

Supplementary Information for

Genetic Variants Associated with Sensitive Skin: A Genome-Wide Association Study in Korean Women

Seoyoung Kim ^{1,2,†}, Kyung-Won Hong ^{3,†}, Mihyun Oh ¹, Susun An ¹, Jieun Han ¹, Sodam Park ¹, Goun Kim ¹ and Jae Youl Cho ^{2,*}

Supplementary Tables

Supplementary Table S1. Diagnostic questionnaire and judgment for assessing self-declared sensitive skin.

Questionnaire		Total Score	Weighted value
Weighted value of the general skin status (A) (5–15 points)	Experience of skin discomfort after using cosmetics, sun sensitivity and inflammation, allergy, skin change, skin thickness	5–8 points	1
		9–10 points	2
		11–12 points	3
		≥13 points	4
Weighted value of cosmetic application and skin alternation (B) (0–48 points)	Cosmetic uses (15 questions)	<11 points	1
	Innate skin characteristics (14 questions)	<18 points	2
	Environmental skin changes (9 questions)	<26 points	3
	Living Habits (10 questions)	≥26 point s	4
Estimated sensitive skin			
Sensitive skin diagnostic classification (2*(A)+3*(B))	<10	GRADE I	Non-sensitive
	10-14	GRADE II	Slightly sensitive
	15-17	GRADE III	Moderately sensitive
	≥18	GRADE IV	Strongly sensitive

Sensitive skin can be diagnosed using the [2*(A) + 3*(B)] formula, where A is the weighted value of the general skin status and B is a cosmetic application and skin alteration. A diagnostic value ≤9 indicates non-sensitive skin, whereas however, a score >18 indicates strongly sensitive skin.

Supplementary Table S2. Lead SNPs of sensitive skin GWAS using three genetic modes (additive, dominant, and recessive).

SNP	Chr:Bp	Mapped Gene	eQTL Genes (GTEx Portal)	Ef- fect Al- lele	Effect Allele Frequency				HWE p- value	Additive mode		Dominant mode		Recessive mode	
					This study	EAS	EUR	AMR		OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
rs11689992	2:122364982	chr2q11.3	-	A	0.14	0.1	0.43	0.28	1.00	3.67 (2.18- 6.16)	9.30×10 ⁻⁷	3.66 (2.11- 6.34)	4.00×10 ⁻⁶	7.95 (0.91- 69.13)	6.0×10 ⁻²
rs7614738	3:49273698	USP4	GPX1	C	0.23	0.06	0.48	0.37	0.78	2.34 (1.68- 3.27)	4.96×10 ⁻⁷	2.90 (1.77- 4.77)	2.66×10 ⁻⁵	5.27 (2.02- 13.76)	6.78×10 ⁻⁴
rs12306124	12:26057827	RASSF8	RASSF8	C	0.22	0.22	0.19	0.2	0.23	2.60 (1.72- 3.93)	5.68×10 ⁻⁶	2.08 (1.28- 3.38)	3.06×10 ⁻³	3.40 (1.24- 9.36)	1.80×10 ⁻²
rs10483893	14:78183426	NRXN3	-	A	0.17	0.23	0.42	0.24	0.21	2.93 (1.83- 4.71)	8.15×10 ⁻⁶	2.93 (1.75- 4.91)	4.43×10 ⁻⁵	7.69 (1.63- 36.35)	1.00×10 ⁻²

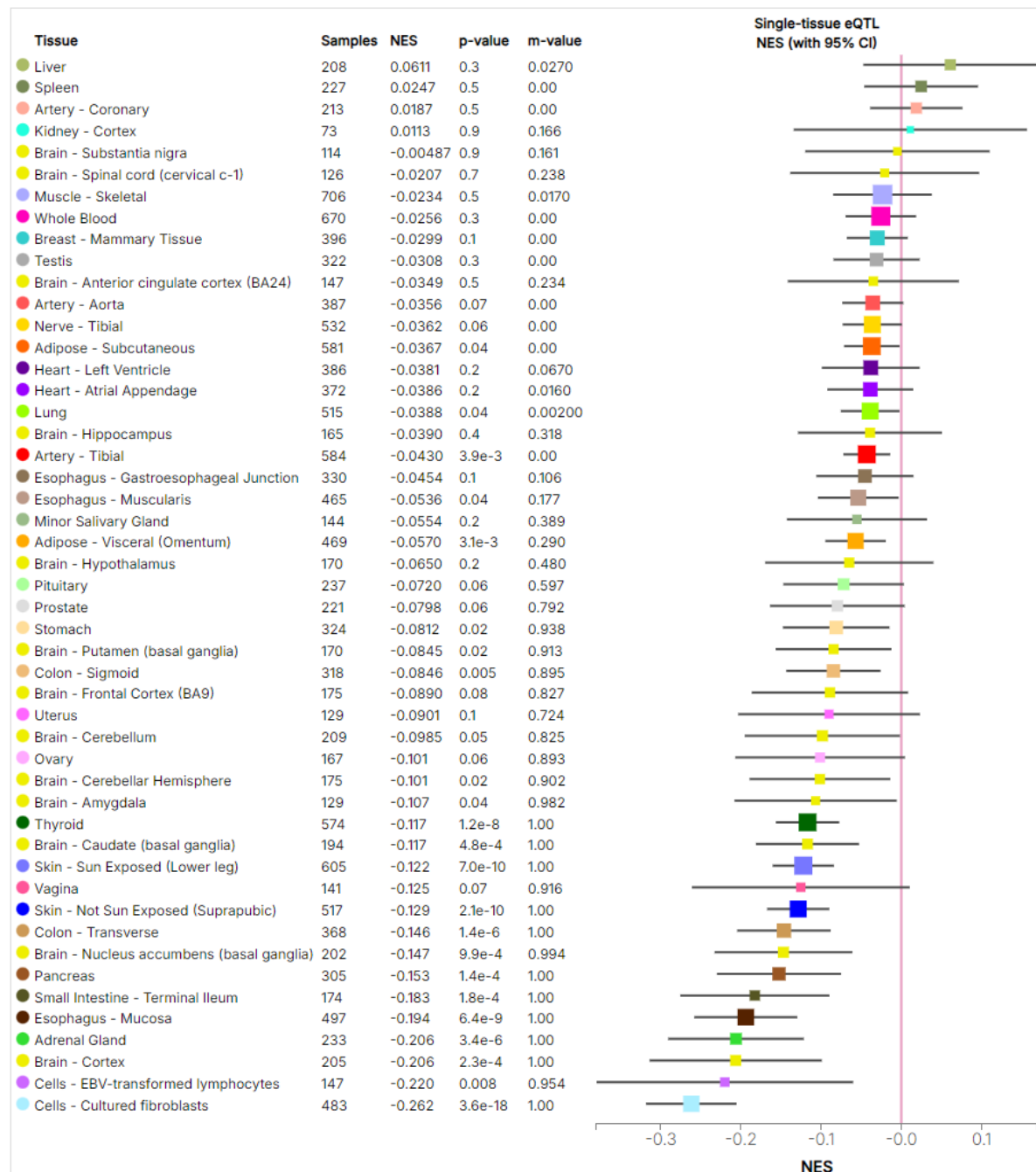
Supplementary Table S3. Distribution of risk allele numbers for each SS grade.

Risk Allele No.	Grade [n (%)]				Total [n]
	Non-Sensitive	Slightly Sensitive	Moderately Sensitive	Severely Sensitive	
0	61 (85.9%)	8 (11.3%)	2 (2.8%)	0 (0%)	71
1	61 (68.5%)	19 (21.3%)	5 (5.6%)	4 (4.5%)	89
2	48 (63.2%)	20 (26.3%)	6 (7.9%)	2 (2.6%)	76
3	11 (26.8%)	23 (56.1%)	4 (9.8%)	3 (7.3%)	41
4	0 (0%)	11 (84.6%)	0 (0%)	2 (15.4%)	13
5	0 (0%)	3 (75%)	1 (25%)	0 (0%)	4
6	0 (0%)	2 (100%)	0 (0%)	0 (0%)	2
Linear regression analysis for grade using the risk allele number					
Odds ratio		CI L95	CI U95	p-value	
1.260		1.181	1.346	2.23954E-11	

Supplementary Figures

Multi-tissue eQTL Comparison

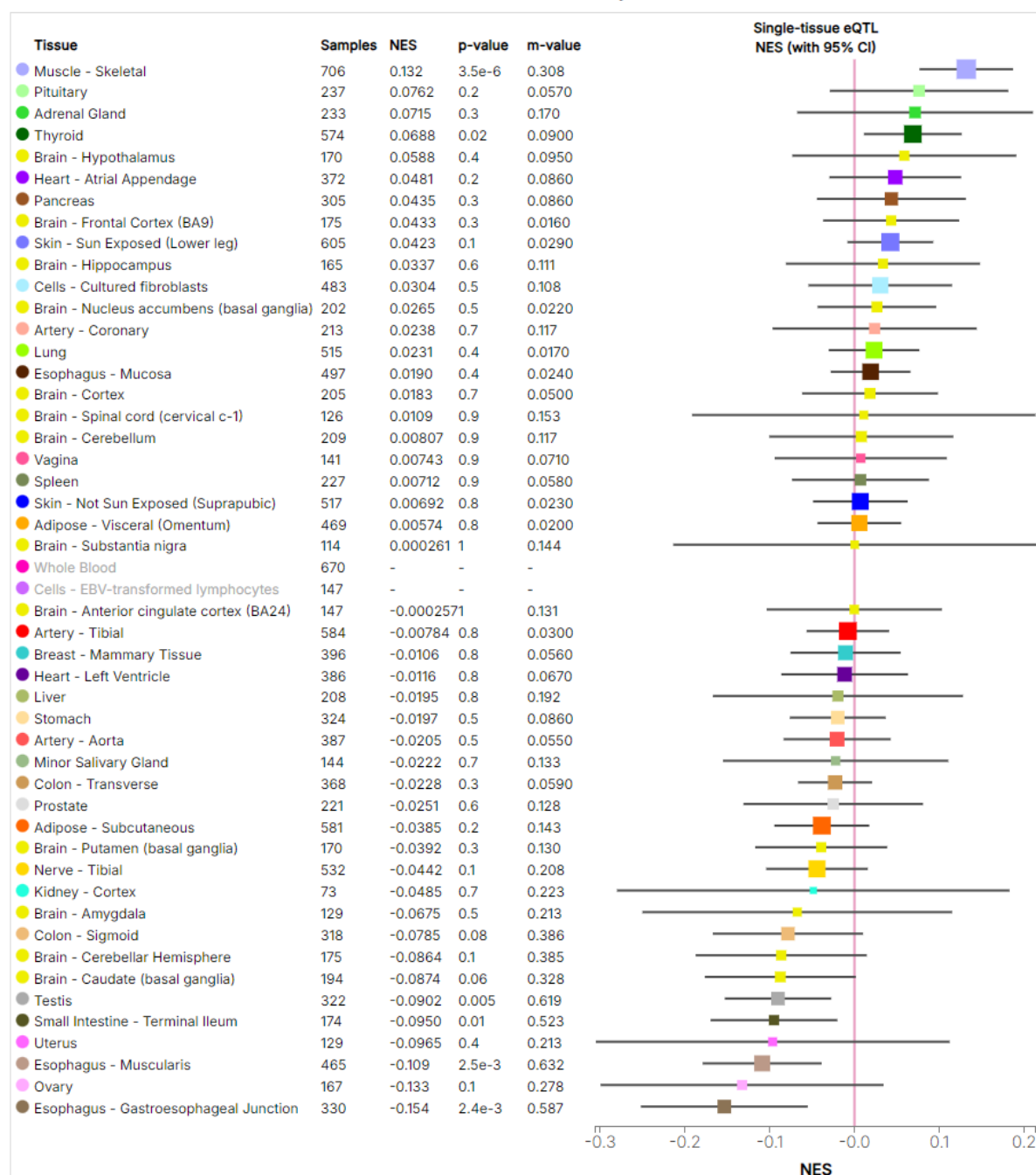
ENSG00000233276.3 GPX1 and chr3_49273698_C_G_b38 eQTL (Meta Analysis RE2 P-Value: 9.204169999999998e-78)



Supplementary Figure S1. GTEx Portal Search for the rs7614738 eQTL for *GPX1*. Sun-exposed skin tissues exhibited a significantly lower expression of the G allele.

Multi-tissue eQTL Comparison

ENSG00000123094.15 RASSF8 and chr12_26057827_G_C_b38 eQTL (Meta Analysis RE2 P-Value: 0.0000192296)



Supplementary Figure S2. GTEX portal search for the rs12306124 eQTL for *RASSF8*. Sun-exposed skin tissues exhibited a higher expression tendency for the C allele.