

**Supplemental table 1. Annotation for the top six SNPs under positive selection in Greenlandic Inuit**

Position <sup>1</sup>	Reference		DAF							PBS
	SNP identification number	Alleles <sup>2</sup>	CEU	CHB	GI	NHS	HPFS	WHI	SCHS	
chr11:61627960	rs74771917	C/T	0.025	0.16	0.98	/	/	/	/	2.67
chr11:61631510	rs3168072	A/T	0.017	0.18	0.98	/	/	/	/	2.64
chr11:61632310	rs12577276	A/G	0.017	0.18	0.98	/	/	/	/	2.64
chr11:61641717	rs7115739	G/T	0.017	0.22	0.98	0.004	0.004	/	/	2.54
chr11:61624414	rs174602	C/T	0.80	0.73	0.01	0.82	0.81	/	/	2.11
chr11:61597212	rs174570	C/T	0.16	0.34	0.99	0.15	0.15	0.14	0.35	2.06

<sup>1</sup>Positions refer to human genome assembly hg19.

<sup>2</sup>Alleles are coded as ancestral/derived states.

PBS, the population branch statistic; DAF, derived allele frequency; CEU, European ancestry; CHB, an Chinese; GI, Greenlandic Inuit

DAFs for each population (CEU, CHB, and GI) and PBS values are reported, along with the genomic position for each SNP.

**Supplemental table 2 Main effect of the *FADS* variants on adiposity in the four cohorts**

Outcomes (kg/m <sup>2</sup> )	<i>FADS</i> SNPs	NHS		HPFS		WHI		SCHS		Pooled	
		Beta ± SE	P	Beta ± SE	P	Beta ± SE	P	Beta ± SE	P	Beta ± SE	P
Baseline BMI	rs174570	0.03 ± 0.10	0.733	-0.05 ± 0.09	0.538	-0.06±0.17	0.72	0.24±0.08	0.002	0.08±0.05	0.06
Baseline BMI	rs174602	0.08 ± 0.10	0.418	-0.05 ± 0.08	0.536	/	/	/	/	0.00 ± 0.03	0.559
Baseline BMI	rs7115739	0.25 ± 0.52	0.634	-0.77 ± 0.43	0.077	/	/	/	/	-0.35 ± 0.14	0.196
Long-term BMI change	rs174570	-0.05 ± 0.06	0.401	0.01 ± 0.05	0.917	-0.02±0.09	0.77	-0.02±0.08	0.85	-0.02±0.03	0.94
Long-term BMI change	rs174602	-0.14 ± 0.06	0.009	0.04 ± 0.05	0.413	/	/	/	/	-0.04 ± 0.01	0.025
Long-term BMI change	rs7115739	0.45 ± 0.29	0.124	-0.23 ± 0.26	0.359	/	/	/	/	0.06 ± 0.08	0.183

Long-term BMI change: BMI change from 1990 to 2000.

Numbers of T carriers/Non-T carriers in the NHS, HPFS, WHI, and SCHS are 1698/9625, 1025/5808, 876/5378, and 1842/3422, respectively.

Effect size (ES) values are  $\beta$  coefficients for relationship between the *FADS* variant rs174570 (additive model) and adiposity.

The general linear model was used to test the genetic association of *FADS* variants with long-term changes in BMI after adjustment for age, source of genotyping data.

**Supplemental table 3 Genetic association of *FADS* variant with long-term changes in body weight according to long chain n-3 PUFAs and fish intakes**

	Difference in long-term changes in weight,			P for interaction
	kg			
<b>Total Fish, serving/day</b>	≤1/wk	1~6/wk	≥1/d	
NHS	-0.69±0.64	-0.13±0.49	1.78±1.64	0.05
HPFS	-0.99±0.85	0.54±0.53	1.52±1.69	0.12
WHI	-0.22±0.42	0.16±0.34	1.26±1.57	0.13
SCHS	-0.42±0.29	-0.44±0.28	0.20±0.29	0.08
Pooled	-0.44±0.22	-0.10±0.18	0.31±0.28	0.01
<b>Food-sourced EPA, g/day</b>	T1	T2	T3	
NHS	-0.77±0.62	-0.25±0.72	0.53±0.64	0.06
HPFS	-1.19±0.82	0.75±0.73	0.72±0.74	0.41
WHI	-0.19±0.42	0.24±0.47	0.14±0.48	0.20
Pooled	-0.50±0.32	0.24±0.34	0.37±0.34	0.10
<b>Food-sourced DHA, g/day</b>	T1	T2	T3	
NHS	-0.53±0.62	-0.39±0.70	0.53±0.65	0.01
HPFS	-1.06±0.82	0.49±0.71	0.89±0.76	0.09
WHI	-0.20±0.43	0.22±0.42	0.30±0.50	0.26
Pooled	-0.43±0.32	0.15±0.32	0.49±0.35	0.01
<b>Food-sourced EPA+DHA, g/day</b>	T1	T2	T3	
NHS	-0.56±0.63	-0.32±0.68	0.49±0.66	0.01
HPFS	-1.25±0.83	0.68±0.73	0.84±0.74	0.09
WHI	-0.02±0.43	0.16±0.44	0.14±0.49	0.23
SCHS	-0.47±0.29	-0.16±0.28	-0.03±0.29	0.10

Pooled	-0.56±0.25	-0.09±0.24	0.14±0.25	0.005
<b>Total EPA+DHA, g/day</b>	<b>T1</b>	<b>T2</b>	<b>T3</b>	
NHS	-0.58±0.63	-0.30±0.68	0.46±0.66	0.02
HPFS	-1.20±0.82	0.75±0.70	0.86±0.77	0.18
WHI	-0.48±0.47	0.64±0.43	0.04±0.47	0.15
Pooled	-0.64±0.34	0.45±0.32	0.32±0.34	0.02

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Data are  $\beta$  coefficients  $\pm$  SE.

Numbers of T carriers/Non-T carriers in the NHS, HPFS, WHI, and SCHS are 1698/9625, 1025/5808, 876/5378, and 1842/3422, respectively.

Frequency of fish intake:  $\leq$  1 serving per week, 1~6 servings per week, and 1 serving per day

Data on baseline fish and fatty acids consumptions were assessed in 1990 (NHS) and 1990 (HPFS).

Data on body weight were assessed in 1990 and 2000 in NHS and 1990 and 2000 in HPFS.

The general linear model was used to test the genetic association with long-term changes in body weight according to baseline long chain n-3 PUFAs and fish intakes after adjustment for age, source of genotyping data, baseline body weight, smoking, alcohol intake, physical activity, total energy intake, alternate healthy eating index, television watching, sugar sweetened beverage, fried food consumption.

Data from three or four cohorts pooled by means of fixed effects meta-analyses (if  $P \geq 0.05$  for heterogeneity between studies).

**Supplemental table 4 Associations of long chain n-3 PUFAs and fish intakes with long-term changes in body weight according to *FADS* genotypes**

Cohorts		Long-term changes in weight, kg			P for trend
Total Fish, serving/day		≤1/wk	1~6/wk	≥1/d	
NHS	Non T carriers	4.91±0.34	5.78±0.24	7.00±0.79	0.008
	T carriers	4.45±0.61	5.64±0.46	9.26±1.44	0.001
HPFS	Non T carriers	0.44±0.06	0.52±0.04	0.56±0.12	0.99
	T carriers	0.25±0.10	0.53±0.07	0.76±0.21	0.08
WHI	Non T carriers	-0.25±0.23	-0.43±0.18	-0.91±0.93	0.50
	T carriers	-0.56±0.37	-0.25±0.28	1.30±1.71	0.13
SCHS	Non T carriers	-3.15±0.23	-3.50±0.21	-3.38±0.21	0.48
	T carriers	-3.68±0.20	-3.41±0.19	-3.34±0.20	0.16
Food-sourced EPA, g/day		T1	T2	T3	
NHS	Non T carriers	4.89±0.33	5.89±0.33	5.95±0.33	0.24
	T carriers	4.45±0.59	5.52±0.63	6.46±0.61	0.34
HPFS	Non T carriers	0.50±0.05	0.54±0.05	0.45±0.05	0.15
	T carriers	0.29±0.10	0.54±0.09	0.52±0.09	0.66
WHI	Non T carriers	-0.30±0.25	-0.54±0.24	-0.29±0.24	0.42
	T carriers	-0.51±0.39	-0.36±0.37	-0.15±0.38	0.14
Food-sourced DHA, g/day		T1	T2	T3	
NHS	Non T carriers	4.78±0.33	5.56±0.34	6.32±0.33	0.14
	T carriers	4.50±0.60	5.07±0.63	6.77±0.61	0.004
HPFS	Non T carriers	0.48±0.05	0.54±0.05	0.46±0.06	0.40
	T carriers	0.27±0.10	0.50±0.09	0.59±0.09	0.15
WHI	Non T carriers	-0.41±0.25	-0.25±0.24	-0.45±0.25	0.51

	T carriers	-0.71±0.39	-0.15±0.37	-0.16±0.39	0.18
<b>Food-sourced EPA+DHA, g/day</b>		T1	T2	T3	
NHS	Non T carriers	4.69±0.34	5.45±0.33	6.51±0.33	0.02
	T carriers	4.44±0.61	5.00±0.61	6.92±0.61	0.0003
HPFS	Non T carriers	0.48±0.05	0.53±0.05	0.47±0.05	0.93
	T carriers	0.26±0.10	0.49±0.09	0.59±0.09	0.08
WHI	Non T carriers	-0.44±0.24	-0.23±0.23	-0.43±0.24	0.47
	T carriers	-0.52±0.38	-0.15±0.37	-0.33±0.38	0.15
SCHS	Non T carriers	-3.44±0.21	-3.58±0.22	-3.05±0.21	0.89
	T carriers	-3.73±0.19	-3.57±0.19	-3.12±0.19	0.12
<b>Total EPA+DHA, g/day</b>		T1	T2	T3	
NHS	Non T carriers	4.74±0.34	5.55±0.32	6.36±0.34	0.81
	T carriers	4.49±0.61	5.16±0.60	6.70±0.61	0.03
HPFS	Non T carriers	0.49±0.05	0.53±0.05	0.47±0.06	0.24
	T carriers	0.26±0.10	0.51±0.09	0.58±0.09	0.33
WHI	Non T carriers	0.32±0.27	-0.84±0.23	-0.60±0.28	0.19
	T carriers	-0.26±0.45	-0.21±0.37	-0.02±0.11	0.08

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Data on baseline fish and fatty acids consumptions were assessed in 1990 (NHS) and 1990 (HPFS).

Numbers of T carriers/Non-T carriers in the NHS, HPFS, WHI, and SCHS are 1698/9625, 1025/5808, 876/5378, and 1842/3422, respectively.

Data on body weight were assessed in 1990 and 2000 in NHS and 1990 and 2000 in HPFS.

The general linear model was used to test the associations of long chain n-3 PUFAs and fish intakes with long-term changes in body weight by *FADS* genotypes after adjustment for age, source of genotyping data, baseline body weight, smoking, alcohol intake, physical activity, total energy intake, alternate healthy eating index, television watching, sugar sweetened beverage, fried food consumption.

Data from two cohorts pooled by means of fixed effects meta-analyses (if  $P \geq 0.05$  for heterogeneity between studies) or random effects meta-analyses (if  $P < 0.05$  for heterogeneity between studies).

**Supplemental Table 5 Associations of long chain n-3 PUFAs and fish intakes with long-term changes in BMI according to *FADS* genotypes**

Diets	<i>FADS</i> genotypes	Long chain n-3 PUFAs and fish intakes			P for trend	P for interaction*
		Categories of diets				
Food-sourced EPA, g/day		T1	T2	T3		
NHS	Non-T carriers	0.82±0.06	1.00±0.06	1.01±0.06	0.24	0.05
	T carriers	0.72±0.10	0.94±0.11	1.10±0.11	0.29	
HPFS	Non-T carriers	0.48±0.05	0.54±0.05	0.47±0.05	0.72	0.37
	T carriers	0.23±0.11	0.54±0.10	0.52±0.09	0.45	
WHI	Non-T carriers	0.10±0.09	0.09±0.09	0.45±0.09	0.21	0.02
	T carriers	-0.08±0.15	0.23±0.15	0.46±0.15	0.003	
Pooled	Non-T carriers	0.54±0.04	0.63±0.04	0.65±0.04	0.35	0.01
	T carriers	0.39±0.07	0.63±0.07	0.70±0.06	0.01	
Food-sourced DHA, g/day		T1	T2	T3		
NHS	Non-T carriers	0.80±0.06	0.94±0.06	1.08±0.06	0.14	0.009
	T carriers	0.74±0.10	0.83±0.11	1.17±0.10	0.002	
HPFS	Non-T carriers	0.46±0.05	0.54±0.05	0.49±0.05	0.99	0.05
	T carriers	0.24±0.10	0.49±0.10	0.58±0.09	0.05	
WHI	Non-T carriers	0.03±0.09	0.20±0.09	0.42±0.09	0.03	0.06
	T carriers	-0.10±0.15	0.33±0.15	0.39±0.15	0.006	
Pooled	Non-T carriers	0.51±0.04	0.63±0.04	0.68±0.04	0.1	0.002
	T carriers	0.38±0.06	0.58±0.07	0.77±0.06	7×10 <sup>-4</sup>	

Data are means ± SE.

<sup>1</sup>P for interaction was generated from dominant model of *FADS* rs174570 (CC vs CT+TT).

Numbers of T carriers/Non-T carriers in the NHS, HPFS, WHI, and SCHS are 1698/9625, 1025/5808, 876/5378, and 1842/3422, respectively.

Data on BMI, long chain n-3 PUFAs consumptions were assessed at baseline in the NHS (1990), the HPFS (1990), the WHI (1994-1998), and the SCHS (1993-1998), respectively.

Data on follow-up BMI was assessed in 2000 in the NHS and HPFS, in the sixth follow-up year in the

WHI, and from 2006 to 2010 in the SCHS, respectively.

Long-term BMI changes were calculated based on the changes in BMI from baseline to follow-up year in the four cohorts, respectively.

The general linear model was used to test the associations of long chain n-3 PUFAs and fish intakes with long-term changes in BMI by *FADS* genotypes after adjustment for age, source of genotyping data, baseline BMI, smoking, alcohol intake, physical activity, total energy intake, alternate healthy eating index, television watching, sugar sweetened beverage, fried food consumption.

The results were pooled by means of fixed effects meta-analyses (if  $P \geq 0.05$  for heterogeneity between studies).

Registration: [www.clinicaltrials.gov](http://www.clinicaltrials.gov). Registration ID: NCT03348566