

Supplementary information

Supplementary Table 1a – Free T4 by genotype of 16 SNPs across three *DIO* genes in WATTs

SNP	common homozygous		heterozygous		minor homozygous		p for trend	
	mean fT4 (95%CI)	n	mean fT4 (95%CI)	n	mean fT4 (95%CI)	n	unadj	adj ^a
<i>DIO1</i>								
rs11206237	21.0 (20.6, 21.3)	399	21.2 (20.5, 21.9)	130	21.5 (19.9, 23.1)	16	0.43	0.34
rs11206244	20.8 (20.3, 21.3)	239	21.2 (20.7, 21.7)	238	21.6 (20.7, 22.5)	69	0.09	0.08
rs2235544	21.7 (21.1, 22.3)	143	21.1 (20.6, 21.5)	288	20.4 (19.7, 21.0)	111	0.005	0.007
rs2268181	21.1 (20.7, 21.4)	387	21.0 (20.4, 21.7)	140	21.7 (20.3, 23.0)	19	0.69	0.57
rs2294511	21.0 (20.5, 21.5)	240	21.3 (20.8, 21.8)	248	20.8 (19.9, 21.6)	56	0.88	0.89
rs2294512	21.1 (20.7, 21.6)	252	21.2 (20.7, 21.6)	245	20.4 (19.2, 21.6)	50	0.41	0.30
rs4926616	21.2 (20.7, 21.7)	245	20.9 (20.5, 21.4)	236	21.0 (20.1, 22.0)	56	0.56	0.55
rs731828	20.9 (20.3, 21.4)	183	21.2 (20.8, 21.6)	278	21.1 (20.3, 21.8)	84	0.50	0.61
rs7527713	21.0 (20.7, 21.4)	362	21.1 (20.4, 21.7)	157	21.0 (20.7, 21.4)	26	0.55	0.43
<i>DIO2</i>								
rs225011	21.2 (20.6, 21.7)	172	21.2 (20.7, 21.6)	264	20.7 (20.0, 21.4)	107	0.32	0.33
rs225014	21.3 (20.8, 21.8)	223	21.0 (20.5, 21.4)	236	20.7 (19.9, 21.4)	87	0.12	0.13
rs225015	21.2 (20.7, 21.7)	237	21.1 (20.6, 21.5)	236	20.6 (19.7, 21.5)	71	0.30	0.31
<i>DIO3</i>								
rs17716499	20.9 (20.4, 21.4)	202	21.2 (20.8, 21.7)	248	20.9 (20.1, 21.8)	95	0.80	0.84
rs7150269	20.7 (20.1, 21.2)	169	21.5 (21.0, 21.9)	254	20.8 (20.1, 21.4)	121	0.64	0.65
rs8011440	20.8 (20.3, 21.3)	215	21.4 (20.9, 21.9)	246	20.8 (20.0, 21.6)	85	0.65	0.60
rs945006	21.0 (20.7, 21.4)	438	21.4 (20.7, 22.1)	92	20.4 (16.8, 24.1)	10	0.58	0.64

^a – adjusted for age and sex

Supplementary Table 1b- Free T3 by genotype in WATTS cohort

SNP	common homozygous		heterozygous		minor homozygous		p for trend	
	mean fT3 (95%CI)	n	mean fT3 (95%CI)	n	mean fT3 (95%CI)	n	unadj	adj ^a
<i>DIO1</i>								
rs11206237	3.83 (3.76, 3.90)	399	3.86 (3.75, 3.97)	130	4.11 (3.73, 4.49)	16	0.22	0.32
rs11206244	3.91 (3.81, 4.00)	239	3.84 (3.75, 3.93)	238	3.69 (3.53, 3.85)	69	0.03	0.02
rs2235544	3.75 (3.65, 3.86)	143	3.88 (3.80, 3.96)	288	3.91 (3.76, 4.07)	111	0.06	0.09
rs2268181	3.84 (3.76, 3.91)	387	3.86 (3.75, 3.96)	140	4.13 (3.80, 4.45)	19	0.23	0.37
rs2294511	3.93 (3.84, 4.02)	240	3.81 (3.72, 3.90)	248	3.72 (3.53, 3.91)	56	0.02	0.02
rs2294512	3.83 (3.74, 3.92)	252	3.82 (3.74, 3.91)	245	4.08 (3.83, 4.33)	50	0.13	0.05
rs4926616	3.90 (3.81, 3.99)	245	3.82 (3.72, 3.92)	236	3.82 (3.63, 4.00)	56	0.24	0.25
rs731828	3.78 (3.67, 3.88)	183	3.89 (3.80, 3.97)	278	3.91 (3.74, 4.07)	84	0.10	0.05
rs7527713	3.84 (3.76, 3.92)	362	3.86 (3.77, 3.96)	157	3.94 (3.66, 4.22)	26	0.50	0.75
<i>DIO2</i>								
rs225011	3.80 (3.69, 3.90)	172	3.89 (3.80, 3.98)	264	3.83 (3.70, 3.96)	107	0.54	0.58
rs225014	3.86 (3.76, 3.97)	223	3.82 (3.74, 3.91)	236	3.89 (3.75, 4.04)	87	0.98	0.95
rs225015	3.85 (3.75, 3.95)	237	3.85 (3.76, 3.94)	236	3.87 (3.71, 4.02)	71	0.93	0.99
<i>DIO3</i>								
rs17716499	3.90 (3.80, 4.00)	202	3.79 (3.70, 3.88)	248	3.91 (3.76, 4.05)	95	0.69	0.76
rs7150269	3.85 (3.75, 3.95)	169	3.89 (3.80, 3.99)	254	3.77 (3.65, 3.90)	121	0.47	0.49
rs8011440	3.85 (3.76, 3.95)	215	3.87 (3.78, 3.96)	246	3.79 (3.65, 3.94)	85	0.64	0.53
rs945006	3.83 (3.76, 3.90)	438	3.94 (3.77, 4.10)	92	3.85 (3.38, 4.32)	10	0.28	0.20

^a – adjusted for age and sex

Supplementary Table 1c - serum TSH by genotype in WATTS cohort

SNP	common homozygous		heterozygous		minor homozygous		p for trend	
	mean TSH (95% CI)	n	mean TSH (95% CI)	n	mean TSH (95% CI)	n	unadj	adj ^a
<i>DIO1</i>								
rs11206237	0.71 (0.61, 0.82)	399	0.64 (0.50, 0.81)	130	0.65 (0.31, 1.36)	16	0.50	0.40
rs11206244	0.67 (0.55, 0.81)	239	0.68 (0.56, 0.82)	238	0.76 (0.55, 1.06)	69	0.59	0.60
rs2235544	0.67 (0.53, 0.85)	143	0.65 (0.55, 0.78)	288	0.79 (0.61, 1.03)	111	0.42	0.45
rs2268181	0.71 (0.61, 0.82)	387	0.64 (0.51, 0.82)	140	0.54 (0.29, 1.04)	19	0.35	0.27
rs2294511	0.67 (0.56, 0.81)	240	0.62 (0.52, 0.76)	248	1.02 (0.72, 1.45)	56	0.27	0.29
rs2294512	0.68 (0.57, 0.81)	252	0.67 (0.55, 0.81)	245	0.74 (0.47, 1.15)	50	0.85	0.79
rs4926616	0.60 (0.50, 0.73)	245	0.70 (0.58, 0.85)	236	1.03 (0.70, 1.50)	56	0.02	0.02
rs731828	0.80 (0.64, 0.99)	183	0.63 (0.53, 0.75)	278	0.63 (0.45, 0.89)	84	0.14	0.23
rs7527713	0.70 (0.59, 0.81)	362	0.66 (0.53, 0.82)	157	0.67 (0.39, 1.15)	26	0.75	0.62
<i>DIO2</i>								
rs225011	0.71 (0.58, 0.89)	172	0.65 (0.54, 0.78)	264	0.73 (0.54, 0.98)	107	0.99	0.83
rs225014	0.64 (0.53, 0.77)	223	0.73 (0.60, 0.89)	236	0.69 (0.49, 0.97)	87	0.47	0.38
rs225015	0.67 (0.56, 0.80)	237	0.68 (0.56, 0.88)	236	0.75 (0.51, 1.10)	71	0.62	0.52
<i>DIO3</i>								
rs17716499	0.67 (0.55, 0.83)	202	0.65 (0.54, 0.78)	248	0.80 (0.58, 1.10)	95	0.46	0.38
rs7150269	0.75 (0.60, 0.94)	169	0.56 (0.47, 0.68)	254	0.89 (0.68, 1.16)	121	0.55	0.54
rs8011440	0.74 (0.61, 0.90)	215	0.58 (0.48, 0.70)	246	0.90 (0.66, 1.22)	85	0.82	0.78
rs945006	0.67 (0.58, 0.77)	438	0.77 (0.57, 1.03)	92	1.03 (0.40, 2.65)	10	0.24	0.24

^a – adjusted for age and sex

Supplementary Table 1d - Reverse T3 by genotype in WATTS cohort

SNP	common homozygous		heterozygous		minor homozygous		p for trend	
	mean rT3 (95% CI)	n	mean rT3 (95% CI)	n	mean rT3 (95% CI)	n	unadj	adj ^a
rs11206237	0.40 (0.39, 0.42)	399	0.39 (0.37, 0.42)	130	0.38 (0.33, 0.43)	16	0.24	0.25
rs11206244	0.39 (0.38, 0.41)	239	0.40 (0.39, 0.42)	238	0.42 (0.38, 0.45)	69	0.23	0.23
rs2235544	0.43 (0.41, 0.46)	143	0.39 (0.38, 0.41)	288	0.39 (0.36, 0.41)	111	0.004	0.004
rs2268181	0.41 (0.39, 0.42)	387	0.39 (0.36, 0.41)	140	0.38 (0.34, 0.43)	19	0.11	0.12
rs2294511	0.39 (0.38, 0.41)	240	0.41 (0.39, 0.43)	248	0.39 (0.36, 0.42)	56	0.46	0.50
rs2294512	0.40 (0.38, 0.42)	252	0.40 (0.39, 0.42)	245	0.40 (0.36, 0.44)	50	0.88	0.96
rs4926616	0.39 (0.38, 0.41)	245	0.41 (0.39, 0.43)	236	0.40 (0.37, 0.44)	56	0.31	0.32
rs731828	0.39 (0.37, 0.41)	183	0.41 (0.40, 0.43)	278	0.40 (0.37, 0.43)	84	0.24	0.19
rs7527713	0.40 (0.39, 0.42)	362	0.40 (0.38, 0.42)	157	0.38 (0.34, 0.43)	26	0.40	0.43
D2								
rs225011	0.41 (0.39, 0.43)	172	0.40 (0.38, 0.42)	264	0.39 (0.36, 0.41)	107	0.18	0.25
rs225014	0.41 (0.39, 0.43)	223	0.39 (0.38, 0.41)	236	0.40 (0.37, 0.42)	87	0.21	0.27
rs225015	0.41 (0.39, 0.43)	237	0.40 (0.38, 0.41)	236	0.39 (0.36, 0.42)	71	0.29	0.34
D3								
rs17716499	0.39 (0.37, 0.41)	202	0.41 (0.40, 0.43)	248	0.39 (0.36, 0.42)	95	0.74	0.72
rs7150269	0.38 (0.36, 0.40)	169	0.41 (0.40, 0.43)	254	0.40 (0.37, 0.42)	121	0.34	0.36
rs8011440	0.40 (0.38, 0.42)	215	0.40 (0.39, 0.42)	246	0.39 (0.36, 0.42)	85	0.84	0.89
rs945006	0.40 (0.38, 0.41)	438	0.43 (0.40, 0.45)	92	0.39 (0.25, 0.53)	10	0.12	0.12

^a – adjusted for age and sex