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Supplemental Material to:

Paula L Hyland, Laura S Burke, Ruth M Pfeiffer,
Melissa Rotunno, David Sun, Prasad Patil, Xiaolin Wu,
Margaret A Tucker, Alisa M Goldstein,
and Xiaohong Rose Yang

Constitutional promoter methylation and risk of familial melanoma

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Table S1. *P*-values for association between overall methylation of each gene-specific promoter and demographic or cutaneous malignant melanoma (CMM) risk factors among non-carrier controls.

Risk Factor	***CDH1***	***COL1A2***	***DAPK1***	***DDIT4L***	***HSPB6***	***LOX***	***MAGE-A3 (females)***	***MAGE-A3 (males)***	***MT1G***	***NPM2***	***p14ARF***	***p16***	***PTEN***	***RASSF1***	***TNFRSF10C***	***TNFRSF10D***
Age at blood draw	0.179	0.070	0.748	**0.001**	0.932	0.506	0.984	0.878	0.881	0.312	**0.003**	0.122	0.656	0.529	0.494	0.261
Gender	0.806	**0.038**	0.858	0.198	0.134	0.280	--	--	0.100	0.078	0.748	**0.027**	0.701	0.674	0.060	0.557
Dysplastic nevi	0.875	**0.042**	0.940	0.847	0.967	**0.035**	0.311	**<.0001**	0.405	0.697	**<.0001**	0.579	0.375	0.462	0.889	0.237
Moles	**0.048**	**0.012**	0.847	0.425	0.414	0.608	0.524	**0.004**	0.225	0.679	0.280	**0.032**	0.174	0.787	0.250	**0.013**
Freckles	0.199	0.560	0.193	0.097	0.304	0.324	0.497	**0.049**	0.112	0.556	0.575	0.653	0.789	0.847	0.774	0.706
Solar injury	0.962	0.523	0.183	0.619	0.741	0.626	0.376	**<.0001**	0.625	0.927	0.995	0.404	0.767	0.889	0.680	0.839
Tanning ability	0.744	0.513	0.784	0.157	0.975	0.672	0.080	**<.0001**	0.932	0.516	0.870	0.374	0.422	0.353	0.364	0.374
Skin type	0.315	0.628	0.633	0.700	0.648	0.785	0.511	**0.0001**	0.578	0.315	0.923	0.836	**0.035**	0.449	0.218	0.588
Eye color	**0.009**	0.678	**0.007**	**0.0004**	**0.012**	**0.005**	0.252	0.069	0.183	**0.003**	0.466	0.371	**0.019**	0.172	0.084	0.308
Hair color	**0.004**	0.480	**0.014**	0.477	**0.013**	0.104	**0.014**	**<.0001**	**0.011**	**0.005**	0.763	0.291	0.245	0.251	0.066	0.106
MC1R	**0.019**	0.593	0.144	**0.016**	0.358	0.459	0.685	**<.0001**	0.660	0.924	0.234	**0.041**	**0.028**	**0.004**	0.880	0.245

P-values were obtained using a generalized estimating equation and adjusting for familial correlation. The significance of each risk factor in non-carrier controls (n= 90) was assessed with all of the other risk factors included in the model. *P*-values <0.05 are bolded. Normality testing of residuals was met for each gene target with the exception of *RASSF1*, *DAPK1* and *CDH1*. For *CDH1* and *DAPK1,* data normality was achieved using log transformation. For *RASSF1*, normality of residuals was not achieved.

Table S2. Association between gene-specific promoter methylation and CMM status.

	Model 1				**Model 2**			
Promoter	**OR**	**95% CI**		***P***	**OR**	**95% CI**		***P***
CDH1	0.78	0.66	0.91	**0.002**	0.84	0.71	1.00	0.052
COL1A2	1.00	0.98	1.02	0.906	1.00	0.97	1.03	0.991
DAPK1	0.76	0.63	0.93	0.007	0.78	0.61	1.01	0.056
DDIT4L	0.77	0.54	1.11	0.166	0.72	0.49	1.08	0.115
HSPB6	0.98	0.95	1.01	0.188	0.98	0.93	1.02	0.286
LOX	0.84	0.68	1.03	0.096	1.01	0.78	1.30	0.952
MAGE-A3 (females)	0.64	0.50	0.82	**0.001**	0.75	0.63	0.89	**0.002**
MAGE-A3 (males)	0.81	0.66	1.01	0.060				
MT1G	0.86	0.79	0.94	**0.001**	0.88	0.80	0.97	0.011
NPM2	0.79	0.51	1.21	0.275	0.82	0.53	1.27	0.372
p14ARF	0.30	0.12	0.74	0.009	0.28	0.10	0.77	0.013
p16	0.75	0.42	1.32	0.319	0.64	0.35	1.18	0.155
PTEN	0.52	0.29	0.95	0.034	0.51	0.26	0.98	0.044
RASSF1	0.29	0.11	0.81	0.018	0.30	0.10	0.86	0.026
TNFRSF10C	0.63	0.50	0.80	**<0.001**	0.64	0.47	0.87	0.004
TNFRSF10D	0.61	0.43	0.87	0.006	0.57	0.39	0.84	0.004

Model 1: Adjusted for age, sex and *CDKN2A* mutation status.

Model 2: Adjusted for age, sex, *CDKN2A* mutation status, moles and hair color.

P-values (*P*) were obtained by comparing CMM cases to unaffected individuals using a generalized estimating equation and adjusting for familial correlation. *P*-value surviving Bonferroni correction for multiple comparisons (0.05/15, *P*= 0.003) are bolded.