	2008	FEMALE	AA-	T1D	8.4	1/1/2012	No history	No history	
SAXU2	FAXU	NO	no	2004	FEMALE	Unknown	Control			No history	No history	
SAZE1	FAZE	NO	no	2004	MALE	AA+	T1D	7.5	10/1/2009	No history	No history	
SAZE2	FAZE	NO	no	2005	MALE	Unknown	Control			No history	No history	
SEBU1	FEBU	NO	no	2000	FEMALE	Unknown	T1D	7.3	5/1/2012	No history	No history	
SEBU2	FEBU	NO	no	1997	MALE	Unknown	Control			No history	No history	
SEBY1	FEBY	NO	no	2004	FEMALE	AA+	T1D	7.7	11/1/2008	No history	No history	
SEBY2	FEBY	NO	no	2004	FEMALE	Unknown	Control			No history	No history	
SECU1	FECU	NO	no	2002	MALE	Unknown	T1D	7.8	5/1/2010	AA-	AA-	
SECU2	FECU	NO	no	2004	MALE	Unknown	T1D	7.6	10/1/2010	AA-	AA-	
SECU3	FECU	NO	no	2008	MALE	AA-	Control			AA-	AA-	
SECY1	FECY	NO	no	2003	MALE	AA+	T1D	11.7	12/1/2012	No history	No history	positive
SECY2	FECY	NO	no	2008	FEMALE	AA+	Control			No history	No history	positive
SEGY1	FEGY	NO	no	2007	FEMALE	AA+	T1D	8.2	4/1/2013	No history	No history	
SEHA1	FEHA	NO	no	2000	FEMALE	Unknown	T1D	10.1	10/1/2002	No history	No history	
SEHA2	FEHA	NO	no	2007	FEMALE	Unknown	Control			No history	No history	
SEHU1	FEHU	YES	yes	2005	MALE	Unknown	Control			No history	No history	
SEHY1	FEHY	NO	no	1999	FEMALE	AA+	T1D	9.7	6/1/2010	No history	No history	positive
SEHY2	FEHY	NO	no	2004	FEMALE	Unknown	Control			No history	No history	
SEJO1	FEJO	NO	no	1997	FEMALE	Unknown	T1D	8.1	11/1/1999	No history	No history	
SEJO2	FEJO	NO	no	2001	FEMALE	Unknown	Control			No history	No history	
SEKA1	FEKA	NO	no	1999	FEMALE	Unknown	T1D	9.4	4/1/2007	Unknown	Unknown	
SELE1	FELE	NO	no	2009	FEMALE	Unknown	T1D	8.3	12/1/2012	No history	No history	
SELE2	FELE	NO	no	2006	MALE	AA-	Control			No history	No history	
SEMU1	FEMU	NO	no	1997	FEMALE	AA+	T1D	11.7	11/1/2007	No history	T1D	positive

SEMU2	FEMU	NO	no	2001	FEMALE	Unknown	Control			No history	T1D	
SEMY1	FEMY	NO	no	1998	FEMALE	AA+	T1D	7.2	4/1/2012	No history	No history	negative
SEMY2	FEMY	NO	no	1999	MALE	AA-	Control			No history	No history	
SEMY3	FEMY	NO	no	2005	MALE	AA+	Control			No history	No history	positive
SENO1	FENO	NO	no	1999	MALE	AA-	T1D	8.5	10/1/2008	Unknown	Unknown	negative
SENO2	FENO	NO	no	2001	FEMALE	Unknown	Control			Unknown	Unknown	
SEPO1	FEPO	NO	yes	2001	MALE	Unknown	Control			No history	No history	
SEPO2	FEPO	NO	no	2004	FEMALE	AA+	Control			No history	No history	positive
SEPO3	FEPO	NO	yes	2006	MALE	AA-	Control			No history	No history	
SETA1	FETA	NO	no	1997	MALE	AA-	T1D	10.9	1/1/2004	No history	No history	
SETA2	FETA	NO	no	1995	FEMALE	Unknown	Control			No history	No history	
SETY1	FETY	NO	no	2001	FEMALE	AA-	T1D	8.2	7/1/2003	AA-	No history	
SETY2	FETY	NO	no	2008	MALE	AA+	T1D	9.1	7/1/2010	AA-	No history	negative
SETY3	FETY	NO	no	2003	MALE	AA-	Control			AA-	No history	
SETY4	FETY	NO	no	2009	MALE	AA-	Control			AA-	No history	
SEVA1	FEVA	NO	no	2001	MALE	Unknown	T1D	10	11/1/2011	No history	No history	
SEVA2	FEVA	NO	no	1999	MALE	AA-	Control			No history	No history	
SEVI1	FEVI	NO	no	2006	FEMALE	AA-	Control			AA+	AA-	
SEVI2	FEVI	NO	no	1998	MALE	AA-	Control			AA+	AA-	
SEVI3	FEVI	NO	no	2002	MALE	AA+	T1D	8.1	2/1/2011	AA+	AA-	
SIBU1	FIBU	NO	no	2000	MALE	AA+	T1D	6.6	8/1/2013	No history	No history	positive
SIBU2	FIBU	NO	no	2002	FEMALE	Unknown	Control			No history	No history	
SICA1	FICA	NO	no	2008	MALE	AA-	Control			T1D	No history	
SICA2	FICA	NO	no	2011	FEMALE	AA-	Control			T1D	No history	
SICE1	FICE	NO	no	2003	FEMALE	AA+	T1D	8	12/1/2010	AA-	Unknown	
SICE2	FICE	NO	no	2006	MALE	AA+	Control			AA-	Unknown	
SICO1	FICO	NO	no	1999	MALE	AA+	T1D	8.4	2/1/2010	AA-	T1D	
SICO2	FICO	NO	no	1997	MALE	AA-	Control			AA-	T1D	
SICO3	FICO	NO	no	2007	MALE	Unknown	Control			AA-	T1D	
SIDI1	FIDI	NO	no	1999	MALE	AA-	Control			No history	No history	
SIDI2	FIDI	NO	no	2001	FEMALE	AA-	Control			No history	No history	

SIDI3	FIDI	NO	no	2004	MALE	AA+	T1D	5.5	7/1/2012	No history	No history	positive
SIDI4	FIDI	NO	no	2007	MALE	AA+	Control			No history	No history	
SIGA1	FIGA	NO	no	1999	MALE	AA+	T1D	8.6	2/1/2011	Unknown	Unknown	positive
SIGA2	FIGA	NO	no	1994	MALE	Unknown	Control			Unknown	Unknown	
SIGE1	FIGE	NO	no	2001	MALE	Unknown	T1D	7.6	3/1/2001	Unknown	No history	
SIGE2	FIGE	NO	no	2000	MALE	Unknown	Control			Unknown	No history	
SIGU1	FIGU	NO	no	1999	MALE	AA+	T1D	5.73	9/1/2011	No history	No history	positive
SIGU2	FIGU	NO	no	1997	FEMALE	Unknown	Control			No history	No history	
SIHU1	FIHU	NO	no	2004	MALE	AA-	T1D	6.4	9/1/2008	No history	No history	
SIHU2	FIHU	NO	no	2003	MALE	Unknown	Control			No history	No history	
SIJI1	FIJI	NO	no	2002	MALE	AA-	T1D	6.8	10/1/2011	No history	No history	negative
SIJI2	FIJI	NO	no	1999	FEMALE	Unknown	Control			No history	No history	
SIKE1	FIKE	NO	no	1998	MALE	Unknown	T1D	12.6	12/1/2002	No history	No history	
SIKE2	FIKE	NO	no	2002	MALE	Unknown	Control			No history	No history	
SIRI1	FIRI	NO	no	2004	FEMALE	AA+	T1D	7.3	3/1/2011	No history	No history	positive
SIRI2	FIRI	NO	no	2000	MALE	Unknown	Control			No history	No history	
SIRU1	FIRU	NO	no	2001	MALE	Unknown	T1D	8.9	6/1/2004	No history	No history	
SIRU2	FIRU	NO	no	2003	FEMALE	Unknown	Control			No history	No history	
SITI1	FITI	NO	no	1997	MALE	AA+	T1D	7.2	5/1/2009	No history	Other	
SITY1	FITY	NO	no	1997	MALE	Unknown	T1D	9.3	2/1/2003	No history	Other	
SITY2	FITY	NO	no	1994	MALE	Unknown	Control			No history	Other	
SIXO1	FIXO	NO	no	2001	MALE	AA+	T1D	13.9	4/1/2003	No history	Unknown	
SIXO2	FIXO	NO	no	2006	MALE	Unknown	Control			No history	Unknown	
SOCA1	FOCA	NO	no	2008	MALE	Unknown	T1D	7.9	8/1/2011	No history	No history	
SOGU1	FOGU	NO	no	1997	FEMALE	AA+	T1D	10.2	3/1/2011	No history	Unknown	
SOGU2	FOGU	NO	no	2001	MALE	AA-	Control			No history	Unknown	
SOHA1	FOHA	NO	no	1999	MALE	AA-	T1D	6.5	5/1/2007	No history	No history	negative
SOHA2	FOHA	NO	no	1996	FEMALE	Unknown	Control			No history	No history	
SOHE1	FOHE	NO	no	2006	FEMALE	Unknown	T1D	8.6	5/1/2013	No history	Unknown	
SOLI1	FOLI	YES	unknown	2003	FEMALE	Unknown	T1D	6.7	8/1/2011	No history	No history	
SOLI2	FOLI	NO	no	2005	MALE	Unknown	Control			No history	No history	

SOLY1	FOLY	NO	no	1997	FEMALE	AA-	T1D	13	2/1/2008	Unknown	Other	
SOLY2	FOLY	NO	no	2000	FEMALE	Unknown	Control			Unknown	Other	
SONY1	FONY	NO	no	2004	MALE	AA+	T1D	9.1	8/1/2010	Unknown	Unknown	
SONY2	FONY	NO	no	2005	MALE	Unknown	Control			Unknown	Unknown	
SOPA1	FOPA	NO	no	1998	MALE	AA+	T1D	14.9	11/1/2010	No history	No history	negative
SOPA2	FOPA	NO	no	2003	FEMALE	Unknown	Control			No history	No history	
SOPI1	FOPI	NO	no	2003	MALE	AA+	T1D	9.2	2/1/2011	No history	No history	positive
SOPI2	FOPI	NO	no	2001	MALE	AA+	T1D	5.9	4/1/2013	No history	No history	positive
SOPI3	FOPI	NO	no	2008	MALE	Unknown	Control			No history	No history	
SOP01	FOPO	NO	no	2005	FEMALE	AA-	T1D	7.2	12/1/2012	No history	No history	negative
SOP02	FOPO	NO	no	2003	FEMALE	Unknown	Control			No history	No history	
SORY1	FORY	NO	no	1998	FEMALE	Unknown	T1D	7.6	4/1/2000	Unknown	Unknown	
SORY2	FORY	NO	no	2000	FEMALE	AA+	T1D	8.4	12/1/2006	Unknown	Unknown	positive
SORY3	FORY	NO	no	2002	FEMALE	Unknown	Control			Unknown	Unknown	
SORY4	FORY	NO	no	2004	FEMALE	Unknown	Control			Unknown	Unknown	
SOTO1	FOTO	NO	no	2006	FEMALE	AA+	T1D	9.4	12/1/2007	No history	No history	positive
SOTO2	FOTO	NO	no	2003	FEMALE	Unknown	Control			No history	No history	
SOVE1	FOVE	NO	no	1998	FEMALE	AA-	T1D	7.2	11/1/2008	No history	No history	
SOVE2	FOVE	NO	no	1995	FEMALE	Unknown	Control			No history	No history	
SOWI1	FOWI	NO	no	2002	FEMALE	AA+	T1D	9.4	4/1/2009	T1D	No history	negative
SOWI2	FOWI	NO	no	2007	FEMALE	AA-	Control			T1D	No history	
SOXA1	FOXA	NO	no	2004	MALE	AA+	T1D	10	7/1/2013	Other	No history	positive
SOXA2	FOXA	NO	no	2006	FEMALE	AA-	Control			Other	No history	
SOXU1	FOXU	NO	no	2003	FEMALE	AA+	T1D	9.8	3/1/2012	No history	T1D	positive
SOXU2	FOXU	NO	no	2000	FEMALE	Unknown	Control			No history	T1D	
SOZI1	FOZI	NO	no	1998	FEMALE	AA+	T1D	8.3	4/1/2008	AA-	Unknown	positive
SOZI2	FOZI	NO	no	1997	FEMALE	AA-	Control			AA-	Unknown	
SOZU1	FOZU	NO	no	2001	FEMALE	AA+	T1D	7.7	2/1/2004	No history	No history	positive
SOZU2	FOZU	NO	no	2002	FEMALE	Unknown	Control			No history	No history	
SUBU1	FUBU	NO	no	2000	FEMALE	AA-	T1D	9.3	6/1/2007	No history	No history	negative
SUBU2	FUBU	NO	no	2005	MALE	AA-	Control			No history	No history	

SUC01	FUCO	NO	no	1997	FEMALE	AA+	T1D	7.2	4/1/2009	No history	No history	positive
SUC02	FUCO	NO	no	2000	MALE	Unknown	Control			No history	No history	
SUDY1	FUDY	NO	no	2001	FEMALE	AA-	T1D	14.9	10/1/2010	No history	Unknown	
SUDY2	FUDY	NO	no	2006	MALE	Unknown	Control			No history	Unknown	
SUHA1	FUHA	NO	no	2004	FEMALE	AA-	T1D	6.9	9/1/2011	No history	No history	
SUHA2	FUHA	YES	yes	2002	FEMALE	AA-	Control			No history	AA-	
SUHE1	FUHE	NO	no	1998	FEMALE	AA+	T1D	6.2	2/1/2013	No history	No history	positive
SUHE2	FUHE	NO	no	1998	FEMALE	AA-	Control			No history	No history	
SUJA1	FUJA	NO	no	2002	MALE	Unknown	T1D	8.5	7/1/2012	No history	Unknown	
SUJA2	FUJA	NO	no	2000	MALE	AA-	Control			No history	Unknown	
SUJ11	FUJI	NO	no	1999	FEMALE	AA+	T1D	7.4	7/1/2012	No history	No history	positive
SUJ12	FUJI	NO	no	1997	MALE	Unknown	Control			No history	No history	
SUKA1	FUKA	NO	no	1998	MALE	Unknown	T1D	5.5	1/1/2011	No history	No history	
SUKA2	FUKA	NO	no	2000	MALE	Unknown	Control			No history	No history	
SUKI1	FUKI	NO	no	2000	MALE	Unknown	T1D	7.3	7/1/2004	No history	No history	
SUKI2	FUKI	NO	no	2004	FEMALE	AA+	Control			No history	No history	
SULI1	FULI	NO	no	2001	MALE	AA+	T1D	8.1	12/1/2010	No history	No history	negative
SULI2	FULI	NO	no	2005	MALE	Unknown	Control			No history	No history	
SUNU2	FUNU	NO	no	1999	FEMALE	AA+	T1D	7.6	10/1/2011	No history	No history	positive
SUPE1	FUPE	NO	no	2003	FEMALE	Unknown	T1D	13	8/1/2008	No history	No history	
SUPE2	FUPE	NO	no	2001	FEMALE	Unknown	T1D	13.6	8/1/2010	No history	No history	
SUPE3	FUPE	NO	no	2006	FEMALE	AA-	Control			No history	No history	
SURO1	FURO	NO	no	1997	FEMALE	Unknown	T1D	7.7	10/1/2008	No history	No history	
SURO2	FURO	NO	no	1997	MALE	Unknown	Control			No history	No history	
SUTO1	FUTO	NO	no	1998	FEMALE	AA+	T1D	7.5	3/1/2005	No history	No history	negative
SUTO2	FUTO	NO	no	2000	MALE	Unknown	Control		N/A	No history	No history	
SUVA1	FUVA	NO	no	2006	MALE	Unknown	Control			No history	No history	
SUVA2	FUVA	NO	no	2004	MALE	AA+	T1D	6.7	1/1/2012	AA-	AA-	positive
SUWA1	FUWA	NO	no	2001	FEMALE	Unknown	T1D	8.1	8/1/2003	No history	No history	
SUWA2	FUWA	NO	no	2005	FEMALE	AA-	T1D	7.5	3/1/2007	No history	No history	negative
SUWA3	FUWA	NO	no	2008	FEMALE	AA-	Control			No history	No history	

SUXO1	FUXO	NO	no	2000	FEMALE	Unknown	T1D	7.4	3/1/2005	No history	No history	
SUXO2	FUXO	NO	no	2004	MALE	Unknown	Control			No history	No history	
SUZA1	FUZA	NO	no	2002	MALE	Unknown	T1D	7.7	12/1/2010	No history	No history	
SUZI1	FUZI	NO	unknown	2001	FEMALE	Unknown	T1D	9.4	10/1/2007	No history	Unknown	
SUZI2	FUZI	NO	no	2007	MALE	AA-	Control			No history	Unknown	
SYCU1	FYCU	NO	no	2004	MALE	AA+	T1D	7.6	5/1/2010	No history	No history	
SYCU2	FYCU	NO	no	2001	FEMALE	Unknown	Control			No history	No history	
SYDU1	FYDU	NO	yes	2007	MALE	AA+	T1D	7.5	6/1/2009	No history	No history	
SYGI1	FYGI	NO	no	2003	MALE	AA+	T1D	6.6	9/1/2013	No history	No history	positive
SYGI2	FYGI	NO	no	2001	MALE	Unknown	Control			No history	No history	
SYHA1	FYHA	NO	no	2003	FEMALE	AA+	T1D	7.9	6/1/2013	No history	No history	
SYHA2	FYHA	NO	no	2007	FEMALE	AA-	Control			No history	No history	
SYKI1	FYKI	NO	no	2004	MALE	AA+	Control			No history	AA+	positive
SYKY2	FYKY	NO	no	1998	MALE	Unknown	Control			No history	No history	
STYLE1	FYLE	NO	no	2004	FEMALE	AA-	T1D	7.6	6/1/2008	No history	No history	
STYLE2	FYLE	NO	no	2001	FEMALE	Unknown	Control			No history	No history	
SYLU1	FYLU	NO	no	2005	FEMALE	AA+	T1D	11.2	11/1/2010	No history	No history	positive
SYLU2	FYLU	NO	no	2006	MALE	Unknown	Control			No history	No history	
SYPY1	FYPY	NO	no	1999	MALE	Unknown	T1D	7.9	5/1/2007	Unknown	Unknown	
SYPY2	FYPY	NO	no	2001	MALE	Unknown	Control			Unknown	Unknown	
SYRO1	FYRO	NO	no	2001	MALE	AA+	T1D	6.6	3/1/2012	Unknown	Unknown	positive
SYRO2	FYRO	NO	no	2003	MALE	Unknown	Control			Unknown	Unknown	
SYRO3	FYRO	NO	no	1999	MALE	Unknown	Control			Unknown	Unknown	
SYTE1	FYTE	NO	unknown	2005	FEMALE	Unknown	T1D	8.1	10/1/2010	AA-	AA-	
SYTE2	FYTE	NO	no	2006	MALE	AA-	Control			AA-	AA-	
SYTO1	FYTO	NO	no	1998	MALE	Unknown	T1D	6	8/1/2013	No history	No history	
SYTO2	FYTO	NO	yes	2001	MALE	Unknown	Control			No history	No history	
SYTY1	FYTY	NO	no	1998	MALE	Unknown	T1D	7.6	8/1/2004	Unknown	Unknown	
SYTY2	FYTY	NO	no	2000	MALE	Unknown	Control			Unknown	Unknown	
SYVA1	FYVA	NO	no	2004	MALE	Unknown	T1D	7.4	7/1/2013	No history	No history	
SYVA2	FYVA	NO	no	2005	FEMALE	AA+	T1D	7.5	1/1/2012	No history	No history	positive

SYVA3	FYVA	NO	no	2005	FEMALE	AA-	Control			No history	No history	
SYVO1	FYVO	NO	no	2002	FEMALE	AA+	T1D	7.6	3/1/2011	No history	No history	positive
SYVO2	FYVO	NO	no	2004	FEMALE	AA-	Control			No history	No history	
SYWE1	FYWE	NO	no	2005	FEMALE	AA+	T1D	7.3	12/1/2011	No history	No history	positive
SYWE2	FYWE	NO	no	2003	FEMALE	Unknown	Control			No history	No history	
SYWI1	FYWI	NO	no	2006	FEMALE	AA-	T1D	7.6	4/1/2012	AA-	AA-	negative
SYXE1	FYXE	NO	no	2008	MALE	AA+	T1D	8.6	10/1/2010	No history	No history	positive
SYXE2	FYXE	NO	no	2002	MALE	AA-	Control			No history	No history	
SYZU1	FYZU	YES	yes	2005	MALE	AA+	T1D	7.5	8/1/2011	No history	No history	positive
SYZU2	FYZU	NO	no	2001	MALE	Unknown	Control			No history	No history	

Information on gender, age, family medical history, date of T1D onset, glutamic acid decarboxylase (GAD65) autoantibody test results, a one-time HbA_{1C} value for subjects in the T1D cohort, and the occurrence of infections and antibiotic usage over the three months prior to specimen collection were recorded. *A1c: hemoglobin A1c level (per cent of total hemoglobin in blood); # either T1D positive, autoantibody-positive or autoantibody-negative status is denoted; AA+, autoantibody positive; AA-, autoantibody negative; control: healthy sibling of T1D patient.

Supplementary Data, Dataset S1: Alpha Diversity Analyses of Gut Microbiota Based on 16S rRNA Phylogenetic Surveys

FIGURE 1: ALPHA DIVERSITY OF MICROBIOTA IN T1D PATIENTS COMPARED TO HEALTHY SIBLING CONTROLS USING THE SHANNON INDEX, THE SIMPSON INDEX, AND THE INV SIMPSON ALPHA DIVERSITY MEASURES. WILCOXON RANK SUM TESTS RETURNED P-VALUES OF 0.61, 0.35 AND 0.35, RESPECTIVELY, SUGGESTING THE ABSENCE OF STATISTICALLY SIGNIFICANT DIFFERENCES IN ALPHA DIVERSITY. THE 16S rDNA DATA FOR THE SURVEY OF GUT MICROBIOTA WERE OBTAINED FROM ANALYSES OF 205 STOOL SAMPLES CONSISTING OF 99 T1D PATIENTS AND 106 HEALTHY SIBLINGS AS THE CONTROL GROUP.1

FIGURE 2: HEATMAP BASED ON NMDS ORDINATION USING BRAY-CURTIS DISSIMILARITY REPRESENTING THE DISTRIBUTION OF DIFFERENT PHYLA IN HEALTHY SIBLING VS T1D SAMPLES. AT PHYLUM LEVEL, THERE IS NO DISSIMILARITY BETWEEN THE T1D AND HEALTHY SIBLING COHORTS. THE T1D STATUS IS INDICATED AT THE BOTTOM OF THE GRAPHIC: LEFT SIDE, HEATHY SIBLING “CONTROLS”; RIGHT SIDE, “T1D” PATIENTS. BRIGHTER COLORS INDICATE HIGH OVERALL ABUNDANCES OF PHYLA AS INDICATED IN THE MATRIX ON THE RIGHT.2

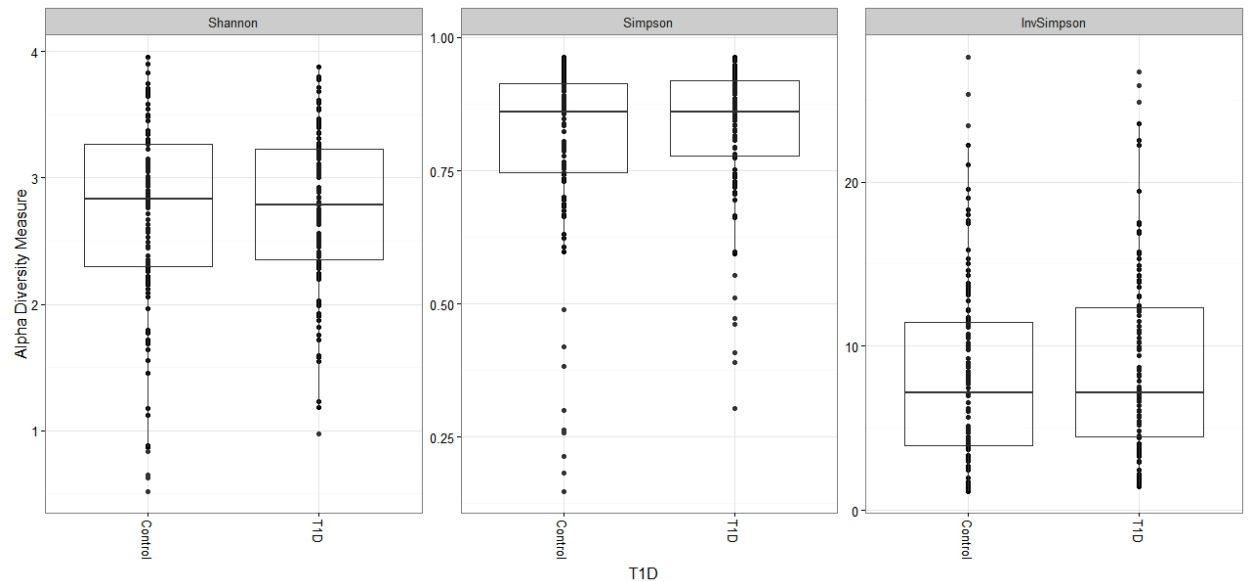


Figure 1: Alpha diversity of microbiota in T1D patients compared to healthy sibling controls using the Shannon index, the Simpson index, and the InvSimpson alpha diversity measures. Wilcoxon rank sum tests returned p-values of 0.61, 0.35 and 0.35, respectively, suggesting the absence of statistically significant differences in alpha diversity. The 16S rDNA data for the survey of gut microbiota were obtained from analyses of 205 stool samples consisting of 99 T1D patients and 106 healthy siblings as the control group.

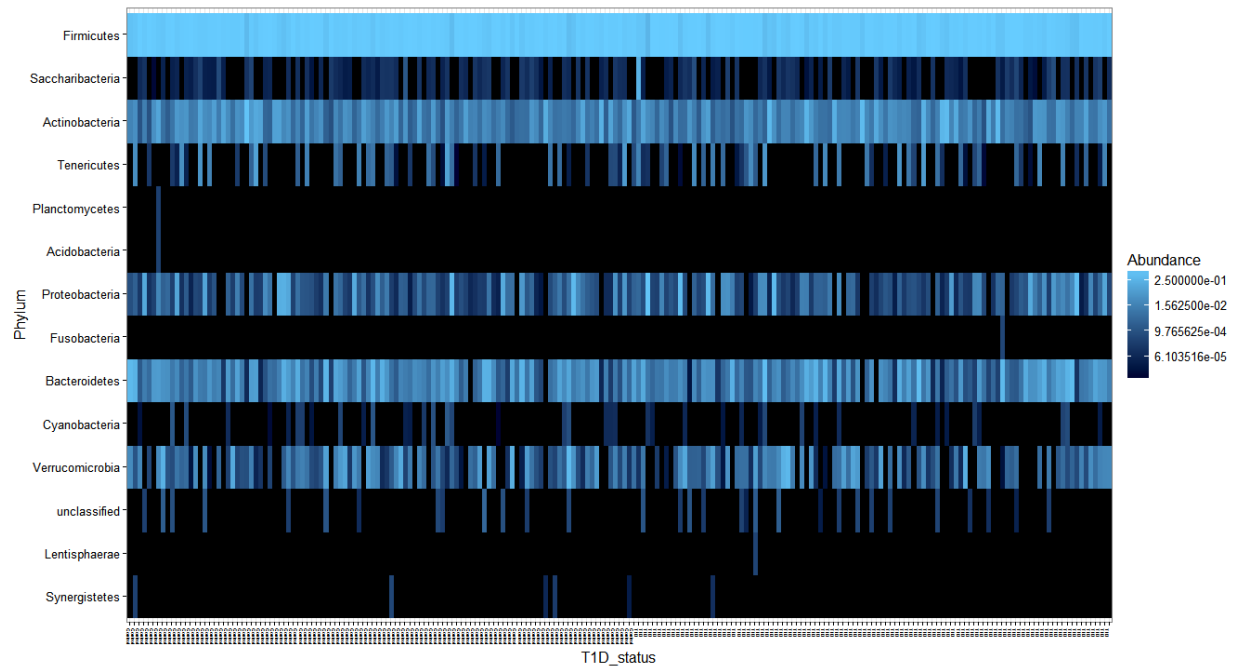


Figure 2: Heatmap based on NMDS ordination using Bray-Curtis dissimilarity representing the distribution of different phyla in healthy sibling vs T1D samples. At phylum level, there is no dissimilarity between the T1D and healthy sibling cohorts. The T1D status is indicated at the bottom of the graphic: left side, healthy sibling “Controls”; right side, “T1D” patients. Brighter colors indicate high overall abundances of phyla as indicated in the matrix on the right.

Supplementary Data, Dataset S2: Urinary Proteome Analyses Including Data Imputation and Differential Abundances Comparing T1D Patients vs. Healthy Siblings.

FIGURE 1: HISTOGRAM GENERATED USING LOG TRANSFORMED EXPRESSION VALUES OF ALL PROTEINS BEFORE AND AFTER APPLYING THE LSIMPUTE IMPUTATION ALGORITHM.	1
FIGURE 2: EXPRESSION LEVELS OF PROTEINS INCREASED AND DECREASED IN ABUNDANCE IN T1D PATIENTS COMPARED TO HEALTHY SIBLINGS (TOP AND BOTTOM, RESPECTIVELY).	6
FIGURE 3: PROTEINS ARRANGED BY MEAN DECREASE ACCURACY AND MEAN DECREASE GINI OBTAINED USING THE IMPORTANCE FUNCTION IN RANDOM FOREST (METHODS ARE DESCRIBED IN THE MATERIALS AND METHODS SECTION).....	17
FIGURE 4: PROTEIN-PROTEIN INTERACTION NETWORK COMPRISED OF ABUNDANCE-INCREASED AND ABUNDANCE-DECREASED PROTEINS INCLUDING THOSE WITH FOLD CHANGES OF GREATER THAN +1.3/-1.3. PROTEINS ARE ARRANGED IN SUBCELLULAR LAYOUT.	18
TABLE 1: FOLD CHANGE VALUE ALONG WITH ADJUSTED P-VALUES OBTAINED USING THE LIMMA PACKAGE FOR IDENTIFICATION OF DIFFERENTIALLY EXPRESSED PROTEINS IN T1D PATIENT VS. HEALTHY SIBLING COHORTS.	2
TABLE 2: A 3-BIOMARKER PANEL WITH ROC VALUES GREATER THAN 0.80. USING FEATURE SELECTION, WE SELECTED 44 PROTEINS AND CHECKED THE ROC VALUES OF ALL POSSIBLE COMBINATION OF 3-BIOMARKER.	4
TABLE 3: FOLD CHANGE VALUE ALONG WITH ADJUSTED P-VALUES OBTAINED USING THE LIMMA PACKAGE FOR IDENTIFICATION OF THE DIFFERENTIALLY EXPRESSED PROTEINS IN THE T1D PATIENTS WITH MODERATELY AND HIGHLY INCREASED LEVELS OF HbA1c AND THEIR HEALTHY SIBLING.	6
TABLE 4: UPREGULATED GO TERMS BASED ON PROTEINS INCREASED IN ABUNDANCE IN THE URINARY PROTEOME (T1D VS. HEALTHY SIBLINGS).....	9
TABLE 5: ENRICHED KEGG PATHWAYS BASED ON PROTEINS INCREASED IN ABUNDANCE IN THE URINARY PROTEOME (T1D VS. HEALTHY SIBLINGS).....	11
TABLE 6: DEPLETED GO TERMS BASED ON PROTEINS INCREASED IN ABUNDANCE IN THE URINARY PROTEOME (T1D VS. HEALTHY SIBLINGS)	12
TABLE 7: DEPLETED KEGG PATHWAYS BASED ON PROTEINS INCREASED IN ABUNDANCE IN THE URINARY PROTEOME (T1D VS. HEALTHY SIBLINGS)	15

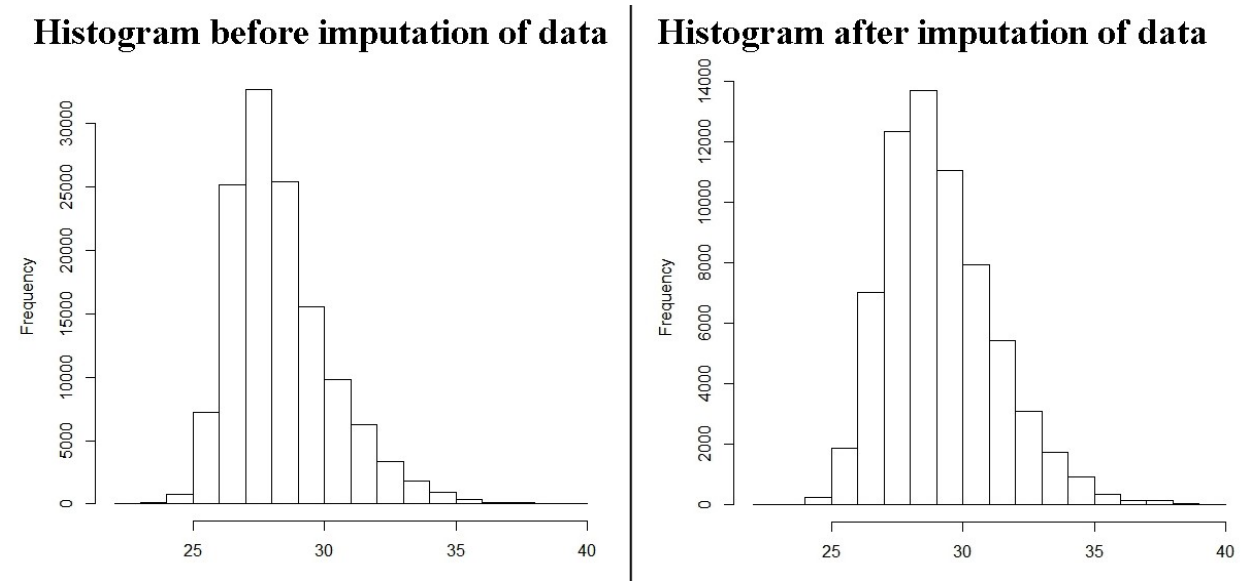


Figure 1: Histogram generated using log transformed expression values of all proteins before and after applying the LSimpute imputation algorithm.

Missing values were imputed using the LSimpute algorithm with the LSimpute_adaptive option as described by Mordes, J.P., et al., Rat Models of Type 1 Diabetes: Genetics, Environment, and Autoimmunity. ILAR Journal, 2004. 45(3): p. 278-291.

Table 1: Fold change value along with adjusted p-values obtained using the Limma package for identification of differentially expressed proteins in T1D patient vs. healthy sibling cohorts.

Protein Name	adjPVal	Fold change	ROC	Protein Name	adjPVal	Fold change	ROC
LRG1	0	2.84	0.7065	COL12A1	0	-1.47	0.4410
CD14	0	1.91	0.6925	UMOD	0.01	-1.45	0.5463
AZGP1	0	1.8	0.6186	SDC4	0	-1.39	0.4804
KV305	0	1.75	0.5687	FGFR2	0	-1.37	0.6030
NAGA	0	1.75	0.7131	RNASE2	0.01	-1.37	0.5443
CTSD	0	1.71	0.6320	CD44	0.03	-1.37	0.4863
GM2A	0	1.7	0.5330	TNC	0	-1.37	0.6027
GNS	0	1.62	0.6157	BCAN	0	-1.36	0.5322
CTSC	0	1.61	0.6342	INAFM2	0	-1.36	0.5734
A1BG	0	1.58	0.6314	GPRC5B	0	-1.35	0.6098
IGLL5	0	1.57	0.4396	CD320	0.01	-1.35	0.4008
IGHM	0	1.57	0.6036	FN1	0.01	-1.34	0.4798
CP	0	1.56	0.5500	AMY2A	0	-1.33	0.6145
CPE	0	1.52	0.6340	PTPRN	0.01	-1.33	0.5733
CTSB	0	1.51	0.5960	MUC1	0	-1.33	0.6255
IGLC2	0	1.51	0.5805	CD300A	0	-1.33	0.5384
CPQ	0	1.5	0.5251	ICOSLG	0.03	-1.32	0.4928
IGHG2	0	1.49	0.6284	SPP1	0.01	-1.31	0.5611
SERPINA6	0	1.48	0.6338	NGFR	0.02	-1.31	0.4834
LUM	0	1.44	0.5384	ACAN	0.04	-1.3	0.5557
ENPEP	0	1.42	0.6063	FZD4	0	-1.28	0.5285
PI16	0	1.42	0.5207	COMP	0.01	-1.28	0.5304
SERPINA7	0	1.4	0.4980	COL5A2	0.01	-1.28	0.4600
SH3BGR13	0.02	1.39	0.5599	DLST	0.01	-1.28	0.5463
ENDOD1	0	1.39	0.6145	RNASE1	0.03	-1.27	0.6604
ANTXR1	0	1.39	0.6716	AFM	0.01	-1.27	0.6295
DPP7	0	1.38	0.6692	CDH2	0	-1.26	0.5179
CDH1	0.02	1.36	0.5702	DLK1	0.03	-1.26	0.5913
AMBP	0	1.36	0.5001	KIAA0319L	0	-1.25	0.5252
ASAH1	0	1.36	0.6116	NOTCH3	0.01	-1.25	0.6437
ELANE	0.03	1.35	0.4914	PTPRJ	0.01	-1.25	0.5703
CTSH	0	1.35	0.5706	ATP6AP1	0	-1.25	0.5764
NAGLU	0.02	1.35	0.5609	COL14A1	0.01	-1.24	0.6219
AGRN	0	1.33	0.6751	MYLK	0	-1.24	0.6390
KV204	0	1.33	0.5010	VCAN	0.01	-1.24	0.5886
HEXB	0	1.31	0.6893	GOLM1	0.02	-1.23	0.6495
LTF	0.04	1.3	0.5283	CHGB	0	-1.23	0.5721
CTSZ	0	1.3	0.5968	PECAM1	0.04	-1.22	0.5266

PGLYRP2	0.01	1.29	0.5516	CPM	0.03	-1.22	0.5133
GALNS	0	1.27	0.5505	FGFR1	0.01	-1.21	0.5705
TMEM106B	0	1.27	0.5894	ITGB1	0	-1.21	0.5944
VCAM1	0	1.26	0.5609	APP	0.01	-1.21	0.5948
ISLR	0	1.26	0.6187	GNB1	0.01	-1.21	0.6353
NHLRC3	0	1.26	0.6062	CALB1	0.01	-1.21	0.5335
CLMP	0.03	1.24	0.5176	MUC20	0	-1.2	0.5742
C1RL	0.03	1.24	0.5332	CSF1	0.04	-1.2	0.5335
CETP	0	1.24	0.5513	CREB3L3	0	-1.2	0.5644
CTSA	0.02	1.24	0.5207	SDCBP	0.04	-1.2	0.5125
CDH11	0.04	1.23	0.5141	GPRC5A	0	-1.2	0.5423
FUCA1	0	1.22	0.6675	IGFLR1	0.04	-1.19	0.5464
HEXA	0.01	1.22	0.4707	VTN	0.03	-1.19	0.5382
SGSH	0.01	1.21	0.4261	PVRL3	0	-1.18	0.6167
MPO	0.04	1.21	0.5030	ROR2	0.03	-1.18	0.5408
LDHA	0.01	1.21	0.5538	FABP3	0.01	-1.18	0.4933
PLBD2	0	1.21	0.6035	SMO	0	-1.17	0.5612
NEU1	0.01	1.2	0.5274	DCHS1	0	-1.17	0.5684
DDAH2	0	1.2	0.6674	CLSTN1	0.05	-1.17	0.5600
GSTP1	0.01	1.2	0.5640	CD99L2	0.01	-1.17	0.6124
ACE2	0	1.2	0.4663	ITFG1	0	-1.17	0.5766
BTB	0.01	1.2	0.5379	PDCD1	0.02	-1.17	0.5613
KV105	0.03	1.19	0.4722	LRRC19	0	-1.15	0.5884
ALDOA	0.01	1.19	0.5329	IL2RB	0	-1.13	0.4940
PLD3	0	1.19	0.5202	BROX	0.02	-1.13	0.5002
RNASET2	0.01	1.18	0.5997	GPR56	0.03	-1.13	0.5361
NAPSA	0.03	1.18	0.5480	SEZ6L2	0.01	-1.13	0.5554
SIAE	0.02	1.18	0.5351	LAMC1	0	-1.12	0.5411
LV301	0.02	1.16	0.5854	PROM2	0.02	-1.11	0.5631
QPRT	0.01	1.15	0.5128	VPS4B	0.01	-1.11	0.5055
APOM	0	1.15	0.5738	PTK7	0.03	-1.1	0.5678
NRXN3	0.05	1.15	0.6076	SDF4	0.02	-1.1	0.6077
PFN1	0.02	1.14	0.4691	CANT1	0.01	-1.1	0.5458
CLN5	0.04	1.12	0.5766				
DNASE2	0.01	1.1	0.5012				

Proteins are listed with short names as denoted in the UniProt database <http://www.uniprot.org/>; adj.P.Val: adjusted p-value using multiple testing corrections (Benjamini Hochberg test); ROC: receiver operating characteristic curve analysis for binary classifications. The moderated t-statistic (t) is used for data interpretation, it an ordinary t-statistic except that the standard errors have been moderated across genes, effectively borrowing information from the ensemble of genes to aid with inference about each individual gene.

Table 2: A 3-biomarker panel with ROC values greater than 0.80. Using feature selection, we selected 44 proteins and checked the ROC values of all possible combination of 3-biomarker.

3-Biomarker			ROC	3-Biomarker			ROC
LRG1	CPQ	MYLK	0.84	PLBD2	NAGA	KV305	0.81
DDAH2	NAGA	SDF4	0.83	CTSC	ANTXR1	SDF4	0.81
LRG1	NAGA	MYLK	0.83	CTSC	PLBD2	GPRC5B	0.81
CTSB	NAGA	KV305	0.83	CTSD	PLBD2	SDF4	0.81
AGRN	NAGA	KV305	0.83	NAGA	KV305	SDF4	0.81
AGRN	HEXB	DDAH2	0.83	CPE	MUC1	SDF4	0.81
LRG1	CPQ	SDF4	0.82	LRG1	CALB1	MYLK	0.81
HEXB	NAGA	KV305	0.82	AGRN	CTSD	LRG1	0.81
AGRN	CTSD	ANTXR1	0.82	LRG1	CALB1	NAGA	0.80
ANTXR1	SDF4	GPRC5B	0.82	HEXB	NAGA	SDF4	0.80
CTSB	NAGA	MUC1	0.82	NAGA	KV305	MYLK	0.80
LRG1	CPQ	MUC1	0.82	LRG1	CPQ	CALB1	0.80
LRG1	CPQ	GPRC5B	0.82	CPE	LRG1	MUC1	0.80
LRG1	CPQ	ANTXR1	0.82	CPE	CPQ	MUC1	0.80
LRG1	PLBD2	CPQ	0.82	AGRN	DDAH2	CPQ	0.80
LRG1	CPQ	NHLRC3	0.82	AGRN	NAGA	GPRC5B	0.80
PLBD2	FUCA1	KV305	0.82	CTSC	APP	NOTCH3	0.80
GNS	ANTXR1	GPRC5B	0.82	PGLYRP2	LRG1	NAGA	0.80
DDAH2	APP	NAGA	0.82	AZGP1	LRG1	CTSC	0.80
UMOD	ANTXR1	GPRC5B	0.82	AGRN	PLBD2	PVRL3	0.80
AGRN	ANTXR1	MUC20	0.82	HEXA	LRG1	MYLK	0.80
CTSD	DDAH2	APP	0.81	AGRN	FUCA1	MYLK	0.80
APP	NAGA	KV305	0.81	TNC	GNS	GPRC5B	0.80
LRG1	CPQ	PVRL3	0.81	HEXB	ALDOA	DDAH2	0.80
HEXB	NAGA	GNB1	0.81	CTSD	ANTXR1	NOTCH3	0.80
TNC	NAGA	SDF4	0.81	GNS	NHLRC3	GPRC5B	0.80
HEXB	LRG1	MYLK	0.81	NAGA	GPRC5B	FGFR2	0.80
LRG1	NAGA	GPRC5B	0.81	LRG1	DDAH2	CPQ	0.80
CTSB	NAGA	SDF4	0.81	LRG1	PLBD2	GPRC5B	0.80
AGRN	LRG1	CPQ	0.81	APP	NAGA	GPRC5B	0.80
HEXB	DDAH2	NAGA	0.81	LRG1	GNS	MYLK	0.80
PGLYRP2	APP	NAGA	0.81	TNC	HEXB	LRG1	0.80
LRG1	NAGA	SDF4	0.81	LRG1	CPQ	APP	0.80
AGRN	CTSC	PLBD2	0.81	HEXA	LRG1	CPQ	0.80
AGRN	DDAH2	NAGA	0.81	CPE	FUCA1	SDF4	0.80
AZGP1	LRG1	MYLK	0.81	AZGP1	CTSC	NHLRC3	0.80
AGRN	CTSD	PLBD2	0.81	UMOD	HEXB	LRG1	0.80
LRG1	CTSB	MYLK	0.81	IGHM	NAGA	SDF4	0.80
ASA1	LRG1	CPQ	0.81	CTSC	GPRC5B	NOTCH3	0.80

AGRN	CTSC	MUC20	0.81	TNC	PGLYRP2	GNS	0.80
CPE	LRG1	SDF4	0.81	CTSB	NAGA	GNB1	0.80
LRG1	CPQ	GNB1	0.81	CTSD	LRG1	SDF4	0.80
HEXB	NAGA	MYLK	0.81	ANTXR1	CTSZ	GPRC5B	0.80
IGHM	DDAH2	NAGA	0.81	CTSC	PLBD2	KV305	0.80
CTSD	ANTXR1	GPRC5B	0.81	CTSC	APP	CALB1	0.80
TNC	ANTXR1	SDF4	0.81	FUCA1	NAGA	SDF4	0.80
IGHG2	LRG1	CPQ	0.81	CTSC	SDF4	GPRC5B	0.80
LRG1	APP	MYLK	0.81	DDAH2	NAGA	PVRL3	0.80
HEXB	APP	NAGA	0.81	CPE	NAGA	SDF4	0.80
CPE	PLBD2	SDF4	0.81	NAGA	NHLRC3	GPRC5B	0.80
AGRN	FUCA1	ANTXR1	0.81	AGRN	CTSC	NAGA	0.80
AGRN	NAGA	MYLK	0.81	CTSC	PLBD2	SDF4	0.80
HEXB	CTSD	ANTXR1	0.81	TNC	LRG1	CPQ	0.80
HEXA	NAGA	KV305	0.81	GNS	CTSC	GPRC5B	0.80
LRG1	CPQ	ITFG1	0.81	AZGP1	CPE	SDC4	0.80
DDAH2	NAGA	MUC20	0.81	IGHG2	DDAH2	NAGA	0.80
AGRN	ANTXR1	GPRC5B	0.81	PLBD2	FUCA1	PVRL3	0.80
DDAH2	NAGA	NHLRC3	0.81	HEXA	APP	ANTXR1	0.80
CTSD	LRG1	APP	0.81	CTSC	NAGA	KV305	0.80
AGRN	HEXB	NAGA	0.81	CPE	PGLYRP2	LRG1	0.80
HEXB	LRG1	NAGA	0.81	CPE	LRG1	GPRC5B	0.80
AZGP1	CTSC	GPRC5B	0.81	GNS	PLBD2	KV305	0.80
CPE	LRG1	CPQ	0.81	CTSD	PLBD2	APP	0.80
AGRN	NAGA	SDF4	0.81	CTSC	NAGA	SDF4	0.80
NAGA	GNB1	MYLK	0.81	AMBP	ANTXR1	GPRC5B	0.80
NAGA	MYLK	PVRL3	0.81	TNC	GNS	ANTXR1	0.80
LRG1	CTSB	NAGA	0.81	AZGP1	CTSC	CALB1	0.80
AGRN	CTSC	NOTCH3	0.81	PGLYRP2	NAGA	SDF4	0.80
IGHM	DDAH2	MUC20	0.81	PGLYRP2	CTSB	NAGA	0.80
AMY2A	CTSD	DDAH2	0.81	LRG1	GNS	GPRC5B	0.80
AGRN	CTSB	NAGA	0.81	LRG1	KV305	MYLK	0.80
PGLYRP2	LRG1	GNS	0.81	PLBD2	FUCA1	SDF4	0.80
LRG1	CTSC	SDF4	0.81	LRG1	CTSC	GPRC5B	0.80
AGRN	CTSD	DDAH2	0.81	AGRN	ASAH1	ANTXR1	0.80
PGLYRP2	LRG1	CPQ	0.81	AMBP	CPE	CTSC	0.80
CPE	SDF4	GPRC5B	0.81	FUCA1	ANTXR1	SDF4	0.80
CPE	LRG1	APP	0.81	DDAH2	CTSB	NAGA	0.80
LRG1	CTSC	CALB1	0.81	CTSB	GPRC5B	NOTCH3	0.80
NAGA	MYLK	FGFR2	0.81	HEXB	NAGA	GPRC5B	0.80
FUCA1	ANTXR1	MYLK	0.81	AZGP1	CPE	GPRC5B	0.80

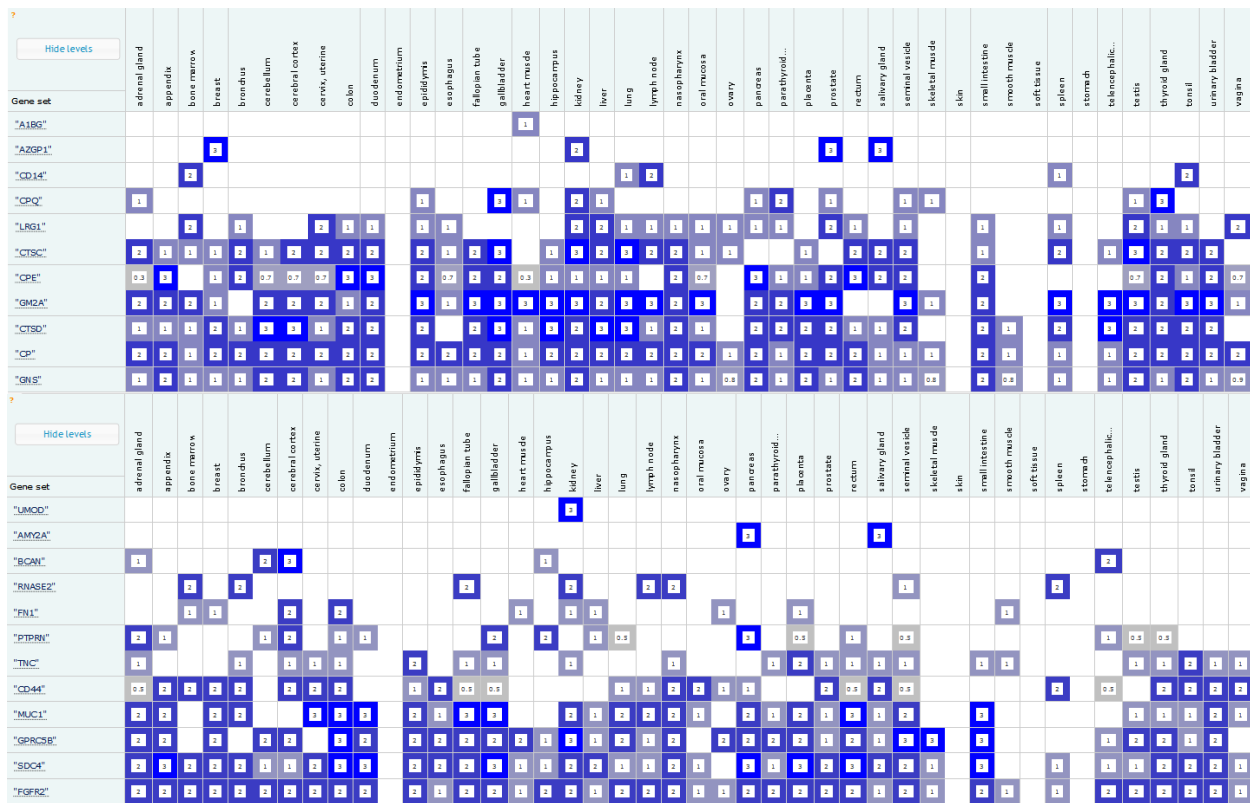


Figure 2: Expression levels of proteins increased and decreased in abundance in T1D patients compared to healthy siblings (top and bottom, respectively).

The four qualitative expression values: 'Not detected', 'Low', 'Medium' and 'High' were converted to values 0 to 3 respectively. Greater color saturation expression means higher expression or higher values (0 - 3). The data is obtained from E-PROT-3 - Human immunochemistry data on 83 different normal cell types from 44 tissue types from the Human Protein Atlas project (<http://www.ebi.ac.uk/arrayexpress/experiments/E-PROT-3/>).

Table 3: Fold change value along with adjusted p-values obtained using the Limma package for identification of the differentially expressed proteins in the T1D patients with moderately and highly increased levels of HbA1c and their healthy sibling.

Gene	Medium Level HbA1C		High Level HbA1C	
	adj.P.Val	Fold change	adj.P.Val	Fold change
LRG1	0.00	2.51	0.00	3.49
CTSD	0.01	1.49	0.00	2.39
CP			0.00	2.21
A1BG			0.00	2.16
IGHM	0.04	1.53	0.00	2.03
AZGP1	0.01	1.67	0.03	2.02
CD14	0.01	1.74	0.01	2.01
NAGA	0.00	1.66	0.00	2.00

IGHG2	0.04	1.49	0.02	1.94
IGLC2	0.02	1.50	0.01	1.90
SERPINA6	0.04	1.41	0.00	1.88
GNS	0.01	1.48	0.01	1.82
LUM			0.01	1.72
ACPP			0.04	1.67
CTSC	0.00	1.53	0.00	1.67
CTSB	0.04	1.41	0.05	1.65
C4A			0.00	1.60
CPE	0.00	1.48	0.00	1.57
SERPINA7	0.01	1.47	0.03	1.55
FAM3C			0.00	1.54
ACE2			0.00	1.54
ISLR			0.00	1.53
LDHA			0.00	1.53
PGLS			0.04	1.51
CTSZ			0.00	1.51
ASAH1			0.01	1.49
DPP7	0.00	1.39	0.01	1.48
BTD			0.00	1.47
ENDOD1	0.02	1.27	0.01	1.46
FUCA1	0.03	1.19	0.00	1.37
NRXN3			0.02	1.37
DPEP1			0.04	1.37
SIAE			0.05	1.37
PKM			0.04	1.27
APOM			0.05	1.25
VPS4B			0.05	-1.21
ITGB1	0.02	-1.18	0.05	-1.29
SPINT1			0.04	-1.35
KIAA0319L	0.03	-1.22	0.01	-1.42
COL14A1			0.05	-1.42
APP			0.02	-1.44
CD300LG			0.04	-1.45
PECAM1			0.05	-1.47
IGFLR1			0.03	-1.47
CPZ			0.05	-1.49
COL5A2			0.05	-1.55
DLST			0.04	-1.55
COMP			0.02	-1.57
BAMBI			0.04	-1.62
BCAN			0.02	-1.72
TNC			0.02	-1.72

CD320	0.05	-1.41	0.01	-1.77
RNASE2			0.02	-1.87
FN1			0.00	-2.00
C6			0.01	-2.00
COL12A1			0.00	-2.29
AGRN	0.04	1.36		
AMY2A	0.04	-1.27		
ANTXR1	0.00	1.37		
ANXA5	0.04	-1.25		
ATP6AP1	0.01	-1.29		
CALB1	0.03	-1.27		
CD300A	0.02	-1.37		
CDH2	0.02	-1.32		
CETP	0.01	1.22		
CHGB	0.02	-1.25		
CPM	0.03	-1.31		
CPQ	0.02	1.43		
CREB3L3	0.01	-1.24		
CSF1	0.02	-1.33		
CTSH	0.01	1.45		
ENPEP	0.00	1.48		
FBLN1	0.03	1.29		
FGFR1	0.01	-1.30		
FGFR2	0.01	-1.36		
FZD4	0.02	-1.35		
GM2A	0.01	1.92		
GPRC5A	0.02	-1.24		
GPRC5B	0.00	-1.44		
HEXB	0.04	1.25		
ICOSLG	0.05	-1.46		
INAFM2	0.01	-1.43		
ITFG1	0.02	-1.17		
KV204	0.02	1.31		
KV305	0.00	1.89		
LAMC1	0.04	-1.13		
LRRC19	0.01	-1.20		
MUC1	0.01	-1.42		
MYLK	0.01	-1.30		
NOTCH3	0.04	-1.31		
PI16	0.02	1.50		
PLBD2	0.04	1.18		
PTGDS	0.04	1.66		
PTPRJ	0.02	-1.30		

PTPRN	0.04	-1.35		
SDC4	0.00	-1.70		
SERPINB3	0.03	1.57		
SMO	0.01	-1.23		
TMEM106B	0.01	1.24		
VCAN	0.01	-1.39		

We used the HbA1c ranges of $n \leq 6.5$ (normal), $6.5 > n < 9$ (medium) and $n \geq 9$ (high) to define the groups for comparative analyses. No entry indicates that a protein was not differentially abundant in a given comparison. Proteins are listed with short names as denoted in the UniProt database <http://www.uniprot.org/>; adj.P.Val: adjusted p-value using multiple testing corrections (Benjamini Hochberg test). The moderated t-statistic (t) is used for data interpretation, it an ordinary t-statistic except that the standard errors have been moderated across genes, effectively borrowing information from the ensemble of genes to aid with inference about each individual gene.

Table 4: Upregulated GO Terms Based on Proteins Increased in Abundance in the Urinary Proteome (T1D vs. Healthy Siblings)

Biological Process					
Term ID	Description	frequency	log ₁₀ p-value	uniqueness	dispensability
GO:0007040	lysosome organization	0.00064	-1.4763	0.93	0
GO:0008152	metabolic process	0.54733	-3.1636	0.99	0
GO:0009057	macromolecule catabolic process	0.02264	-7.8729	0.65	0
GO:0034284	response to monosaccharide	0.0041	-2.0274	0.9	0
GO:0044117	growth of symbiont in host	0.00084	-2.3104	0.87	0
GO:0044256	protein digestion	0.00005	-1.9115	0.91	0
GO:0042445	hormone metabolic process	0.00448	-1.8743	0.83	0.06
GO:0043603	cellular amide metabolic process	0.0048	-3.7779	0.85	0.06
GO:0002221	pattern recognition receptor signaling pathway	0.00406	-1.9369	0.84	0.07
GO:0009056	catabolic process	0.07851	-8.0716	0.89	0.09
GO:0006790	sulfur compound metabolic process	0.00742	-1.3088	0.88	0.1
GO:0006643	membrane lipid metabolic process	0.00449	-3.5422	0.72	0.11
GO:0005975	carbohydrate metabolic process	0.03046	-3.5683	0.86	0.13
GO:0006807	nitrogen compound metabolic process	0.26566	-5.5638	0.87	0.14
GO:0018196	peptidyl-asparagine modification	0.00114	-2.1993	0.83	0.16
GO:1901135	carbohydrate derivative metabolic process	0.10573	-3.1802	0.84	0.17
GO:0032682	negative regulation of chemokine production	0.00013	-1.4669	0.88	0.17
GO:0006022	aminoglycan metabolic process	0.00332	-2.4431	0.75	0.18
GO:0044268	multicellular organismal protein metabolic process	0.00011	-1.9115	0.79	0.19

GO:0060177	regulation of angiotensin metabolic process	0.00018	-1.6835	0.84	0.19
GO:0090305	nucleic acid phosphodiester bond hydrolysis	0.00647	-1.7528	0.81	0.2
GO:0044710	single-organism metabolic process	0.26477	-3.0725	0.86	0.21
GO:0043436	oxoacid metabolic process	0.03077	-1.4558	0.76	0.22
GO:0034367	macromolecular complex remodeling	0.0004	-1.3078	0.95	0.24
GO:0019882	antigen processing and presentation	0.24721	-1.3078	0.97	0.25
GO:0071704	organic substance metabolic process	0.42826	-3.1691	0.86	0.25
GO:1901564	organonitrogen compound metabolic process	0.11844	-5.9788	0.79	0.27
GO:0006629	lipid metabolic process	0.03159	-1.3706	0.79	0.28
GO:0016137	glycoside metabolic process	0.0003	-1.4669	0.8	0.29
GO:0006488	dolichol-linked oligosaccharide biosynthetic process	0.00039	-1.4669	0.81	0.3
GO:0044238	primary metabolic process	0.41881	-2.5427	0.86	0.32
GO:0044237	cellular metabolic process	0.42121	-1.7478	0.85	0.32
GO:0006518	peptide metabolic process	0.0035	-1.9929	0.78	0.33
GO:0043129	surfactant homeostasis	0.00023	-1.4669	0.88	0.35
GO:0044266	multicellular organismal macromolecule catabolic process	0.00005	-1.9115	0.76	0.35
GO:0044281	small molecule metabolic process	0.13539	-2.3605	0.78	0.36
GO:0001991	regulation of systemic arterial blood pressure by circulatory renin-angiotensin	0.00032	-1.6835	0.83	0.36
GO:0071827	plasma lipoprotein particle organization	0.00054	-1.3078	0.87	0.36
GO:0016139	glycoside catabolic process	0.00008	-1.9115	0.71	0.37
GO:0097067	cellular response to thyroid hormone stimulus	0.00016	-1.4669	0.9	0.37
GO:0071825	protein-lipid complex subunit organization	0.00056	-1.3078	0.95	0.37
GO:0009313	oligosaccharide catabolic process	0.00011	-2.3104	0.69	0.38
GO:0009100	glycoprotein metabolic process	0.00923	-1.8275	0.74	0.39
Cellular Component					
Term ID	Description	frequency	log ₁₀ p-value	uniqueness	dispensability
GO:0005576	extracellular region	0.08277	-1.8362	0.94	0
GO:0005764	lysosome	0.01077	-9.8508	0.52	0
GO:0031974	membrane-enclosed lumen	0.07246	-1.9387	0.94	0
GO:0043226	organelle	0.44898	-1.7881	0.96	0
GO:0005622	intracellular	0.52068	-1.9023	0.95	0.01
GO:0070062	extracellular vesicular exosome	0.03528	-4.3215	0.56	0.14
GO:0031982	vesicle	0.0566	-3.3752	0.76	0.14

GO:0031906	late endosome lumen	0.00041	-1.4669	0.59	0.15
GO:0005773	vacuole	0.01212	-9.71	0.7	0.21
GO:0043231	intracellular membrane-bounded organelle	0.3802	-3.1348	0.61	0.26
GO:0044444	cytoplasmic part	0.27658	-2.5435	0.73	0.32
GO:0044422	organelle part	0.21569	-1.9339	0.71	0.35
GO:0005737	cytoplasm	0.35493	-1.9719	0.78	0.36
GO:0044424	intracellular part	0.49419	-1.8996	0.79	0.37
Molecular Function					
Term ID	Description	frequency	log ₁₀ p-value	uniqueness	dispensability
GO:0003824	catalytic activity	0.36343	-8.8539	0.96	0
GO:0005246	calcium channel regulator activity	0.00084	-1.9115	0.93	0
GO:0015929	hexosaminidase activity	0.00063	-4.0851	0.49	0
GO:0016019	peptidoglycan receptor activity	0.00006	-1.4669	0.93	0
GO:0016505	peptidase activator activity involved in apoptotic process	0.0003	-1.9115	0.89	0
GO:0016757	transferase activity, transferring glycosyl groups	0.01761	-1.9486	0.71	0.11
GO:0016787	hydrolase activity	0.11239	-9.9172	0.68	0.21
GO:0070011	peptidase activity, acting on L-amino acid peptides	0.03135	-3.4269	0.3	0.36
GO:0008375	acetylglucosaminyltransferase activity	0.00156	-1.4669	0.75	0.37

*Frequency = frequency of the GO term in the underlying reference database – the EBI GOA database;

*According to Revigo article “Uniqueness and Dispensability values are anticorrelated, though not perfectly, since ‘uniqueness’ measures whether the term is an outlier when compared semantically to the whole list (without regard for the p-values), while the ‘dispensability’ compares a term to other semantically close terms and is assigned based both on the semantic distance and the supplied p-values.”

Table 5: Enriched KEGG Pathways Based on Proteins Increased in Abundance in the Urinary Proteome (T1D vs. Healthy Siblings)

KEGG number	Pathway	N	Up	Down	P.Up	P.Down
hsa04142	Lysosome	38	20	1	1.64E-22	0.734164
hsa01100	Metabolic pathways	51	12	3	1.74E-08	0.244853
hsa00531	Glycosaminoglycan degradation	9	6	0	6.68E-08	1
hsa04210	Apoptosis	8	5	0	1.55E-06	1
hsa00511	Other glycan degradation	8	4	0	6.38E-05	1
hsa00603	Glycosphingolipid biosynthesis - globo series	4	3	0	0.000129	1

hsa00520	Amino sugar and nucleotide sugar metabolism	2	2	0	0.001054	1
hsa04614	Renin-angiotensin system	8	3	0	0.001645	1
hsa00604	Glycosphingolipid biosynthesis - ganglio series	3	2	0	0.003098	1
hsa05202	Transcriptional misregulation in cancer	12	3	2	0.005894	0.059136
hsa04071	Sphingolipid signaling pathway	4	2	0	0.006066	1
hsa00600	Sphingolipid metabolism	5	2	0	0.009901	1
hsa04064	NF-kappa B signaling pathway	5	2	0	0.009901	1
hsa05130	Pathogenic Escherichia coli infection	6	2	1	0.014544	0.186407
hsa04066	HIF-1 signaling pathway	7	2	0	0.019941	1
hsa05132	Salmonella infection	7	2	0	0.019941	1
hsa00565	Ether lipid metabolism	1	1	0	0.032884	1
hsa00780	Biotin metabolism	1	1	0	0.032884	1
hsa05216	Thyroid cancer	1	1	0	0.032884	1
hsa00010	Glycolysis / Gluconeogenesis	11	2	0	0.048063	1

*N = Total number of proteins in the particular pathway; Up = Number of protein upregulated in a particular pathway; P.Up = p.value of the up regulated proteins; Down = Number of protein downregulated in a particular pathway; P.down = p.value of the down regulated proteins. Wilcoxon rank-sum test implemented in the Limma package is used for performing the statistical test as described in Young, M. D., Wakefield, M. J., Smyth, G. K., Oshlack, A. (2010). Gene ontology analysis for RNA-seq: accounting for selection bias. Genome Biology 11, R14.

Table 6: Depleted GO Terms Based on Proteins Increased in Abundance in the Urinary Proteome (T1D vs. Healthy Siblings)

Biological Process					
Term ID	Description	frequency	log ₁₀ p-value	uniqueness	dispensability
GO:0007155	cell adhesion	0.02821	-2.2984	0.97	0
GO:0022610	biological adhesion	0.02826	-2.1685	0.99	0
GO:0023052	signaling	0.17329	-1.9746	1	0
GO:0033280	response to vitamin D	0.00068	-2.8173	0.9	0
GO:0040007	growth	0.0216	-2.6879	0.99	0
GO:0040011	locomotion	0.03285	-2.3881	0.99	0
GO:0045165	cell fate commitment	0.0062	-4.8827	0.64	0
GO:0051674	localization of cell	0.0257	-1.8847	0.98	0
GO:0001503	ossification	0.00817	-2.6047	0.74	0.02
GO:0031399	regulation of protein modification process	0.02771	-4.6345	0.75	0.05

GO:0060242	contact inhibition	0.00013	-1.8726	0.94	0.06
GO:0007528	neuromuscular junction development	0.00106	-2.2534	0.91	0.07
GO:0006928	cellular component movement	0.0383	-1.9471	0.9	0.1
GO:0007049	cell cycle	0.03703	-1.5569	0.9	0.13
GO:0007154	cell communication	0.17535	-1.7721	0.88	0.17
GO:0006793	phosphorus metabolic process	0.17457	-3.1912	0.91	0.19
GO:0007265	Ras protein signal transduction	0.0156	-4.2941	0.74	0.23
GO:0098727	maintenance of cell number	0.00003	-2.2534	0.8	0.23
GO:0051726	regulation of cell cycle	0.01952	-2.458	0.8	0.23
GO:0051961	negative regulation of nervous system development	0.00021	-2.7455	0.64	0.26
GO:0048873	homeostasis of number of cells within a tissue	0.00068	-2.2534	0.76	0.27
GO:0042636	negative regulation of hair cycle	0.00001	-1.8726	0.77	0.28
GO:0007632	visual behavior	0.00112	-1.8726	0.76	0.28
GO:0030166	proteoglycan biosynthetic process	0.00088	-1.8934	0.92	0.28
GO:0043412	macromolecule modification	0.10189	-2.5813	0.94	0.29
GO:0048522	positive regulation of cellular process	0.08548	-2.4722	0.81	0.29
GO:0021769	orbitofrontal cortex development	0.00008	-1.8726	0.7	0.32
GO:0060322	head development	0.00238	-2.4509	0.7	0.32
GO:0072073	kidney epithelium development	0.00349	-4.8477	0.58	0.33
GO:0060560	developmental growth involved in morphogenesis	0.00399	-4.4067	0.62	0.34
GO:0001553	luteinization	0.0003	-1.8726	0.7	0.35
GO:0030030	cell projection organization	0.02744	-2.1683	0.88	0.35
GO:0060173	limb development	0.005	-2.3441	0.66	0.35
GO:0008347	glial cell migration	0.00034	-2.3441	0.64	0.36
GO:0048736	appendage development	0.005	-2.3441	0.67	0.37
GO:0007044	cell-substrate junction assembly	0.00174	-1.6852	0.91	0.37
GO:0023014	signal transduction by phosphorylation	0.01554	-3.3921	0.73	0.37
GO:0007267	cell-cell signaling	0.02522	-3.0673	0.85	0.37
GO:0007169	transmembrane receptor protein tyrosine kinase signaling pathway	0.01599	-2.5084	0.76	0.37

GO:0007268	synaptic transmission	0.01611	-2.0541	0.85	0.37
GO:0051338	regulation of transferase activity	0.01829	-3.2832	0.85	0.37
GO:0055025	positive regulation of cardiac muscle tissue development	0.00003	-1.8726	0.64	0.38
Cellular Component					
Term ID	Description	frequency	log ₁₀ p-value	uniqueness	dispensability
GO:0005593	FACIT collagen trimer	0.00008	-1.8726	0.94	0
GO:0005614	interstitial matrix	0.00032	-1.4296	0.94	0
GO:0016020	membrane	0.63613	-2.3417	0.99	0
GO:0044441	ciliary part	0.00545	-3.1001	0.61	0
GO:0045202	synapse	0.01727	-3.3902	0.96	0
GO:0060076	excitatory synapse	0.00051	-2.8173	0.84	0
GO:0098589	membrane region	0.0268	-2.1122	0.92	0
GO:0032154	cleavage furrow	0.00037	-1.8726	0.9	0
GO:0032153	cell division site	0.00044	-1.8726	0.96	0
GO:0042995	cell projection	0.04192	-2.3448	0.96	0.01
GO:0031252	cell leading edge	0.00744	-1.6828	0.96	0.01
GO:0012505	endomembrane system	0.07341	-1.7342	0.96	0.01
GO:0071944	cell periphery	0.37689	-1.5483	0.96	0.01
GO:0045121	membrane raft	0.0067	-2.1993	0.83	0.07
GO:0043235	receptor complex	0.00706	-1.3071	0.96	0.08
GO:0005887	integral component of plasma membrane	0.02577	-2.0536	0.87	0.08
GO:0005794	Golgi apparatus	0.02939	-2.0665	0.82	0.1
GO:0031224	intrinsic component of membrane	0.29207	-4.6596	0.9	0.12
GO:0045334	clathrin-coated endocytic vesicle	0.00098	-1.8934	0.88	0.18
GO:0044425	membrane part	0.54114	-3.847	0.92	0.18
GO:0005819	spindle	0.00487	-1.4246	0.84	0.23
GO:0031226	intrinsic component of plasma membrane	0.02681	-1.7594	0.87	0.24
GO:0044459	plasma membrane part	0.31687	-2.1265	0.85	0.26
GO:0044444	cytoplasmic part	0.27658	-1.6493	0.91	0.28
GO:0098588	bounding membrane of organelle	0.03352	-1.9511	0.8	0.28
GO:0016021	integral component of membrane	0.28962	-4.383	0.88	0.36
Molecular Function					
Term ID	Description	frequency	log ₁₀ p-value	uniqueness	dispensability
GO:0004522	ribonuclease activity	0.00005	-1.8726	0.91	0

GO:0004872	receptor activity	0.05395	-1.4333	0.96	0
GO:0005201	extracellular matrix structural constituent	0.00211	-1.4244	0.96	0
GO:0019903	protein phosphatase binding	0.00175	-1.8726	0.82	0
GO:0038023	signaling receptor activity	0.04623	-2.3554	0.81	0
GO:0060089	molecular transducer activity	0.05605	-1.4333	0.96	0
GO:0005540	hyaluronic acid binding	0.00101	-1.6301	0.78	0.02
GO:0044212	transcription regulatory region DNA binding	0.01419	-1.4296	0.62	0.02
GO:0019842	vitamin binding	0.00235	-1.4246	0.77	0.02
GO:0097367	carbohydrate derivative binding	0.10136	-1.5715	0.92	0.03
GO:0045545	syndecan binding	0.00007	-1.8726	0.87	0.17
GO:0045295	gamma-catenin binding	0.00019	-1.4296	0.87	0.19
GO:0030507	spectrin binding	0.00027	-1.8726	0.86	0.19
GO:0017134	fibroblast growth factor binding	0.00045	-1.4296	0.86	0.2
GO:0017147	Wnt-protein binding	0.00065	-1.4246	0.86	0.2
GO:0005518	collagen binding	0.002	-1.6828	0.85	0.22
GO:0019899	enzyme binding	0.02942	-1.3292	0.83	0.28
GO:0016462	pyrophosphatase activity	0.03346	-1.3916	0.87	0.29
GO:0005539	glycosaminoglycan binding	0.00447	-1.3013	0.75	0.33
GO:0001067	regulatory region nucleic acid binding	0.01504	-1.4296	0.72	0.38
GO:0071936	coreceptor activity involved in Wnt signaling pathway	0.00001	-1.4296	0.87	0.38

*Frequency = frequency of the GO term in the underlying reference database – the EBI GOA database;

*According to Revigo article “Uniqueness and Dispensability values are anticorrelated, though not perfectly, since ‘uniqueness’ measures whether the term is an outlier when compared semantically to the whole list (without regard for the p-values), while the ‘dispensability’ compares a term to other semantically close terms and is assigned based both on the semantic distance and the supplied p-values.”

Table 7: Depleted KEGG Pathways Based on Proteins Increased in Abundance in the Urinary Proteome (T1D vs. Healthy Siblings)

KEGG number	Pathway	N	Up	Down	P.Up	P.Down
hsa04151	PI3K-Akt signaling pathway	29	0	14	1	1.13E-14
hsa04512	ECM-receptor interaction	22	1	9	0.523986	8.02E-09
hsa05200	Pathways in cancer	20	2	8	0.138111	7.61E-08
hsa04510	Focal adhesion	25	0	8	1	5.78E-07
hsa05205	Proteoglycans in cancer	26	1	8	0.584721	8.15E-07

hsa04514	Cell adhesion molecules (CAMs)	31	3	8	0.078287	3.64E-06
hsa04014	Ras signaling pathway	11	0	5	1	1.35E-05
hsa04015	Rap1 signaling pathway	14	2	5	0.074755	5.42E-05
hsa04810	Regulation of actin cytoskeleton	16	2	5	0.094621	0.000113
hsa05222	Small cell lung cancer	5	0	3	1	0.00034
hsa04550	Signaling pathways regulating pluripotency of stem cells	6	0	3	1	0.000664
hsa04725	Cholinergic synapse	2	0	2	1	0.00111
hsa04726	Serotonergic synapse	2	0	2	1	0.00111
hsa05215	Prostate cancer	7	1	3	0.20916	0.001134
hsa05206	MicroRNAs in cancer	9	0	3	1	0.002596
hsa04022	cGMP-PKG signaling pathway	3	0	2	1	0.003259
hsa04728	Dopaminergic synapse	3	0	2	1	0.003259
hsa05217	Basal cell carcinoma	3	0	2	1	0.003259
hsa04520	Adherens junction	10	1	3	0.285135	0.003622
hsa04916	Melanogenesis	4	0	2	1	0.006378
hsa04144	Endocytosis	13	0	3	1	0.008044
hsa04060	Cytokine-cytokine receptor interaction	14	0	3	1	0.01
hsa05100	Bacterial invasion of epithelial cells	5	1	2	0.154198	0.010404
hsa05131	Shigellosis	5	1	2	0.154198	0.010404
hsa05161	Hepatitis B	5	0	2	1	0.010404
hsa04668	TNF signaling pathway	6	1	2	0.182129	0.015274
hsa05230	Central carbon metabolism in cancer	6	1	2	0.182129	0.015274
hsa05323	Rheumatoid arthritis	6	0	2	1	0.015274
hsa05412	Arrhythmogenic right ventricular cardiomyopathy (ARVC)	6	0	2	1	0.015274
hsa04145	Phagosome	17	2	3	0.105071	0.017413
hsa05166	HTLV-I infection	7	1	2	0.20916	0.02093
hsa05034	Alcoholism	7	0	2	1	0.02093
hsa05145	Toxoplasmosis	7	0	2	1	0.02093
hsa04974	Protein digestion and absorption	19	1	3	0.472838	0.02368
hsa00240	Pyrimidine metabolism	1	0	1	1	0.033727
hsa00310	Lysine degradation	1	0	1	1	0.033727
hsa04211	Longevity regulating pathway	1	0	1	1	0.033727

hsa04320	Dorso-ventral axis formation	1	0	1	1	0.033727
hsa04330	Notch signaling pathway	1	0	1	1	0.033727
hsa04660	T cell receptor signaling pathway	1	0	1	1	0.033727
hsa04723	Retrograde endocannabinoid signaling	1	0	1	1	0.033727
hsa04724	Glutamatergic synapse	1	0	1	1	0.033727
hsa04727	GABAergic synapse	1	0	1	1	0.033727
hsa04911	Insulin secretion	1	0	1	1	0.033727
hsa04931	Insulin resistance	1	0	1	1	0.033727
hsa05016	Huntington's disease	1	0	1	1	0.033727
hsa05030	Cocaine addiction	1	0	1	1	0.033727
hsa05032	Morphine addiction	1	0	1	1	0.033727
hsa04640	Hematopoietic cell lineage	9	1	2	0.260636	0.034379
hsa05144	Malaria	9	1	2	0.260636	0.034379
hsa04611	Platelet activation	9	0	2	1	0.034379

*N = Total number of proteins in the particular pathway; Up = Number of protein upregulated in a particular pathway; P.Up = p.value of the up regulated proteins; Down = Number of protein downregulated in a particular pathway; P.down = p.value of the down regulated proteins. Wilcoxon rank-sum test implemented in the Limma package is used for performing the statistical test as described in Young, M. D., Wakefield, M. J., Smyth, G. K., Oshlack, A. (2010). Gene ontology analysis for RNA-seq: accounting for selection bias. Genome Biology 11, R14.

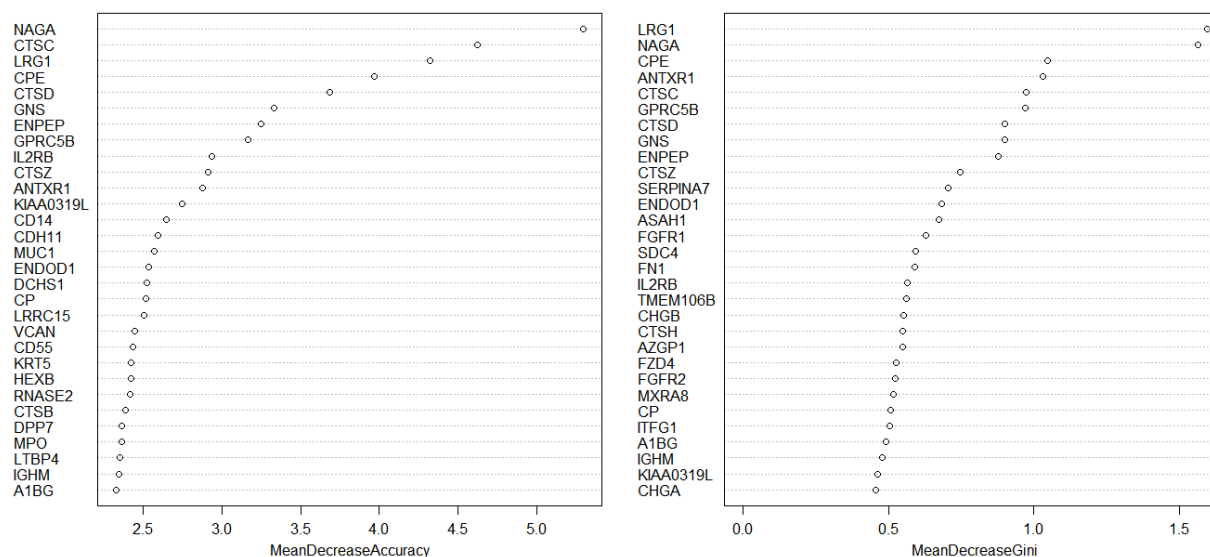


Figure 3: Proteins arranged by mean decrease accuracy and mean decrease gini obtained using the importance function in Random Forest (methods are described in the Materials and Methods section).

The mean decrease accuracy represents the significance of a variable in the model, the higher the value the more important the variable in classification of the T1D and healthy siblings. The GINI index describes the overall explanatory power of the variables; the value denotes how much a

particular predictor variable plays a greater role in partitioning the protein expression data into the either T1D group or healthy siblings. Proteins are listed according to their short names in the UniProt database.

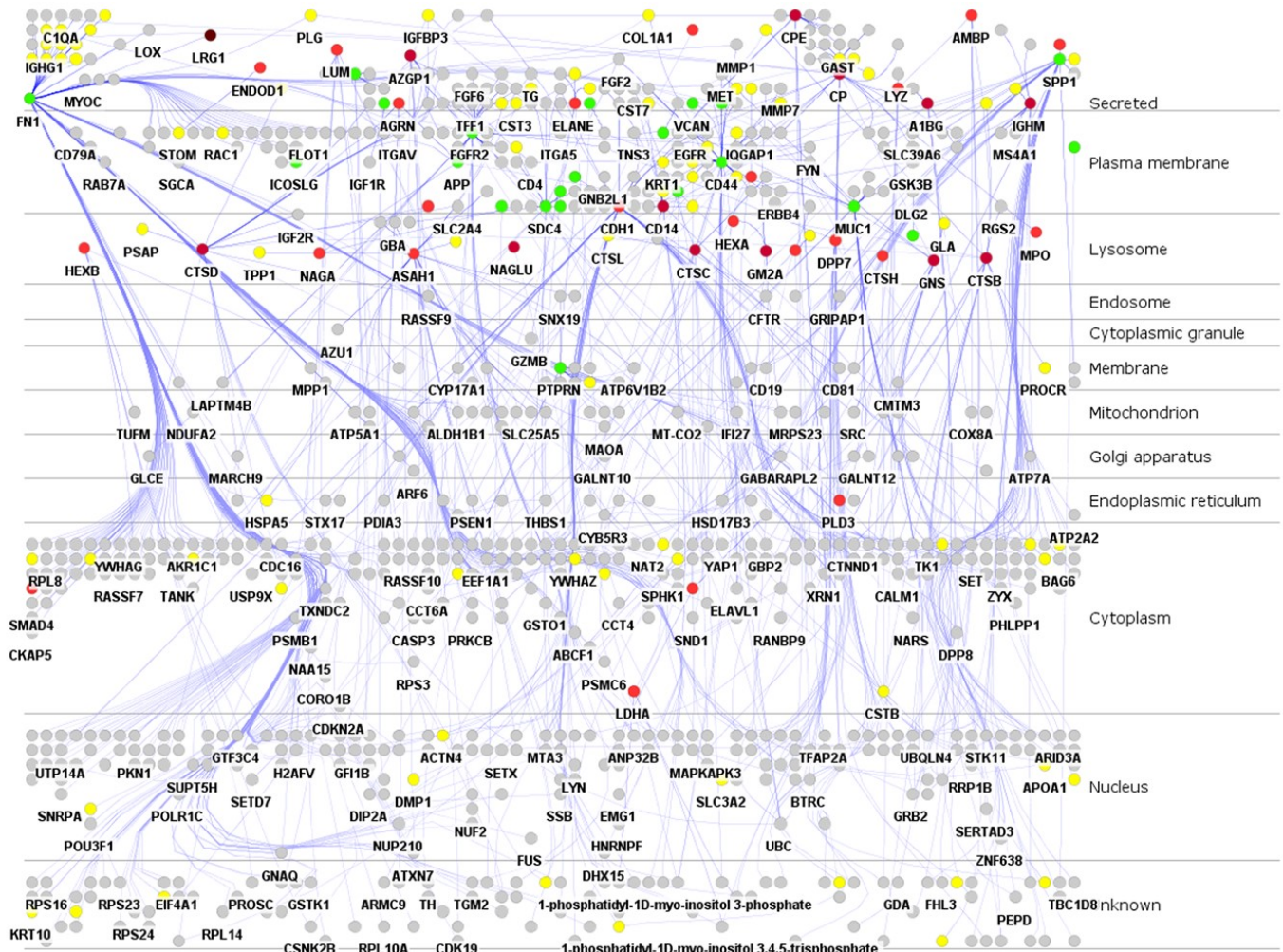


Figure 4: Protein-protein interaction network comprised of abundance-increased and abundance-decreased proteins including those with fold changes of greater than +1.2/-1.2.

Proteins are arranged in subcellular layout obtained from uniprot. For some proteins, there are multiple subcellular locations present in uniprot, we obtained the relevant subcellular location according to the present study. The shade of red indicates the fold change in abundance (light red = > 1.2 and < 1.5 ; medium red = > 1.5 and < 2.0 ; dark red = > 2.0). Only LRG1 has fold change above 2.0 in the above network. A green denotes downregulated protein with fold change > -1.0 and < -1.5 . A yellow color denotes the absence of statistically significant changes of connected proteins in the network. A grey color denotes protein absence in our proteome datasets. The network analysis was performed using data from the IntAct and PINA2 databases. The network analysis was performed using the software tool Cytoscape. Reference: Shannon, P., et al., Cytoscape: a software environment for integrated models of biomolecular interaction networks. *Genome Res*, 2003. 13(11): p. 2498-504.