

ONLINE RESOURCE

Breast tumor DNA methylation patterns associated with smoking in the Carolina Breast Cancer Study

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Table S1. CpG loci differentially methylated at p<0.05 in current vs. never smokers by HR status.

Probe	CpG ID	Chr	Mean Beta Never	Coefficient <u>Current vs. never</u>	Mean Beta <u>Current</u>	% Change vs Never	p-value	FDR-adjusted p-value	Coefficient <u>Former vs. never</u>	Mean Beta <u>Former</u>	p-value	FDR-adjusted p-value	Coefficient <u>Ever vs. never</u>	Mean Beta <u>Ever</u>	p-value	FDR-adjusted p-value
HR- (n=107 CpGs in current vs never smokers)																
CDKN1A_P242_F	cg23305046	6	0.0652	2.210	0.0901	38.19	0.000	0.000	0.827	0.0626	0.104	0.446	1.345	0.0770	0.000	0.067
IL12B_E25_F	cg18307303	5	0.8696	-0.465	0.8314	-4.39	0.000	0.065	-0.296	0.8497	0.012	0.286	-0.373	0.8401	0.000	0.076
MCC_P196_R	cg19728002	5	0.0541	-0.820	0.0476	-12.01	0.000	0.122	-0.405	0.0408	0.077	0.411	-0.624	0.0443	0.000	0.120
FGF1_P357_R	cg05353098	5	0.6871	-0.517	0.5879	-14.44	0.000	0.132	-0.125	0.6694	0.414	0.684	-0.324	0.6270	0.008	0.267
PIK3R1_P307_F	cg03473299	5	0.9073	-0.353	0.8838	-2.59	0.001	0.132	0.007	0.9037	0.955	0.984	-0.174	0.8933	0.051	0.377
TRIM29_E189_F	cg26414304	11	0.7605	-0.491	0.6870	-9.66	0.001	0.184	-0.212	0.7234	0.173	0.520	-0.347	0.7045	0.006	0.251
ACVR1_P983_F	cg10122840	2	0.8544	-0.473	0.7959	-6.85	0.001	0.199	-0.177	0.8347	0.266	0.591	-0.330	0.8145	0.009	0.268
MAPK9_P1175_F	cg05023457	5	0.9145	-0.402	0.8878	-2.92	0.002	0.231	-0.094	0.9066	0.527	0.763	-0.250	0.8968	0.030	0.336
MC2R_P1025_F	cg00358505	18	0.4793	-0.490	0.4090	-14.67	0.003	0.251	-0.257	0.4467	0.108	0.448	-0.374	0.4271	0.004	0.251
APBA1_E99_R	cg18505908	9	0.1270	0.434	0.1622	27.72	0.003	0.251	-0.096	0.1272	0.588	0.810	0.178	0.1454	0.174	0.520
CYP2E1_E53_R	cg23093817	10	0.7554	-0.457	0.6742	-10.75	0.003	0.251	-0.278	0.7111	0.086	0.421	-0.371	0.6919	0.005	0.251
ZIM3_P451_R	cg16859188	19	0.9297	-0.433	0.9104	-2.08	0.004	0.251	-0.057	0.9262	0.743	0.885	-0.231	0.9180	0.077	0.411
DSC2_P407_R	cg20887958	18	0.8565	-0.392	0.8149	-4.86	0.004	0.251	-0.241	0.8242	0.086	0.421	-0.316	0.8194	0.006	0.251
CDM_seq_21_S260_R	cg18682265	X	0.3964	-0.382	0.3251	-17.99	0.005	0.251	-0.155	0.3597	0.222	0.554	-0.269	0.3417	0.010	0.271
EPHA2_P340_R	cg20350808	1	0.4335	-0.365	0.3549	-18.13	0.005	0.251	-0.136	0.3935	0.277	0.594	-0.252	0.3734	0.013	0.298
BMPR1A_E88_F	cg14602437	10	0.7188	-0.334	0.6564	-8.68	0.005	0.251	-0.113	0.6920	0.367	0.651	-0.227	0.6735	0.022	0.317
FRK_P258_F	cg26557270	6	0.6436	-0.487	0.5366	-16.63	0.005	0.251	-0.160	0.6165	0.369	0.653	-0.326	0.5749	0.022	0.317
MAP3K8_P1036_F	cg21555918	10	0.6421	-0.418	0.5836	-9.11	0.005	0.251	-0.293	0.5777	0.050	0.377	-0.356	0.5808	0.003	0.251
MST1R_E42_R	cg03714052	3	0.5684	-0.440	0.4522	-20.44	0.005	0.251	-0.116	0.5458	0.458	0.709	-0.279	0.4970	0.028	0.332
UGT1A1_E11_F	cg03607648	2	0.9567	-0.369	0.9490	-0.80	0.006	0.251	-0.121	0.9542	0.413	0.684	-0.242	0.9515	0.036	0.351
SNCG_P98_R	cg03677069	10	0.6472	-0.372	0.5833	-9.87	0.006	0.251	-0.105	0.6202	0.446	0.705	-0.240	0.6010	0.030	0.336
ITGA6_P718_R	cg03085296	2	0.9225	-0.363	0.9003	-2.41	0.006	0.251	-0.202	0.9071	0.150	0.498	-0.283	0.9036	0.012	0.286
RARA_E128_R	cg00848035	17	0.2640	-0.449	0.1852	-29.85	0.006	0.251	-0.316	0.1954	0.046	0.369	-0.384	0.1901	0.002	0.231
MYCL1_P502_R	cg27650434	1	0.1159	-0.375	0.0886	-23.55	0.007	0.253	-0.225	0.0996	0.084	0.421	-0.302	0.0939	0.004	0.251
HGF_P1293_R	cg14690980	7	0.9236	-0.383	0.9071	-1.79	0.007	0.254	-0.334	0.8998	0.015	0.298	-0.356	0.9036	0.002	0.231
CSF2_P605_F	cg21708430	5	0.8866	-0.306	0.8648	-2.46	0.007	0.259	-0.151	0.8771	0.208	0.548	-0.228	0.8707	0.017	0.306
ACVR1_E328_R	cg09919801	2	0.7775	-0.435	0.6933	-10.83	0.008	0.259	-0.171	0.7431	0.314	0.618	-0.303	0.7171	0.026	0.331
BCL2L2_E172_F	cg09582636	14	0.0962	0.287	0.1083	12.58	0.008	0.267	0.054	0.0925	0.662	0.848	0.177	0.1008	0.060	0.385
BGN_E282_R	cg00993428	X	0.7072	-0.348	0.6408	-9.39	0.009	0.268	-0.161	0.6805	0.243	0.577	-0.257	0.6598	0.020	0.314
CTSL_P264_R	cg20035138	9	0.4556	-0.359	0.3768	-17.30	0.010	0.272	-0.235	0.4131	0.087	0.425	-0.297	0.3942	0.007	0.259
MCF2_E195_F	cg20900840	X	0.8476	-0.352	0.8090	-4.55	0.010	0.272	-0.126	0.8326	0.382	0.663	-0.236	0.8203	0.040	0.356
CTGF_P693_R	cg15155239	6	0.8080	-0.410	0.7308	-9.55	0.011	0.277	-0.033	0.7999	0.857	0.942	-0.236	0.7639	0.090	0.429
EPHA2_P203_F	cg15146752	1	0.5861	-0.380	0.5034	-14.11	0.011	0.277	-0.097	0.5584	0.515	0.755	-0.240	0.5297	0.046	0.368
SEPT9_P374_F	cg11617283	17	0.4313	-0.490	0.3552	-17.64	0.012	0.286	-0.157	0.3750	0.386	0.666	-0.312	0.3647	0.035	0.351
HOXC6_P456_R	cg02491017	12	0.2176	-0.426	0.1789	-17.78	0.013	0.298	-0.288	0.1830	0.074	0.410	-0.357	0.1809	0.006	0.251
RARRES1_P57_R	cg12199224	3	0.7029	-0.238	0.6714	-4.48	0.014	0.298	-0.115	0.6642	0.235	0.567	-0.176	0.6680	0.024	0.331
PTHR1_E36_R	cg21954799	3	0.9055	-0.324	0.8831	-2.47	0.014	0.298	-0.171	0.8950	0.225	0.557	-0.249	0.8888	0.026	0.331
CCKAR_P270_F	cg12336680	4	0.8503	-0.300	0.7996	-5.96	0.014	0.298	-0.261	0.8182	0.034	0.350	-0.280	0.8085	0.006	0.251
VBP1_P12_R	cg16091746	X	0.5217	-0.322	0.4388	-15.89	0.015	0.298	-0.032	0.5138	0.809	0.922	-0.179	0.4747	0.090	0.429
GPC3_E72_F	cg27496708	X	0.7230	-0.337	0.6627	-8.34	0.015	0.298	-0.230	0.6613	0.102	0.443	-0.284	0.6620	0.012	0.294
CYP2E1_P416_F	cg17336072	10	0.7988	-0.410	0.7473	-6.45	0.015	0.298	-0.277	0.7605	0.108	0.448	-0.344	0.7536	0.014	0.298
GUCY2D_P48_R	cg18094470	17	0.3178	0.366	0.3926	23.54	0.015	0.298	-0.027	0.3096	0.868	0.947	0.180	0.3529	0.156	0.503

SLC14A1_P369_R	cg00377772	18	0.7573	-0.343	0.7006	-7.49	0.016	0.300	-0.302	0.6927	0.032	0.344	-0.322	0.6968	0.005	0.251
TRIP6_P1090_F	cg09357642	7	0.6303	-0.349	0.5629	-10.69	0.016	0.300	-0.218	0.5761	0.129	0.472	-0.283	0.5692	0.015	0.298
HSPA2_P162_R	cg05316932	14	0.8962	-0.332	0.8717	-2.73	0.017	0.305	-0.208	0.8769	0.143	0.492	-0.269	0.8742	0.020	0.314
TRIM29_P135_F	cg24593464	11	0.7623	-0.339	0.7122	-6.57	0.017	0.306	-0.139	0.7379	0.348	0.641	-0.239	0.7245	0.043	0.365
SNURF_P78_F	cg15999943	15	0.7719	-0.364	0.7180	-6.98	0.017	0.306	-0.304	0.7151	0.044	0.368	-0.334	0.7166	0.007	0.259
LOX_P313_R	cg08623535	5	0.2852	-0.412	0.2234	-21.67	0.017	0.307	-0.293	0.2321	0.084	0.421	-0.353	0.2276	0.009	0.267
TDG_E129_F	cg09857351	12	0.7800	-0.302	0.7404	-5.08	0.018	0.311	-0.234	0.7432	0.071	0.404	-0.267	0.7417	0.011	0.277
MCAM_P265_R	cg19017850	11	0.2808	-0.333	0.2192	-21.94	0.019	0.314	-0.126	0.2398	0.349	0.641	-0.231	0.2291	0.035	0.350
VAMP8_P241_F	cg05486094	2	0.5886	-0.276	0.5422	-7.88	0.020	0.314	-0.164	0.5499	0.166	0.514	-0.221	0.5459	0.021	0.316
MAGEA1_P926_F	cg03363189	X	0.8920	-0.380	0.8707	-2.39	0.020	0.314	-0.081	0.8857	0.652	0.842	-0.227	0.8779	0.102	0.443
S100A2_E36_R	cg09232826	1	0.5736	-0.357	0.5106	-10.98	0.020	0.314	-0.179	0.5473	0.242	0.576	-0.268	0.5282	0.029	0.336
SPI1_E205_F	cg07675031	11	0.5855	-0.251	0.5337	-8.47	0.020	0.314	-0.121	0.5627	0.264	0.591	-0.186	0.5476	0.032	0.344
HDAC7A_P344_F	cg25755806	12	0.9108	-0.371	0.8577	-5.83	0.020	0.314	0.014	0.9095	0.945	0.983	-0.218	0.8825	0.133	0.477
PRKCDBP_P352_R	cg21590521	11	0.2438	-0.406	0.2049	-16.00	0.020	0.314	-0.182	0.2085	0.265	0.591	-0.294	0.2066	0.027	0.332
SNCG_P53_F	cg12027410	10	0.6535	-0.394	0.5725	-12.39	0.021	0.317	-0.284	0.5866	0.098	0.442	-0.339	0.5792	0.015	0.298
TYRO3_P366_F	cg10391513	15	0.2479	-0.323	0.1899	-23.40	0.023	0.324	-0.347	0.1844	0.018	0.311	-0.335	0.1873	0.003	0.251
ZP3_P220_F	cg14667235	7	0.7647	-0.354	0.7146	-6.55	0.024	0.331	-0.162	0.7282	0.318	0.621	-0.256	0.7211	0.048	0.372
GRPR_P200_R	cg26196133	X	0.7302	-0.307	0.6812	-6.71	0.025	0.331	-0.258	0.6823	0.059	0.382	-0.282	0.6817	0.011	0.278
MECP2_P398_R	cg04941592	X	0.6285	-0.306	0.5613	-10.69	0.026	0.331	-0.126	0.5945	0.364	0.649	-0.218	0.5772	0.050	0.377
PTPRH_P255_F	cg17314748	19	0.8994	-0.425	0.8834	-1.78	0.026	0.331	-0.226	0.8847	0.254	0.581	-0.320	0.8840	0.045	0.368
BRCA1_P835_R	cg00579360	17	0.7037	-0.325	0.6393	-9.15	0.026	0.331	-0.106	0.6819	0.486	0.731	-0.217	0.6597	0.072	0.404
KRT5_P308_F	cg03540813	12	0.7591	-0.286	0.7197	-5.19	0.027	0.331	-0.081	0.7401	0.549	0.779	-0.185	0.7295	0.084	0.421
HLA-F_E402_F	cg19070841	6	0.0801	-3.807	0.0551	-31.21	0.027	0.331	2.058	0.0902	0.004	0.251	-0.215	0.0719	0.524	0.760
Xist_seq_80_S47_R	cg11717280	X	0.8000	-0.265	0.7703	-3.71	0.027	0.332	-0.176	0.7726	0.151	0.498	-0.221	0.7714	0.025	0.331
THBS2_E129_F	cg05068443	6	0.1148	0.404	0.1601	39.46	0.028	0.332	-0.193	0.0914	0.454	0.708	0.150	0.1272	0.380	0.662
LEFTY2_P719_F	cg09540507	1	0.8861	-0.392	0.8578	-3.19	0.029	0.336	-0.119	0.8753	0.540	0.769	-0.249	0.8662	0.103	0.443
SERPIN5_P19_R	cg22362057	18	0.7934	-0.366	0.7329	-7.63	0.030	0.336	-0.019	0.7850	0.920	0.973	-0.198	0.7578	0.166	0.513
IL6_E168_F	cg05401786	7	0.2455	-0.284	0.2085	-15.07	0.031	0.340	-0.287	0.1887	0.034	0.349	-0.285	0.1990	0.006	0.251
EPHB1_E202_R	cg23448029	3	0.7920	-0.280	0.7537	-4.84	0.031	0.341	-0.128	0.7609	0.339	0.638	-0.204	0.7572	0.057	0.378
IL13_E75_R	cg20391122	5	0.9255	-0.281	0.9084	-1.85	0.032	0.344	-0.135	0.9184	0.336	0.635	-0.211	0.9132	0.057	0.378
KRT5_E196_R	cg04254916	12	0.8843	-0.349	0.8450	-4.44	0.033	0.346	-0.150	0.8696	0.394	0.671	-0.253	0.8567	0.069	0.399
FGF1_E5_F	cg02259548	5	0.7991	-0.305	0.7553	-5.48	0.033	0.346	-0.138	0.7774	0.359	0.648	-0.223	0.7659	0.061	0.385
HDAC5_E298_F	cg08753986	17	0.4026	-0.207	0.3697	-8.17	0.033	0.346	-0.203	0.3407	0.038	0.351	-0.205	0.3558	0.008	0.267
MCF2_P1024_R	cg13637055	X	0.8422	-0.281	0.8169	-3.00	0.034	0.349	-0.152	0.8229	0.264	0.591	-0.214	0.8198	0.051	0.377
DNAJC15_P65_F	cg05035143	13	0.8359	-0.314	0.8021	-4.04	0.034	0.349	-0.270	0.7903	0.067	0.398	-0.291	0.7964	0.016	0.301
IGFBP7_P297_F	cg10799769	4	0.4365	-0.343	0.3782	-13.36	0.034	0.350	0.003	0.4154	0.984	0.995	-0.167	0.3960	0.186	0.532
IL16_P93_R	cg13639030	15	0.5989	-0.306	0.5342	-10.80	0.035	0.350	-0.262	0.5388	0.072	0.404	-0.284	0.5364	0.015	0.298
TNK1_P221_F	cg26000767	17	0.4806	-0.295	0.4149	-13.67	0.036	0.351	-0.232	0.4169	0.099	0.442	-0.263	0.4158	0.019	0.311
PTHR1_P170_R	cg04041000	3	0.8938	-0.454	0.8619	-3.57	0.036	0.351	-0.279	0.8803	0.224	0.556	-0.357	0.8707	0.052	0.377
IRF7_P277_R	cg01030720	11	0.1619	0.535	0.1952	20.57	0.036	0.351	0.204	0.1711	0.445	0.704	0.369	0.1836	0.085	0.421
ESR1_E298_R	cg17191385	6	0.1579	-0.301	0.1226	-22.36	0.037	0.351	-0.405	0.1124	0.009	0.268	-0.350	0.1178	0.002	0.231
SLC5A8_P38_R	cg13433302	12	0.2205	-0.432	0.1668	-24.35	0.037	0.351	-0.150	0.1834	0.419	0.688	-0.292	0.1748	0.057	0.378
NBL1_E205_R	cg21813747	1	0.7836	-0.317	0.7437	-5.09	0.037	0.351	-0.046	0.7775	0.775	0.903	-0.178	0.7599	0.157	0.503
TNFRSF10D_P70_F	cg04134048	8	0.4346	0.439	0.5100	17.35	0.037	0.351	-0.264	0.3633	0.234	0.567	0.088	0.4398	0.609	0.822
COL6A1_P283_F	cg22734035	21	0.0398	0.497	0.0513	28.89	0.038	0.351	-0.262	0.0288	0.518	0.758	0.238	0.0405	0.307	0.614
DSG1_E292_F	cg20099449	18	0.8737	-0.228	0.8543	-2.22	0.038	0.351	-0.009	0.8736	0.942	0.982	-0.121	0.8635	0.189	0.534
IGFBP5_P9_R	cg20419545	2	0.2434	-0.322	0.1958	-19.56	0.040	0.359	-0.156	0.2265	0.295	0.608	-0.238	0.2105	0.047	0.369
HLA-DQA2_E93_F	cg15869057	6	0.6858	-0.228	0.6501	-5.21	0.040	0.360	-0.338	0.6117	0.002	0.231	-0.283	0.6317	0.002	0.211

SEPT9_P58_R	cg05428394	17	0.6676	-0.379	0.5901	-11.61	0.041	0.360	-0.077	0.6539	0.686	0.859	-0.230	0.6207	0.130	0.472
PRSS8_E134_R	cg27436259	16	0.8046	-0.299	0.7638	-5.07	0.041	0.363	-0.124	0.7861	0.422	0.692	-0.213	0.7744	0.082	0.419
MUSK_P308_F	cg22051739	9	0.8136	-0.242	0.7869	-3.28	0.042	0.363	-0.009	0.8143	0.946	0.984	-0.128	0.8001	0.197	0.541
FLJ20712_P984_R	cg05794098	7	0.6105	-0.275	0.5540	-9.25	0.043	0.365	-0.480	0.4854	0.000	0.132	-0.379	0.5211	0.001	0.145
FANCE_P356_R	cg04035266	6	0.2097	0.358	0.2577	22.89	0.043	0.368	-0.391	0.1658	0.102	0.443	0.030	0.2137	0.850	0.940
PDGFRA_E125_F	cg20629161	4	0.5449	-0.328	0.4732	-13.16	0.044	0.368	-0.293	0.4689	0.067	0.398	-0.310	0.4711	0.016	0.301
PMP22_P975_F	cg08815822	17	0.8172	-0.306	0.7851	-3.93	0.044	0.368	-0.112	0.7972	0.483	0.729	-0.208	0.7909	0.099	0.443
ATP10A_P147_F	cg06932470	15	0.4014	0.364	0.4819	20.05	0.045	0.368	0.250	0.4529	0.171	0.518	0.307	0.4680	0.035	0.351
RARRES1_P426_R	cg13848998	3	0.5410	-0.342	0.4686	-13.38	0.045	0.368	-0.266	0.4720	0.117	0.461	-0.304	0.4702	0.026	0.331
NTRK2_P10_F	cg23399093	9	0.1405	-0.449	0.1020	-27.40	0.045	0.368	-0.604	0.0908	0.015	0.298	-0.524	0.0967	0.004	0.251
TNC_P57_F	cg01250769	9	0.1516	-0.269	0.1260	-16.89	0.045	0.368	-0.123	0.1288	0.346	0.641	-0.199	0.1273	0.056	0.378
GLI3_E148_R	cg12211443	7	0.8793	-0.386	0.8487	-3.48	0.045	0.368	-0.336	0.8521	0.083	0.421	-0.361	0.8503	0.024	0.331
G6PD_P597_F	cg26178557	X	0.7432	-0.281	0.6902	-7.13	0.046	0.368	-0.195	0.7051	0.171	0.518	-0.239	0.6973	0.038	0.351
SFTPC_E13_F	cg11540705	8	0.7611	-0.253	0.7124	-6.40	0.047	0.369	-0.189	0.7350	0.138	0.484	-0.220	0.7233	0.033	0.346
USP29_P282_R	cg16675193	19	0.8961	-0.224	0.8854	-1.19	0.047	0.369	-0.063	0.8918	0.599	0.815	-0.143	0.8885	0.128	0.472
VBP1_E127_F	cg10528799	X	0.7240	-0.297	0.6511	-10.07	0.048	0.371	-0.338	0.6569	0.023	0.324	-0.318	0.6539	0.009	0.268
MMP7_P613_F	cg20645973	11	0.8465	-0.205	0.8296	-2.00	0.048	0.372	0.065	0.8532	0.573	0.798	-0.077	0.8409	0.384	0.664

HR+ (n=22 CpGs in current vs never smokers)

FRZB_E186_R	cg01872931	2	0.3326	0.541	0.4163	25.17	0.001	0.568	0.097	0.3447	0.540	0.998	0.305	0.3797	0.021	0.998
MYCL1_P502_R	cg27650434	1	0.0980	0.395	0.1349	37.65	0.003	0.998	0.436	0.1379	0.001	0.568	0.417	0.1365	0.000	0.550
COL1A1_P117_R	cg10100754	17	0.4786	0.366	0.5582	16.63	0.003	0.998	0.094	0.5032	0.429	0.998	0.223	0.5300	0.025	0.998
CCNA1_E7_F	cg27186533	13	0.3422	0.491	0.4265	24.63	0.007	0.998	0.308	0.4061	0.075	0.998	0.393	0.4161	0.007	0.998
COL1A1_P5_F	cg13069732	17	0.5696	0.361	0.6445	13.15	0.007	0.998	0.013	0.5777	0.915	0.998	0.175	0.6103	0.096	0.998
IGF2AS_P203_F	cg14188639	11	0.5979	0.375	0.6747	12.84	0.010	0.998	0.116	0.6134	0.388	0.998	0.234	0.6433	0.039	0.998
TMEFF2_E94_R	cg10026428	2	0.1812	0.393	0.2349	29.64	0.011	0.998	0.199	0.2093	0.201	0.998	0.291	0.2218	0.024	0.998
TAL1_P817_F	cg26891410	1	0.7654	0.322	0.8125	6.15	0.013	0.998	0.049	0.7714	0.665	0.998	0.176	0.7915	0.071	0.998
BMP4_P199_R	cg09229893	14	0.6169	0.354	0.6968	12.95	0.015	0.998	0.175	0.6525	0.190	0.998	0.257	0.6741	0.022	0.998
IGF2_P1036_R	cg04741015	11	0.1249	0.268	0.1543	23.54	0.015	0.998	0.053	0.1324	0.642	0.998	0.155	0.1431	0.093	0.998
SERPINE1_P519_F	cg19722814	7	0.3282	0.252	0.3822	16.45	0.020	0.998	0.152	0.3530	0.151	0.998	0.200	0.3672	0.024	0.998
CALCA_E174_R	cg09068492	11	0.3740	0.319	0.4317	15.43	0.021	0.998	0.209	0.4204	0.120	0.998	0.261	0.4259	0.020	0.998
PTPRO_E56_F	cg23147819	12	0.0904	0.358	0.1053	16.48	0.024	0.998	0.105	0.0959	0.522	0.998	0.230	0.1005	0.085	0.998
HLF_E192_F	cg05876326	17	0.1001	0.438	0.1325	32.37	0.025	0.998	0.340	0.1340	0.075	0.998	0.382	0.1333	0.020	0.998
RIPK3_P124_F	cg13583230	14	0.5399	0.285	0.6001	11.15	0.026	0.998	0.133	0.5674	0.274	0.998	0.205	0.5834	0.044	0.998
HOXA11_P92_R	cg18977999	7	0.1876	0.296	0.2219	18.28	0.034	0.998	0.102	0.1950	0.464	0.998	0.192	0.2082	0.096	0.998
TAL1_E122_F	cg00875272	1	0.2406	0.301	0.2928	21.7	0.036	0.998	0.071	0.2550	0.630	0.998	0.182	0.2735	0.128	0.998
OAT_P465_F	cg10231486	10	0.1846	0.190	0.2070	12.13	0.036	0.998	0.029	0.1915	0.749	0.998	0.107	0.1991	0.154	0.998
GFI1_P45_R	cg07499339	1	0.3388	0.257	0.3695	9.06	0.037	0.998	-0.080	0.3328	0.521	0.998	0.082	0.3507	0.419	0.998
POMC_P53_F	cg00293936	2	0.0847	0.341	0.1071	26.45	0.040	0.998	0.180	0.0918	0.275	0.998	0.255	0.0993	0.065	0.998
OPCML_P71_F	cg00738841	11	0.2895	0.212	0.3248	12.19	0.045	0.998	0.094	0.3048	0.367	0.998	0.151	0.3145	0.081	0.998
HBI1-52_P659_F	cg18037269	15	0.8875	-0.225	0.8643	-2.61	0.045	0.998	-0.164	0.8709	0.140	0.998	-0.193	0.8677	0.038	0.998

CpG loci differentially methylated in current versus never smokers at $p < 0.05$ were identified from generalized linear models adjusted for age, menopausal status, race (AA vs. non-AA as appropriate), BMI (<25, 25-29, >29), average alcohol consumption (grams per week), and stage (ordinal, 1-4) in HR+ or HR- tumor subsets. Results for current smoking-associated loci are also shown in former and ever smokers.

Table S2. Correlation of methylation with increasing duration of smoking or years since quitting at current smoking-associated CpG loci in HR- breast tumors

Probe	Duration of smoking in years (ever smokers)		Years since quitting smoking (former smokers)	
	Correlation Coefficient	p value	Correlation Coefficient	p value
RARA_E128_R	-0.2600	0.001	0.2732	0.000
HLF_E192_F	-0.2590	0.001	0.2619	0.001
TYRO3_P366_F	-0.2419	0.002	0.2569	0.001
ESR1_E298_R	-0.2290	0.003	0.2407	0.002
MST1R_E42_R	-0.2133	0.006	0.2321	0.003
EPHA2_P340_R	-0.2229	0.004	0.2201	0.005
ACVR1_P983_F	-0.2000	0.011	0.2119	0.007
FLJ20712_P984_R	-0.2366	0.002	0.2116	0.007
HLA_DQA2_E93_F	-0.2113	0.007	0.2081	0.008
SNCG_P53_F	-0.2082	0.008	0.2080	0.008
CTSL_P264_R	-0.2088	0.008	0.2037	0.009
TRIP6_P1090_F	-0.1891	0.016	0.1991	0.011
CDM_seq_21_S260_R	-0.1877	0.017	0.1993	0.011
CCKAR_P270_F	-0.2455	0.002	0.1990	0.011
SLC14A1_P369_R	-0.2102	0.007	0.1983	0.011
FRK_P258_F	-0.1755	0.026	0.1978	0.011
SEPT9_P374_F	-0.1642	0.037	0.1947	0.013
FGF1_P357_R	-0.1749	0.026	0.1933	0.013
TRIM29_E189_F	-0.1671	0.034	0.1923	0.014
CYP2E1_E53_R	-0.2142	0.006	0.1902	0.015
ACVR1_E328_R	-0.1902	0.015	0.1901	0.015
NTRK2_P10_F	-0.2304	0.003	0.1898	0.015
EPHA2_P203_F	-0.1777	0.024	0.1898	0.015
TDG_E129_F	-0.2202	0.005	0.1872	0.017
IL6_E168_F	-0.1793	0.022	0.1869	0.017
SLC5A8_P38_R	-0.1612	0.041	0.1861	0.017
IL12B_E25_F	-0.2058	0.009	0.1825	0.020
PDGFRA_E125_F	-0.1679	0.033	0.1821	0.020
TNK1_P221_F	-0.1558	0.048	0.1810	0.021
CYP2E1_P416_F	-0.1894	0.016	0.1806	0.021
MCAM_P265_R	-0.1177	0.136	0.1796	0.022
SNCG_P98_R	-0.1832	0.020	0.1756	0.025
VBP1_P12_R	-0.1854	0.018	0.1734	0.027
DSC2_P407_R	-0.1552	0.049	0.1729	0.027
GPC3_E72_F	-0.2237	0.004	0.1723	0.028
BRCA1_P835_R	-0.1982	0.012	0.1688	0.031
KRT5_E196_R	-0.1761	0.025	0.1685	0.032
VBP1_E127_F	-0.2218	0.005	0.1665	0.034
HDAC5_E298_F	-0.1530	0.052	0.1657	0.035
RARRES1_P426_R	-0.1622	0.039	0.1651	0.035
MAP3K8_P1036_F	-0.1487	0.059	0.1649	0.036
HOXC6_P456_R	-0.1611	0.041	0.1642	0.036
IGFBP5_P9_R	-0.1624	0.039	0.1626	0.038
IL16_P93_R	-0.1542	0.050	0.1626	0.038
CTGF_P693_R	-0.1803	0.022	0.1623	0.039
MYCL1_P502_R	-0.1512	0.055	0.1598	0.042
IGFBP7_P297_F	-0.1347	0.088	0.1569	0.046
MC2R_P1025_F	-0.1487	0.059	0.1558	0.047
SEPT9_P58_R	-0.1314	0.096	0.1556	0.047
ITGA6_P718_R	-0.1632	0.038	0.1546	0.049
LOX_P313_R	-0.1472	0.062	0.1532	0.051
BGN_E282_R	-0.1684	0.032	0.1518	0.053
PRKCDBP_P352_R	-0.1655	0.035	0.1511	0.054
ATP10A_P147_F	0.1611	0.041	-0.1511	0.054
SNURF_P78_F	-0.1584	0.044	0.1510	0.054
GUCY2D_P48_R	0.0796	0.314	-0.1460	0.063
VAMP8_P241_F	-0.1138	0.150	0.1436	0.068
S100A2_E36_R	-0.1284	0.103	0.1399	0.075
ZP3_P220_F	-0.1042	0.187	0.1377	0.080

BMPR1A_E88_F	-0.0883	0.264	0.1373	0.081
SERPINB5_P19_R	-0.1159	0.142	0.1358	0.084
PRSS8_E134_R	-0.1456	0.065	0.1355	0.085
SPI1_E205_F	-0.1480	0.060	0.1302	0.098
TNC_P57_F	-0.1452	0.065	0.1273	0.105
FGF1_E5_F	-0.1341	0.089	0.1259	0.109
EPHB1_E202_R	-0.1171	0.138	0.1241	0.115
MAPK9_P1175_F	-0.1382	0.080	0.1235	0.116
PIK3R1_P307_F	-0.1073	0.174	0.1172	0.136
MCF2_P1024_R	-0.1491	0.058	0.1170	0.137
NBL1_E205_R	-0.1278	0.105	0.1156	0.142
HSPA2_P162_R	-0.1192	0.131	0.1127	0.152
MECP2_P398_R	-0.1258	0.111	0.1123	0.153
MCF2_E195_F	-0.1109	0.160	0.1112	0.158
KRT5_P308_F	-0.1224	0.121	0.1096	0.164
PTHR1_E36_R	-0.1178	0.136	0.1091	0.166
RARRES1_P57_R	-0.0690	0.383	0.1033	0.190
HGF_P1293_R	-0.1386	0.079	0.0998	0.205
GLI3_E148_R	-0.1136	0.150	0.0980	0.213
G6PD_P597_F	-0.1144	0.147	0.0965	0.220
IL13_E75_R	-0.1011	0.201	0.0936	0.235
DNAJC15_P65_F	-0.0754	0.340	0.0907	0.250
LEFTY2_P719_F	-0.0734	0.353	0.0814	0.302
SFTPC_E13_F	-0.0971	0.219	0.0781	0.322
HDAC7A_P344_F	-0.0898	0.256	0.0767	0.330
TRIM29_P135_F	-0.0696	0.379	0.0748	0.343
MUSK_P308_F	-0.0641	0.418	0.0695	0.378
UGT1A1_E11_F	-0.0875	0.268	0.0639	0.418
IRF7_P277_R	0.0170	0.830	-0.0638	0.418
APBA1_E99_R	0.0441	0.578	-0.0631	0.424
Xist_seq_80_S47_R	-0.0852	0.281	0.0627	0.427
BCL2L2_E172_F	-0.0238	0.763	0.0575	0.466
CSF2_P605_F	-0.0883	0.264	0.0561	0.477
DSG1_E292_F	-0.0501	0.527	0.0534	0.499
CDKN1A_P242_F	-0.1267	0.108	0.0529	0.503
MAGEA1_P926_F	-0.0600	0.448	0.0484	0.539
PTHR1_P170_R	-0.0619	0.434	0.0441	0.577
USP29_P282_R	-0.0381	0.630	0.0431	0.585
ZIM3_P451_R	-0.0482	0.542	0.0420	0.594
TNFRSF10D_P70_F	0.0256	0.746	-0.0420	0.595
PMP22_P975_F	-0.0311	0.694	0.0380	0.630
MMP7_P613_F	-0.0308	0.698	0.0372	0.638
PTPRH_P255_F	-0.0551	0.486	0.0318	0.688
HLA_F_E402_F	0.0201	0.800	-0.0290	0.713
MCC_P196_R	-0.0589	0.457	0.0276	0.726
COL6A1_P283_F	-0.0460	0.561	0.0231	0.770
FANCE_P356_R	-0.0217	0.785	-0.0214	0.786
THBS2_E129_F	0.0002	0.998	-0.0209	0.792

Spearman correlation coefficients and p values were used to test the relationship between increasing duration of smoking among ever smokers or years since quitting among former smokers and tumor methylation at smoking-associated CpG loci identified from GLM. Duration of smoking in years was tested across never smokers and ≤ 10 years, 11-20 years, and >20 years smoked. Years since quitting among former smokers was tested across 0 years (current smokers), ≤ 10 years, 11+ years since smoking cessation.

Table S3. Correlation of methylation and gene expression in TCGA breast tumors for CpG loci differentially methylated in current vs. never smokers

Cancer Panel CpG probe	450K CpG probe	All tumors			HR+			HR-		
		Coefficient	N	p value	Coefficient	N	p value	Coefficient	N	p value
APBA1_E99_R	cg18505908	-0.0478	581	2.50E-01	-0.0589	391	2.45E-01	-0.1167	97	2.55E-01
BMP4_P199_R	cg09229893	-0.4099	581	6.05E-25	-0.4423	391	3.73E-20	-0.3012	97	2.72E-03
CALCA_E174_R	cg09068492	-0.1516	215	2.63E-02	-0.1746	128	4.87E-02	-0.1215	51	3.96E-01
CDKN1A_P242_F	cg23305046	-0.1768	581	1.81E-05	-0.2106	391	2.69E-05	-0.1161	97	2.58E-01
DNAJC15_P65_F	cg05035143	-0.2171	581	1.25E-07	-0.1482	391	3.31E-03	-0.3079	97	2.15E-03
DSG1_E292_F	cg20099449	-0.3542	513	1.31E-16	-0.0317	338	5.62E-01	-0.7035	91	7.48E-15
EPHA2_P203_F	cg15146752	-0.2204	581	8.01E-08	-0.2357	391	2.45E-06	-0.3337	97	8.36E-04
FRK_P258_F	cg26557270	-0.2873	581	1.68E-12	-0.3102	391	3.63E-10	-0.1687	97	9.86E-02
GPC3_E72_F	cg27496708	0.0684	581	9.97E-02	0.0427	391	3.99E-01	0.0213	97	8.36E-01
GRPR_P200_R	cg26196133	0.0997	575	1.68E-02	0.1735	390	5.81E-04	0.1112	93	2.89E-01
HGF_P1293_R	cg14690980	0.1162	581	5.03E-03	0.1055	391	3.70E-02	0.0529	97	6.07E-01
HOXA11_P92_R	cg18977999	-0.0449	580	2.81E-01	-0.0462	391	3.63E-01	-0.0591	96	5.67E-01
HOXC6_P456_R	cg02491017	-0.2757	581	1.35E-11	-0.3683	391	5.28E-14	-0.0872	97	3.96E-01
IGF2AS_P203_F	cg14188639	-0.1353	484	2.85E-03	-0.1644	332	2.66E-03	-0.1636	69	1.79E-01
IGFBP5_P9_R	cg20419545	-0.1779	581	1.61E-05	-0.1766	391	4.50E-04	-0.0663	97	5.19E-01
IL12B_E25_F	cg18307303	0.2860	516	3.58E-11	0.2756	343	2.14E-07	0.2805	89	7.76E-03
KRT5_E196_R	cg04254916	-0.0992	576	1.73E-02	0.0082	388	8.73E-01	-0.5324	97	2.00E-08
LOX_P313_R	cg08623535	-0.1129	581	6.42E-03	-0.1447	391	4.13E-03	-0.1170	97	2.54E-01
MMP7_P613_F	cg20645973	-0.2107	580	3.03E-07	0.0244	390	6.31E-01	-0.4697	97	1.21E-06
MYCL1_P502_R	cg27650434	-0.1720	581	3.09E-05	-0.1131	391	2.54E-02	-0.2277	97	2.49E-02
NBL1_E205_R	cg21813747	-0.0789	581	5.73E-02	-0.0638	391	2.08E-01	0.0155	97	8.80E-01
POMC_P53_F	cg00293936	-0.1870	578	6.04E-06	-0.1257	388	1.32E-02	-0.2278	97	2.48E-02
PRSS8_E134_R	cg27436259	-0.2833	581	3.45E-12	-0.2691	391	6.48E-08	-0.3046	97	2.42E-03
RIPK3_P124_F	cg13583230	-0.7121	581	5.39E-91	-0.7180	391	3.46E-63	-0.6097	97	3.40E-11
SERPINE1_P519_F	cg19722814	-0.1047	581	1.16E-02	-0.0762	391	1.32E-01	-0.1310	97	2.01E-01
SFTPC_E13_F	cg11540705	0.1300	103	1.91E-01	0.2483	53	7.31E-02	0.0450	35	7.97E-01
SLC5A8_P38_R	cg13433302	-0.2212	406	6.83E-06	-0.2612	270	1.38E-05	0.0307	76	7.92E-01
SNCG_P98_R	cg03677069	-0.1766	581	1.87E-05	-0.2211	391	1.02E-05	0.0248	97	8.10E-01
SPI1_E205_F	cg07675031	-0.4957	581	2.35E-37	-0.4881	391	8.49E-25	-0.5888	97	2.26E-10
TAL1_E122_F	cg00875272	-0.1995	581	1.26E-06	-0.1784	391	3.94E-04	0.1227	97	2.31E-01
TAL1_P817_F	cg26891410	-0.0682	581	1.01E-01	-0.1102	391	2.94E-02	0.1838	97	7.15E-02
TNFRSF10D_P70_F	cg04134048	-0.5006	581	3.49E-38	-0.4131	391	1.52E-17	-0.5511	97	4.95E-09
TRIM29_P135_F	cg24593464	-0.2593	581	2.23E-10	-0.0882	391	8.17E-02	-0.5300	97	2.37E-08
UGT1A1_E11_F	cg03607648	0.1866	68	1.28E-01	0.0668	42	6.74E-01	0.3121	15	2.57E-01
USP29_P282_R	cg16675193	-0.1135	22	6.15E-01	0.1781	14	5.43E-01	-0.6075	5	2.77E-01
VAMP8_P241_F	cg05486094	-0.1873	581	5.50E-06	-0.1707	391	7.02E-04	-0.2752	97	6.36E-03
VBP1_P12_R	cg16091746	-0.2854	581	2.39E-12	-0.2608	391	1.69E-07	-0.3059	97	2.31E-03
Xist_seq_80_S47_R	cg11717280	-0.5489	580	6.03E-47	-0.5577	390	2.91E-33	-0.6358	97	2.62E-12
ZP3_P220_F	cg14667235	-0.3102	581	2.02E-14	-0.2970	391	2.10E-09	-0.2230	97	2.81E-02

CpGs are restricted to those that exactly match between the Illumina Cancer Panel I array used in this study and the Illumina 450K methylation platform used in TCGA. Pearson correlation coefficients were calculated in 581 TCGA breast tumors to test the relationship between methylation and RNAseq expression.

Table S4. CpG loci differentially methylated at p<0.05 in current vs. never smokers, by race and HR status

Black cases

HR+ (n=40 CpGs; 40 hyper)

HR- (n=67 CpGs; 52 hypo, 15 hyper)

Probe	Coefficient Current vs. Never	Current Mean Beta	Never Mean Beta	p value	FDR adjusted p value	Probe	Coefficient Current vs. Never	Current Mean Beta	Never Mean Beta	p value	FDR adjusted p value
RIPK4_P172_F	1.0233	0.1733	0.1111	1.55E-05	1.45E-02	BMPR1A_E88_F	-0.6321	0.6046	0.7331	1.33E-04	1.24E-01
SMO_E57_F	1.2224	0.1006	0.0739	4.17E-05	1.95E-02	MAP3K8_P1036_F	-0.7746	0.4220	0.6405	4.72E-04	2.20E-01
MAF_P826_R	0.9624	0.1293	0.0940	1.19E-04	3.70E-02	TNF_P158_F	1.0571	0.1968	0.1086	7.94E-04	2.47E-01
MYCL1_P502_R	0.6765	0.1580	0.0904	7.27E-04	1.60E-01	RASGRF1_P768_F	0.6871	0.1149	0.0891	2.52E-03	4.73E-01
FN1_E469_F	0.8020	0.1643	0.1081	8.84E-04	1.60E-01	LEFTY2_P719_F	-0.7097	0.8870	0.9023	2.53E-03	4.73E-01
POMC_P53_F	0.7541	0.1079	0.0803	1.13E-03	1.60E-01	IGF1_E394_F	-0.4934	0.5468	0.6563	3.74E-03	5.37E-01
HLF_E192_F	0.8922	0.1496	0.0901	1.20E-03	1.60E-01	TNFRSF10A_P91_F	0.6200	0.2364	0.1534	5.41E-03	5.37E-01
ITGA2_P26_R	0.4556	0.0949	0.0700	1.54E-03	1.80E-01	DMP1_E194_F	-0.4308	0.8829	0.9059	5.80E-03	5.37E-01
TNC_P198_F	0.6849	0.3158	0.2272	2.48E-03	2.57E-01	FGF1_P357_R	-0.5877	0.5581	0.6967	7.01E-03	5.37E-01
MYLK_E132_R	0.4817	0.2255	0.1889	2.98E-03	2.60E-01	MC2R_P1025_F	-0.7254	0.3556	0.5094	8.02E-03	5.37E-01
ER_seq_a1_S60_F	0.5030	0.1891	0.1545	3.07E-03	2.60E-01	PIK3R1_P307_F	-0.3442	0.8878	0.9099	8.97E-03	5.37E-01
NTSR1_E109_F	0.7769	0.1192	0.0879	5.52E-03	4.29E-01	POMC_P53_F	0.4499	0.1093	0.0842	9.02E-03	5.37E-01
IGF2AS_P203_F	0.8061	0.7253	0.5771	7.71E-03	5.54E-01	ITGA6_P718_R	-0.4768	0.8856	0.9239	9.10E-03	5.37E-01
Xist_seq_80_S95_R	0.4508	0.8035	0.7447	1.02E-02	6.78E-01	EPHA1_P119_R	0.6752	0.1310	0.1063	9.11E-03	5.37E-01
CDM_seq_21_S260_R	0.4475	0.4417	0.3408	1.37E-02	8.52E-01	HDAC7A_P344_F	-0.8071	0.8472	0.9168	9.13E-03	5.37E-01
DLL1_P386_F	0.6471	0.0845	0.0632	1.56E-02	9.07E-01	DSC2_P407_R	-0.4419	0.8032	0.8515	9.50E-03	5.37E-01
ODC1_P424_F	0.5836	0.0803	0.0681	1.88E-02	9.92E-01	CSF1_P339_F	-3.0064	0.0936	0.1336	1.01E-02	5.37E-01
RET_seq_53_S374_F	0.6445	0.1182	0.0954	2.03E-02	9.92E-01	RBP1_P150_F	-1.7366	0.0708	0.0943	1.04E-02	5.37E-01
PTPRO_E56_F	0.6928	0.1205	0.0935	2.15E-02	9.92E-01	TSP50_E21_R	-0.5170	0.7890	0.8435	1.09E-02	5.37E-01
MYH11_P236_R	0.6674	0.2590	0.1584	2.38E-02	9.92E-01	TRIM29_E189_F	-0.4302	0.6567	0.7629	1.16E-02	5.43E-01
DSP_P440_R	0.4560	0.1046	0.0898	2.48E-02	9.92E-01	RARA_E128_R	-0.6477	0.1304	0.2512	1.34E-02	5.67E-01
CCNA1_E7_F	0.7450	0.4691	0.3446	2.58E-02	9.92E-01	S100A2_P1186_F	-0.5465	0.5530	0.6661	1.41E-02	5.67E-01
CASP2_P192_F	0.6008	0.0886	0.0869	2.60E-02	9.92E-01	DDR1_P332_R	-0.5677	0.3191	0.4672	1.43E-02	5.67E-01
MMP9_P237_R	0.4731	0.2188	0.1804	2.68E-02	9.92E-01	ZP3_P220_F	-0.4898	0.7010	0.7672	1.46E-02	5.67E-01
PMP22_P975_F	0.5174	0.8192	0.7602	2.93E-02	9.92E-01	SPI1_E205_F	-0.3666	0.5343	0.6090	1.59E-02	5.81E-01
TPEF_seq_44_S88_R	0.6158	0.5207	0.4219	3.10E-02	9.92E-01	FASTK_P598_R	-0.3818	0.6121	0.7028	1.73E-02	5.81E-01
EVI2A_P94_R	0.5858	0.8330	0.7915	3.17E-02	9.92E-01	OGG1_E400_F	-0.5321	0.3077	0.4461	1.87E-02	5.81E-01
PCDH1_P264_F	0.4697	0.2499	0.1699	3.24E-02	9.92E-01	FGF1_E5_F	-0.4465	0.7328	0.8092	2.07E-02	5.81E-01
WNT10B_P993_F	0.4384	0.2845	0.2152	3.28E-02	9.92E-01	DNMT3B_P352_R	-0.4352	0.1578	0.2198	2.11E-02	5.81E-01
DST_P262_R	0.3244	0.1105	0.1018	3.44E-02	9.92E-01	TDG_E129_F	-0.3904	0.7523	0.8032	2.15E-02	5.81E-01
PTHR1_P170_R	0.7419	0.9063	0.8488	3.58E-02	9.92E-01	LOX_P313_R	-0.5750	0.1947	0.2935	2.21E-02	5.81E-01
TFAP2C_P765_F	0.7041	0.2014	0.1747	3.64E-02	9.92E-01	SLC5A8_P38_R	-0.5007	0.1451	0.2214	2.31E-02	5.81E-01
CYP1B1_E83_R	0.5170	0.2964	0.2341	3.68E-02	9.92E-01	EPHA2_P203_F	-0.5000	0.4310	0.5725	2.32E-02	5.81E-01
OSM_P34_F	0.4233	0.6574	0.6106	3.95E-02	9.92E-01	FRK_P258_F	-0.5717	0.4995	0.6184	2.34E-02	5.81E-01
GSTM1_P266_F	0.4103	0.5947	0.5405	3.98E-02	9.92E-01	HS3ST2_E145_R	0.7848	0.6934	0.5369	2.36E-02	5.81E-01
ALPL_P278_F	0.6248	0.1180	0.0890	4.04E-02	9.92E-01	TMPRSS4_E83_F	-0.5454	0.8228	0.8992	2.36E-02	5.81E-01
OPCML_E219_R	0.6084	0.3395	0.2667	4.10E-02	9.92E-01	HHIP_P578_R	-0.4281	0.4311	0.4851	2.37E-02	5.81E-01
SMARCA3_P109_R	0.3140	0.1082	0.0902	4.13E-02	9.92E-01	TYRO3_P366_F	-0.4837	0.1739	0.2523	2.37E-02	5.81E-01
TAL1_E122_F	0.5220	0.3039	0.2462	4.26E-02	9.92E-01	MAPK9_P1175_F	-0.4679	0.8756	0.9146	2.60E-02	5.81E-01
FN1_P229_R	0.4222	0.1721	0.1251	4.82E-02	9.92E-01	TNFRSF10D_E27_F	0.8554	0.5489	0.3652	2.66E-02	5.81E-01
						SNCG_P53_F	-0.5126	0.5326	0.6558	2.75E-02	5.81E-01
						COL6A1_P283_F	0.9089	0.0819	0.0398	2.81E-02	5.81E-01
						NPR2_P618_F	-0.6009	0.2791	0.3657	2.85E-02	5.81E-01
						IGSF4C_P533_R	0.4758	0.1285	0.1138	2.92E-02	5.81E-01
						EPHA1_E46_R	0.4703	0.1420	0.1014	2.98E-02	5.81E-01
						TNFRSF10D_P70_F	0.6809	0.5580	0.4029	3.02E-02	5.81E-01
						HBII-52_P563_F	-0.3213	0.8336	0.8465	3.10E-02	5.81E-01
						EPHA2_P340_R	-0.3914	0.3395	0.4393	3.12E-02	5.81E-01
						IL12B_P392_R	-0.4368	0.4844	0.6302	3.14E-02	5.81E-01
						LY6G6E_P45_R	-0.5272	0.8111	0.8833	3.15E-02	5.81E-01
						CD82_P557_R	-0.5025	0.2084	0.2965	3.22E-02	5.81E-01

						CDM_seq_21_S260_R	-0.3723	0.2807	0.3808	3.24E-02	5.81E-01
						CTSL_P264_R	-0.4191	0.3609	0.4678	3.52E-02	6.11E-01
						IL13_E75_R	-0.3706	0.9019	0.9292	3.54E-02	6.11E-01
						MLH3_P25_F	0.3760	0.1298	0.1270	4.15E-02	6.13E-01
						PDGFB_P719_F	-0.3518	0.6507	0.7379	4.16E-02	6.13E-01
						FGF6_P139_R	-0.3494	0.8724	0.8810	4.22E-02	6.13E-01
						GSTM2_P109_R	0.7004	0.5996	0.4203	4.24E-02	6.13E-01
						ITK_P114_F	0.3887	0.8355	0.7663	4.39E-02	6.13E-01
						DSP_P36_F	-0.4002	0.1704	0.2463	4.45E-02	6.13E-01
						SFRP1_P157_F	0.7504	0.1617	0.1326	4.53E-02	6.13E-01
						SNCG_P98_R	-0.4305	0.5465	0.6560	4.54E-02	6.13E-01
						HIF1A_P488_F	-0.3277	0.1292	0.1642	4.55E-02	6.13E-01
						SEPT9_P374_F	-0.5568	0.3614	0.4411	4.58E-02	6.13E-01
						GPX1_P194_F	-0.9304	0.2321	0.3691	4.61E-02	6.13E-01
						TEK_P526_F	-0.3391	0.7507	0.7745	4.66E-02	6.13E-01
						SNURF_P78_F	-0.3657	0.7526	0.7887	4.72E-02	6.13E-01

White cases

HR+ (n=19 CpGs; 5 hypo, 14 hyper)

HR- (n=114 CpGs; 95 hypo, 19 hyper)

Probe	Coefficient Current vs. Never	Current Mean Beta	Never Mean Beta	p value	FDR adjusted p value	Probe	Coefficient Current vs. never	Current Mean Beta	Never Mean Beta	p value	FDR adjusted p value
FRZB_E186_R	0.6328	0.4437	0.3245	2.27E-03	9.97E-01	DKFZP56400823_E45_F	1.2523	0.1326	0.0855	1.72E-04	1.30E-01
BMP4_P199_R	0.5962	0.7163	0.5833	2.88E-03	9.97E-01	HGF_P1293_R	-0.8890	0.8844	0.9286	2.99E-04	1.30E-01
MYCL1_P502_R	0.4056	0.1363	0.1118	4.41E-03	9.97E-01	TIAM1_P188_R	0.8186	0.1124	0.0766	5.37E-04	1.30E-01
KIAA1804_P689_R	-0.4949	0.1020	0.1521	8.92E-03	9.97E-01	MKRN3_P108_F	-0.9164	0.8067	0.8684	5.57E-04	1.30E-01
CTSL_P264_R	-0.3935	0.3438	0.4226	1.44E-02	9.97E-01	MCF2_E195_F	-0.8312	0.7544	0.8445	7.46E-04	1.37E-01
TMEM63A_E63_F	0.3495	0.0968	0.0744	1.49E-02	9.97E-01	p16_seq_47_S188_R	0.8493	0.0969	0.0726	9.30E-04	1.37E-01
LAMB1_E144_R	-0.2676	0.1526	0.1995	1.60E-02	9.97E-01	SOD3_P225_F	-0.6423	0.8945	0.9242	1.03E-03	1.37E-01
MST1R_P392_F	-0.4253	0.1368	0.1673	2.55E-02	9.97E-01	ZIM3_P451_R	-1.0043	0.8933	0.9348	1.32E-03	1.48E-01
PLXDC2_E337_F	0.3671	0.0906	0.0753	2.59E-02	9.97E-01	MCC_P196_R	-1.5974	0.0458	0.0476	1.43E-03	1.48E-01
OPCML_P71_F	0.2931	0.3346	0.3042	3.07E-02	9.97E-01	IL12B_E25_F	-0.6717	0.8150	0.8784	1.72E-03	1.61E-01
HOXA11_P92_R	0.3777	0.2276	0.1739	3.20E-02	9.97E-01	CSF2_P605_F	-0.6072	0.8469	0.8900	2.07E-03	1.76E-01
S100A4_E315_F	-0.3719	0.2881	0.3521	3.29E-02	9.97E-01	WRN_P969_F	-0.7955	0.8517	0.8934	2.73E-03	1.92E-01
ESR2_E66_F	0.5253	0.2316	0.1764	3.67E-02	9.97E-01	ACVR1_P983_F	-0.6915	0.7820	0.8490	2.76E-03	1.92E-01
KDR_E79_F	0.4450	0.1609	0.1149	3.77E-02	9.97E-01	CDKN1A_P242_F	2.5126	0.1232	0.0638	3.00E-03	1.92E-01
COL1A1_P117_R	0.3184	0.5654	0.4898	3.85E-02	9.97E-01	Xist_seq_80_S47_R	-0.5249	0.7326	0.8006	3.19E-03	1.92E-01
BMP4_P123_R	0.3927	0.4154	0.3238	4.03E-02	9.97E-01	PTHR1_E36_R	-0.6837	0.8714	0.9095	3.29E-03	1.92E-01
ASCL1_E24_F	0.4929	0.1374	0.0973	4.04E-02	9.97E-01	CD9_P585_R	-0.7817	0.5085	0.6403	4.15E-03	2.18E-01
CDH11_P203_R	0.4671	0.1202	0.1005	4.22E-02	9.97E-01	VAMP8_P241_F	-0.5719	0.4911	0.6022	4.46E-03	2.18E-01
CCND2_P898_R	0.4135	0.3092	0.2615	4.62E-02	9.97E-01	MECP2_P398_R	-0.6246	0.5374	0.6391	4.53E-03	2.18E-01
						DSC2_P407_R	-0.6764	0.8093	0.8621	4.79E-03	2.18E-01
						PIK3R1_P307_F	-0.5384	0.8735	0.9069	4.91E-03	2.18E-01
						MKRN3_E144_F	-0.8455	0.8196	0.8785	5.15E-03	2.18E-01
						MAP3K9_E17_R	0.8248	0.1849	0.1518	5.65E-03	2.29E-01
						APBA1_E99_R	0.7410	0.1884	0.1046	6.18E-03	2.40E-01
						SERPINB2_P939_F	-0.5712	0.9106	0.9339	7.36E-03	2.61E-01
						BCL2L2_E172_F	0.4963	0.1117	0.0881	7.59E-03	2.61E-01
						TRIM29_P135_F	-0.6032	0.6929	0.7625	7.66E-03	2.61E-01
						IL16_P93_R	-0.6762	0.4553	0.6119	7.82E-03	2.61E-01
						CSF1_P339_F	-2.2168	0.0867	0.0705	9.09E-03	2.84E-01
						G6PD_P597_F	-0.6210	0.6564	0.7403	9.15E-03	2.84E-01
						SLC14A1_P369_R	-0.5970	0.6670	0.7545	9.62E-03	2.90E-01
						MMP7_P613_F	-0.4756	0.8146	0.8591	1.06E-02	3.05E-01
						MAP3K1_E81_F	0.5773	0.2473	0.1773	1.08E-02	3.05E-01
						MYCL1_P502_R	-0.6298	0.0790	0.1086	1.12E-02	3.05E-01
						USP29_P282_R	-0.5115	0.8762	0.9060	1.14E-02	3.05E-01
						RUNX3_E27_R	-0.6135	0.6106	0.7062	1.20E-02	3.07E-01

						MST1R_E42_R	-0.7065	0.4570	0.5757	1.24E-02	3.07E-01
						TAL1_P817_F	-0.5570	0.7534	0.8071	1.25E-02	3.07E-01
						PTPRG_E40_R	0.5163	0.1605	0.1130	1.30E-02	3.12E-01
						CDM_seq_21_S260_R	-0.5777	0.3045	0.4042	1.49E-02	3.24E-01
						ACVR1_E328_R	-0.6722	0.6473	0.7514	1.50E-02	3.24E-01
						RUNX3_P247_F	-0.6162	0.6764	0.7641	1.55E-02	3.24E-01
						IGF2AS_E4_F	0.5061	0.3638	0.2858	1.56E-02	3.24E-01
						PDGFRA_E125_F	-0.7038	0.4298	0.5332	1.56E-02	3.24E-01
						DDR2_P743_R	-0.5003	0.8501	0.8958	1.66E-02	3.24E-01
						NPR2_P1093_F	-0.6505	0.8034	0.8531	1.69E-02	3.24E-01
						MUSK_P308_F	-0.4950	0.7816	0.8263	1.72E-02	3.24E-01
						DES_P1006_R	-0.5146	0.7083	0.7817	1.74E-02	3.24E-01
						PRDM2_P1340_R	-0.4941	0.8675	0.9051	1.77E-02	3.24E-01
						TRIP6_P1090_F	-0.5777	0.5632	0.6274	1.84E-02	3.24E-01
						TRIM29_E189_F	-0.6686	0.6678	0.7505	1.84E-02	3.24E-01
						EPHB3_E0_F	-0.7281	0.0739	0.1067	1.87E-02	3.24E-01
						DKC1_E101_F	-0.4913	0.3446	0.4426	1.90E-02	3.24E-01
						IGFBP1_P12_R	-0.6195	0.4649	0.5521	1.91E-02	3.24E-01
						MAPK9_P1175_F	-0.4957	0.8948	0.9184	1.94E-02	3.24E-01
						MMP9_P237_R	-0.6698	0.1321	0.1923	1.95E-02	3.24E-01
						IL13_E75_R	-0.5303	0.9118	0.9330	2.00E-02	3.24E-01
						HS3ST2_E145_R	-0.8637	0.4129	0.6224	2.05E-02	3.24E-01
						MKRN4_P1320_R	-0.4046	0.8933	0.9200	2.06E-02	3.24E-01
						KRT5_E196_R	-0.5999	0.8442	0.8855	2.08E-02	3.24E-01
						SNURF_P78_F	-0.6010	0.6720	0.7754	2.20E-02	3.33E-01
						MMP7_E59_F	-0.5760	0.3120	0.3515	2.25E-02	3.33E-01
						GSTM2_P453_R	-0.5119	0.6950	0.7705	2.29E-02	3.33E-01
						SERPINB5_P19_R	-0.6402	0.7177	0.7855	2.33E-02	3.33E-01
						EGFR_E295_R	0.4338	0.1098	0.0738	2.34E-02	3.33E-01
						SHB_P691_R	0.3860	0.1342	0.0990	2.36E-02	3.33E-01
						KLK11_P1290_F	-0.4310	0.8277	0.8700	2.39E-02	3.33E-01
						MCF2_P1024_R	-0.5745	0.7839	0.8432	2.53E-02	3.43E-01
						OSM_P188_F	-0.5531	0.6022	0.6360	2.53E-02	3.43E-01
						VBP1_P12_R	-0.5092	0.4175	0.5126	2.64E-02	3.51E-01
						NFKB1_P496_F	-0.5421	0.2458	0.3052	2.71E-02	3.56E-01
						UGT1A1_E11_F	-0.6256	0.9375	0.9594	2.76E-02	3.57E-01
						PMP22_P975_F	-0.5707	0.7537	0.8276	2.84E-02	3.62E-01
						IGFBP1_E48_R	-0.4704	0.5899	0.6747	2.95E-02	3.62E-01
						HOXC6_P456_R	-0.5777	0.1435	0.1866	2.96E-02	3.62E-01
						EMR3_P39_R	-0.4964	0.5322	0.6019	3.04E-02	3.62E-01
						IRF7_P277_R	0.8602	0.2247	0.1668	3.08E-02	3.62E-01
						GRPR_P200_R	-0.4869	0.6662	0.7355	3.11E-02	3.62E-01
						PRKCDBP_P352_R	-0.6685	0.1491	0.2399	3.13E-02	3.62E-01
						BGN_E282_R	-0.4902	0.6120	0.7159	3.18E-02	3.62E-01
						DNMT2_P199_F	-0.4254	0.7981	0.8414	3.18E-02	3.62E-01
						MAGEA1_P926_F	-0.7030	0.8422	0.8891	3.24E-02	3.62E-01
						GADD45A_P737_R	-0.5102	0.2980	0.3597	3.28E-02	3.62E-01
						CYP2E1_E53_R	-0.5996	0.6528	0.7420	3.30E-02	3.62E-01
						DDR2_E331_F	-0.6620	0.8329	0.8733	3.34E-02	3.62E-01
						DSG1_E292_F	-0.4238	0.8544	0.8782	3.36E-02	3.62E-01
						CYP2E1_P416_F	-0.6609	0.7242	0.7946	3.40E-02	3.62E-01
						THY1_P20_R	0.4188	0.3685	0.3278	3.41E-02	3.62E-01
						PITX2_P183_R	-0.4364	0.3397	0.4259	3.49E-02	3.66E-01
						PTCH2_P568_R	-0.4220	0.2931	0.3177	3.66E-02	3.77E-01
						APC_P14_F	-1.0435	0.3421	0.3974	3.79E-02	3.77E-01
						FGF1_P357_R	-0.5109	0.5998	0.6819	3.84E-02	3.77E-01
						S100A2_E36_R	-0.5518	0.4690	0.5800	3.87E-02	3.77E-01
						CTGF_P693_R	-0.6339	0.6779	0.7718	3.93E-02	3.77E-01
						GLA_P112_F	-0.5005	0.7479	0.7976	3.93E-02	3.77E-01
						CHI3L2_E10_F	-0.4443	0.6711	0.7021	3.99E-02	3.77E-01

						FGF2_P229_F	-0.5816	0.3968	0.4626	4.06E-02	3.77E-01
						PLAT_P80_F	-0.4957	0.2613	0.3678	4.07E-02	3.77E-01
						MEST_P62_R	0.6449	0.5935	0.5221	4.10E-02	3.77E-01
						MC2R_E455_F	-0.6017	0.8471	0.8878	4.16E-02	3.77E-01
						ARHGAP9_P518_R	-0.4657	0.8168	0.8583	4.16E-02	3.77E-01
						MEST_E150_F	0.6549	0.5279	0.4584	4.16E-02	3.77E-01
						ZIM3_E203_F	-0.3820	0.9208	0.9343	4.21E-02	3.77E-01
						SNURF_E256_R	-0.4359	0.7424	0.8221	4.25E-02	3.77E-01
						THY1_P149_R	0.5964	0.5217	0.4264	4.28E-02	3.77E-01
						KRT5_P308_F	-0.4597	0.6991	0.7490	4.29E-02	3.77E-01
						GRB10_P260_F	0.3674	0.1002	0.0829	4.45E-02	3.85E-01
						RARRES1_P57_R	-0.2905	0.6705	0.7154	4.46E-02	3.85E-01
						HSPA2_P162_R	-0.4906	0.8532	0.8904	4.50E-02	3.85E-01
						TNC_P198_F	-0.5736	0.2000	0.2340	4.70E-02	3.99E-01
						FRK_P258_F	-0.5725	0.5458	0.6474	4.82E-02	4.04E-01
						PTHLH_P757_F	-0.3188	0.8258	0.8508	4.87E-02	4.04E-01
						PRSS8_E134_R	-0.5228	0.7382	0.8008	4.89E-02	4.04E-01
						RBP1_P150_F	0.6612	0.1149	0.0695	4.99E-02	4.09E-01

Table S5. Top differentially methylated CpG loci in current versus never smokers, stratified by HR status and race

Black cases						White cases					
CpG Probe	CpG ID	Chr	Coef	p value	q value	CpG probe	CpG ID	Chr	Coef	p value	q value
HR+ tumors											
Top 10 differentially methylated											
RIPK4_P172_F	cg19812226	21	1.02331	1.55E-05	1.45E-02	FRZB_E186_R	cg01872931	2	0.63276	2.27E-03	9.97E-01
SMO_E57_F	cg13659980	7	1.22238	4.17E-05	1.95E-02	BMP4_P199_R	cg09229893	14	0.59623	2.88E-03	9.97E-01
MAF_P826_R	cg24274831	16	0.96239	1.19E-04	3.70E-02	MYCL1_P502_R	cg27650434	1	0.40556	4.41E-03	9.97E-01
MYCL1_P502_R	cg27650434	1	0.67652	7.27E-04	1.60E-01	KIAA1804_P689_R	cg09524235	1	-0.49491	8.92E-03	9.97E-01
FN1_E469_F	cg01966735	2	0.80196	8.84E-04	1.60E-01	CTSL_P264_R	cg20035138	9	-0.39349	1.44E-02	9.97E-01
POMC_P53_F	cg00293936	2	0.75408	1.13E-03	1.60E-01	TMEM63A_E63_F	cg09739214	1	0.34952	1.49E-02	9.97E-01
HLF_E192_F	cg05876326	17	0.89222	1.20E-03	1.60E-01	LAMB1_E144_R	cg24971900	7	-0.26764	1.60E-02	9.97E-01
ITGA2_P26_R	cg15676241	5	0.45560	1.54E-03	1.80E-01	MST1R_P392_F	cg03610760	3	-0.42527	2.55E-02	9.97E-01
TNC_P198_F	cg22480835	9	0.68490	2.48E-03	2.57E-01	PLXDC2_E337_F	cg16953926	10	0.36708	2.59E-02	9.97E-01
MYLK_E132_R	cg07455270	3	0.48175	2.98E-03	2.60E-01	OPCML_P71_F	cg00738841	11	0.29313	3.07E-02	9.97E-01
Differentially methylated in both blacks & whites											
MYCL1_P502_R	cg27650434	1	0.595	5.02E-04	2.34E-01	MYCL1_P502_R	cg27650434	1	0.354	1.54E-02	9.96E-01
HR- tumors											
Top 10 differentially methylated											
BMPR1A_E88_F	cg14602437	10	-0.63213	1.33E-04	1.24E-01	DKFZP564O0823_E45_F	cg14481786	4	1.25227	1.72E-04	1.30E-01
MAP3K8_P1036_F	cg21555918	10	-0.77462	4.72E-04	2.20E-01	HGF_P1293_R	cg14690980	7	-0.88901	2.99E-04	1.30E-01
TNF_P158_F	cg26444570	6	1.05709	7.94E-04	2.47E-01	TIAM1_P188_R	cg02217293	21	0.81863	5.37E-04	1.30E-01
RASGRF1_P768_F	cg08522779	15	0.68707	2.52E-03	4.73E-01	MKRN3_P108_F	cg19407225	15	-0.91639	5.57E-04	1.30E-01
LEFTY2_P719_F	cg09540507	1	-0.70971	2.53E-03	4.73E-01	MCF2_E195_F	cg20900840	X	-0.83117	7.46E-04	1.37E-01
IGF1_E394_F	cg17084217	12	-0.49338	3.74E-03	5.37E-01	p16_seq_47_S188_R	cg05238395	9	0.84930	9.30E-04	1.37E-01
TNFRSF10A_P91_F	cg25641272	8	0.61997	5.41E-03	5.37E-01	SOD3_P225_F	cg10307548	4	-0.64232	1.03E-03	1.37E-01
DMP1_E194_F	cg18397653	4	-0.43081	5.80E-03	5.37E-01	ZIM3_P451_R	cg16859188	19	-1.00432	1.32E-03	1.48E-01
FGF1_P357_R	cg05353098	5	-0.58768	7.01E-03	5.37E-01	MCC_P196_R	cg19728002	5	-1.59739	1.43E-03	1.48E-01
MC2R_P1025_F	cg00358505	18	-0.72542	8.02E-03	5.37E-01	IL12B_E25_F	cg18307303	5	-0.67171	1.72E-03	1.61E-01
Differentially methylated in both blacks & whites											
CDM_seq_21_S260_R	cg18682265	X	-0.37231	3.24E-02	5.81E-01	CDM_seq_21_S260_R	cg18682265	X	-0.57768	1.49E-02	3.24E-01
CSF1_P339_F	cg06450700	1	-3.00642	1.01E-02	5.37E-01	CSF1_P339_F	cg06450700	1	-2.21680	9.09E-03	2.84E-01
DSC2_P407_R	cg20887958	18	-0.44191	9.50E-03	5.37E-01	DSC2_P407_R	cg20887958	18	-0.67638	4.79E-03	2.18E-01
FGF1_P357_R	cg05353098	5	-0.58768	7.01E-03	5.37E-01	FGF1_P357_R	cg05353098	5	-0.51093	3.84E-02	3.77E-01
FRK_P258_F	cg26557270	6	-0.57172	2.34E-02	5.81E-01	FRK_P258_F	cg26557270	6	-0.57252	4.82E-02	4.04E-01
IL13_E75_R	cg20391122	5	-0.37063	3.54E-02	6.11E-01	IL13_E75_R	cg20391122	5	-0.53027	2.00E-02	3.24E-01
MAPK9_P1175_F	cg05023457	5	-0.46791	2.60E-02	5.81E-01	MAPK9_P1175_F	cg05023457	5	-0.49570	1.94E-02	3.24E-01
PIK3R1_P307_F	cg03473299	5	-0.34424	8.97E-03	5.37E-01	PIK3R1_P307_F	cg03473299	5	-0.53838	4.91E-03	2.18E-01
SNURF_P78_F	cg15999943	15	-0.36565	4.72E-02	6.13E-01	SNURF_P78_F	cg15999943	15	-0.60101	2.20E-02	3.33E-01
TRIM29_E189_F	cg26414304	11	-0.43017	1.16E-02	5.43E-01	TRIM29_E189_F	cg26414304	11	-0.66864	1.84E-02	3.24E-01

Models were adjusted for age (continuous), race (AA vs. non-AA), menopausal status (premenopausal vs. postmenopausal), BMI (<25, 25-29, >29 kg/m²), alcohol consumption (lifetime consumption in grams/week), and stage (1, 2, 3, 4). Coef; coefficient. Positive coefficients indicate higher methylation in smokers, while negative coefficients indicate lower methylation in smokers. Chr; chromosome.

Table S6. Results of DAVID 6.8 gene ontology analyses

Category	Term	Count	Fold Enrichment	P Value	Benjamini
Current vs never smoking in HR- tumors (top 50 shown)					
GOTERM_BP_ALL	response to stress	45	1.70	5.21E-05	8.37E-02
GOTERM_BP_ALL	response to ethanol	7	9.63	8.43E-05	9.00E-02
GOTERM_BP_ALL	protein metabolic process	48	1.68	2.94E-05	9.40E-02
GOTERM_BP_ALL	peptidyl-amino acid modification	22	2.38	2.14E-04	9.76E-02
GOTERM_BP_ALL	cellular protein metabolic process	44	1.65	1.55E-04	9.89E-02
GOTERM_BP_ALL	rhythmic process	10	4.85	2.01E-04	1.06E-01
GOTERM_BP_ALL	cellular component organization	51	1.50	3.20E-04	1.12E-01
GOTERM_BP_ALL	single-organism process	84	1.16	4.30E-04	1.13E-01
GOTERM_BP_ALL	response to organic substance	41	1.71	1.48E-04	1.17E-01
GOTERM_BP_ALL	multi-organism process	26	2.03	4.92E-04	1.19E-01
GOTERM_BP_ALL	response to alcohol	8	6.14	3.08E-04	1.21E-01
GOTERM_BP_ALL	antigen processing and presentation of exogenous peptide antigen	3	93.14	4.23E-04	1.21E-01
GOTERM_BP_ALL	negative regulation of cellular process	49	1.48	6.20E-04	1.30E-01
GOTERM_BP_ALL	cellular component organization or biogenesis	51	1.48	4.20E-04	1.31E-01
GOTERM_BP_ALL	response to chemical	46	1.53	6.19E-04	1.38E-01
GOTERM_BP_ALL	response to hormone	16	2.65	7.90E-04	1.53E-01
GOTERM_BP_ALL	cell death	33	1.71	1.14E-03	1.66E-01
GOTERM_BP_ALL	cellular response to chemical stimulus	38	1.60	1.21E-03	1.69E-01
GOTERM_BP_ALL	response to steroid hormone	10	3.92	9.44E-04	1.70E-01
GOTERM_BP_ALL	single-organism cellular process	79	1.19	1.01E-03	1.71E-01
GOTERM_BP_ALL	response to organic cyclic compound	16	2.56	1.13E-03	1.73E-01
GOTERM_BP_ALL	cellular protein modification process	38	1.60	1.31E-03	1.73E-01
GOTERM_BP_ALL	protein modification process	38	1.60	1.31E-03	1.73E-01
GOTERM_BP_ALL	antigen processing and presentation of exogenous antigen	3	59.27	1.10E-03	1.76E-01
GOTERM_BP_ALL	response to extracellular stimulus	11	3.38	1.40E-03	1.77E-01
GOTERM_BP_ALL	negative regulation of biological process	50	1.42	1.45E-03	1.77E-01
GOTERM_BP_ALL	apoptotic process	29	1.77	1.70E-03	1.97E-01
GOTERM_BP_ALL	regulation of primary metabolic process	50	1.41	1.85E-03	2.06E-01
GOTERM_BP_ALL	response to nutrient levels	10	3.44	2.31E-03	2.09E-01
GOTERM_BP_ALL	regulation of signaling	42	1.49	2.30E-03	2.15E-01
GOTERM_BP_ALL	response to stimulus	69	1.24	2.50E-03	2.19E-01
GOTERM_BP_ALL	programmed cell death	31	1.69	2.29E-03	2.20E-01
GOTERM_BP_ALL	macromolecule modification	38	1.56	2.14E-03	2.20E-01
GOTERM_BP_ALL	regulation of cell communication	42	1.49	2.22E-03	2.20E-01
GOTERM_BP_ALL	positive regulation of cell activation	12	2.96	2.14E-03	2.26E-01
GOTERM_BP_ALL	regulation of metabolic process	52	1.37	2.78E-03	2.34E-01
GOTERM_BP_ALL	response to oxygen-containing compound	24	1.85	3.17E-03	2.56E-01
GOTERM_BP_ALL	single-organism metabolic process	34	1.59	3.35E-03	2.57E-01
GOTERM_BP_ALL	peptidyl-tyrosine modification	15	2.39	3.28E-03	2.57E-01
GOTERM_BP_ALL	peptidyl-tyrosine phosphorylation	15	2.39	3.28E-03	2.57E-01
GOTERM_BP_ALL	cellular response to stimulus	63	1.27	3.60E-03	2.61E-01
GOTERM_BP_ALL	single-organism localization	30	1.66	3.56E-03	2.64E-01
GOTERM_BP_ALL	response to external stimulus	32	1.61	3.98E-03	2.79E-01
GOTERM_BP_ALL	cellular response to organic substance	33	1.58	4.27E-03	2.84E-01
GOTERM_BP_ALL	response to endogenous stimulus	26	1.75	4.19E-03	2.85E-01
GOTERM_BP_ALL	regulation of cellular metabolic process	49	1.36	4.90E-03	3.01E-01
GOTERM_BP_ALL	phosphorus metabolic process	36	1.52	4.89E-03	3.06E-01
GOTERM_BP_ALL	phosphate-containing compound metabolic process	36	1.52	4.89E-03	3.06E-01
GOTERM_BP_ALL	regulation of response to stimulus	44	1.41	4.88E-03	3.11E-01
GOTERM_BP_ALL	cellular process	88	1.07	5.57E-03	3.29E-01
Current vs never smoking in HR+ tumors					
GOTERM_BP_ALL	biosynthetic process	14	2.30	2.20E-04	5.80E-02
GOTERM_BP_ALL	regulation of RNA biosynthetic process	12	2.90	2.00E-04	6.00E-02
GOTERM_BP_ALL	regulation of RNA metabolic process	12	2.80	2.60E-04	6.00E-02
GOTERM_BP_ALL	regulation of cellular macromolecule biosynthetic process	12	2.70	3.90E-04	6.00E-02
GOTERM_BP_ALL	RNA biosynthetic process	12	2.70	3.70E-04	6.20E-02
GOTERM_BP_ALL	nucleic acid-templated transcription	12	2.80	3.50E-04	6.40E-02
GOTERM_BP_ALL	macromolecule biosynthetic process	13	2.50	3.40E-04	6.90E-02
GOTERM_BP_ALL	organic substance biosynthetic process	14	2.40	1.90E-04	7.00E-02
GOTERM_BP_ALL	regulation of nucleic acid-templated transcription	12	3.00	1.80E-04	8.30E-02
GOTERM_BP_ALL	aromatic compound biosynthetic process	12	2.50	9.10E-04	9.00E-02
GOTERM_BP_ALL	regulation of nitrogen compound metabolic process	12	2.50	1.00E-03	9.10E-02
GOTERM_BP_ALL	heterocycle biosynthetic process	12	2.50	8.30E-04	9.30E-02
GOTERM_BP_ALL	cellular biosynthetic process	13	2.30	8.80E-04	9.30E-02
GOTERM_BP_ALL	transcription, DNA-templated	11	2.70	1.00E-03	9.50E-02
GOTERM_BP_ALL	organic cyclic compound biosynthetic process	12	2.40	1.10E-03	9.50E-02
GOTERM_BP_ALL	nucleobase-containing compound biosynthetic process	12	2.50	8.30E-04	9.90E-02
GOTERM_BP_ALL	regulation of cellular biosynthetic process	12	2.60	7.30E-04	1.00E-01
GOTERM_BP_ALL	regulation of nucleobase-containing compound metabolic process	12	2.50	7.90E-04	1.00E-01
GOTERM_BP_ALL	regulation of transcription, DNA-templated	12	3.00	1.80E-04	1.10E-01
GOTERM_BP_ALL	cellular nitrogen compound biosynthetic process	12	2.40	1.30E-03	1.10E-01
GOTERM_BP_ALL	cellular macromolecule biosynthetic process	12	2.40	1.40E-03	1.10E-01

GOTERM_BP_ALL	regulation of gene expression	12	2.40	1.50E-03	1.10E-01
GOTERM_BP_ALL	positive regulation of cellular biosynthetic process	9	3.30	1.50E-03	1.10E-01
GOTERM_BP_ALL	regulation of transcription involved in G1/S transition of mitotic cell cycle	2	1137	1.70E-03	1.10E-01
GOTERM_BP_ALL	multicellular organismal process	16	1.60	1.70E-03	1.10E-01
GOTERM_BP_ALL	positive regulation of biosynthetic process	9	3.20	2.10E-03	1.30E-01
GOTERM_BP_ALL	regulation of macromolecule biosynthetic process	13	2.80	8.70E-05	1.50E-01
GOTERM_BP_ALL	regulation of biosynthetic process	13	2.70	1.70E-04	1.50E-01
GOTERM_BP_ALL	RNA metabolic process	12	2.20	3.20E-03	1.80E-01
GOTERM_BP_ALL	leukocyte migration	5	6.90	4.00E-03	2.20E-01
GOTERM_BP_ALL	regulation of immune system process	8	3.30	4.50E-03	2.40E-01
GOTERM_BP_ALL	regulation of macromolecule metabolic process	13	1.90	6.40E-03	3.10E-01
GOTERM_BP_ALL	positive regulation of macromolecule biosynthetic process	8	3.10	6.50E-03	3.10E-01
GOTERM_BP_ALL	positive regulation of nucleobase-containing compound metabolic process	8	3.00	7.10E-03	3.20E-01
GOTERM_BP_ALL	monocyte chemotaxis	3	21.9	7.20E-03	3.20E-01
GOTERM_BP_ALL	single-organism biosynthetic process	6	4.30	7.40E-03	3.20E-01
GOTERM_BP_ALL	nucleic acid metabolic process	12	1.90	9.40E-03	3.40E-01
GOTERM_BP_ALL	single-organism cellular process	17	1.30	9.50E-03	3.40E-01
GOTERM_BP_ALL	positive regulation of nitrogen compound metabolic process	8	2.90	8.50E-03	3.50E-01
GOTERM_BP_ALL	nitrogen compound metabolic process	13	1.80	9.20E-03	3.50E-01
GOTERM_BP_ALL	regulation of multicellular organismal process	11	2.10	9.30E-03	3.50E-01
GOTERM_BP_ALL	negative regulation of cell-substrate adhesion	3	19.30	9.20E-03	3.60E-01
GOTERM_BP_ALL	regulation of metabolic process	13	1.80	9.10E-03	3.70E-01
GOTERM_BP_ALL	gene expression	12	1.90	1.10E-02	3.70E-01
GOTERM_BP_ALL	negative regulation of cell adhesion	4	7.80	1.10E-02	3.80E-01
GOTERM_BP_ALL	mitotic cell cycle	5	5.00	1.20E-02	3.80E-01
GOTERM_BP_ALL	regulation of cellular component organization	9	2.40	1.20E-02	3.90E-01
GOTERM_BP_ALL	positive regulation of nucleic acid-templated transcription	7	3.20	1.20E-02	3.90E-01
GOTERM_BP_ALL	positive regulation of transcription, DNA-templated	7	3.20	1.20E-02	3.90E-01
GOTERM_BP_ALL	positive regulation of RNA biosynthetic process	7	3.10	1.30E-02	3.90E-01

Figure S1. Volcano plots illustrating array-wide patterns of breast tumor differential methylation in smokers compared with never smokers. Generalized linear regression (GLM) (logit link) was used to compare breast tumor methylation beta values between ever or current smokers and never smokers, adjusting for age, race, menopausal status, BMI, and alcohol consumption. Volcano plots display patterns of breast tumor differential methylation in each smoking group (ever or current) versus never smokers among (A) all cases, (B) HR+ cases, and (C) HR- cases. Each volcano plot displays the negative log of unadjusted p-values for differences in β (proportion DNA methylated) at each probe on the y axis versus the correlation coefficient for methylation at each CpG locus on the x axis. Probes that fall above the broken line are significant at $p < 0.05$. Probes hypomethylated in smokers have negative coefficients) and probes hypermethylated in smokers have positive coefficients).

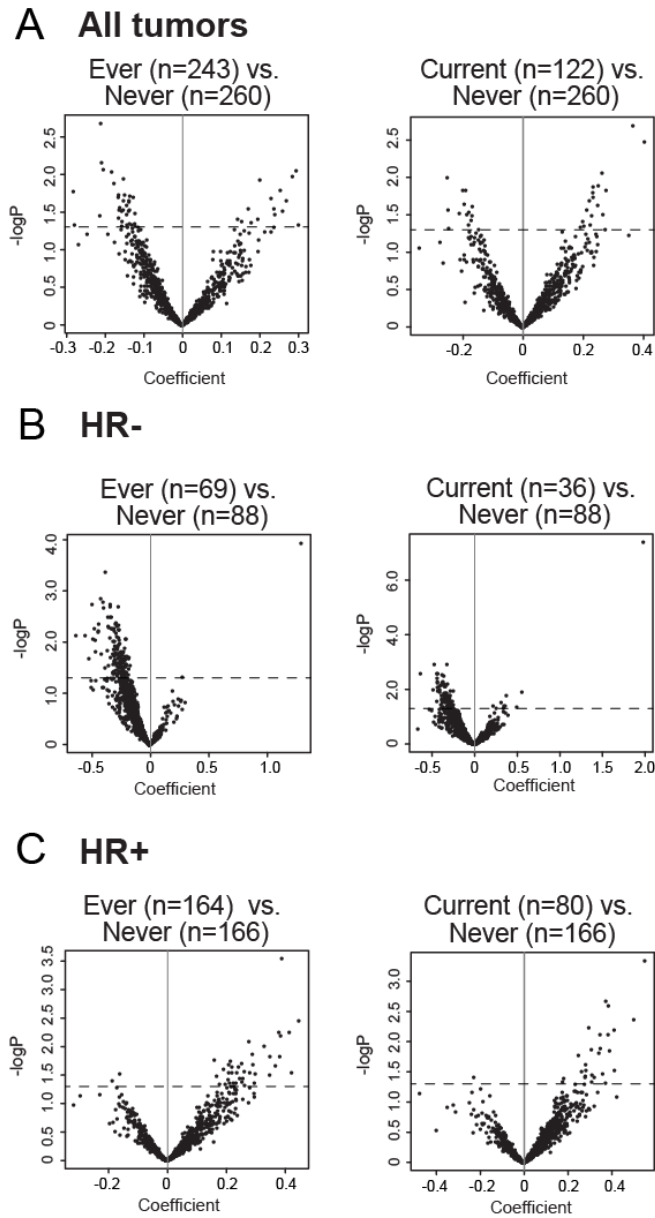
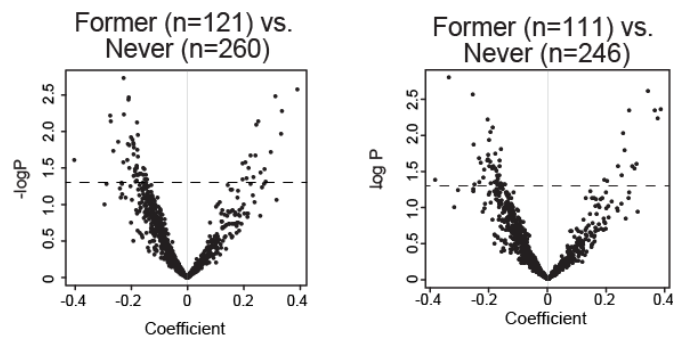
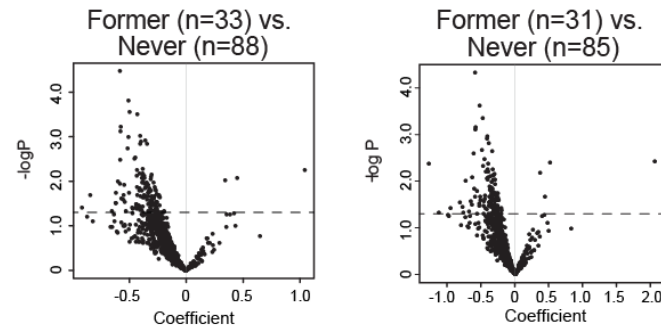


Figure S2. Volcano plots illustrating array-wide patterns of breast tumor differential methylation in former smokers compared with never smokers. Generalized linear regression (GLM) (logit link) was used to compare breast tumor methylation beta values between former and never smokers, adjusting for age, race, menopausal status, BMI, and alcohol consumption (left side). Models on the right side were additionally adjusted for clinical stage (1-4). Volcano plots display patterns of breast tumor differential methylation in former smokers versus never smokers among (A) all cases, (B) HR- cases, and (C) HR+ cases. Each volcano plot displays the negative log of unadjusted p-values for differences in β (proportion DNA methylated) at each probe on the y axis versus the correlation coefficient for methylation at each CpG locus on the x axis. Probes that fall above the broken line are significant at $p < 0.05$. Probes hypomethylated in smokers have negative coefficients) and probes hypermethylated in smokers have positive coefficients.

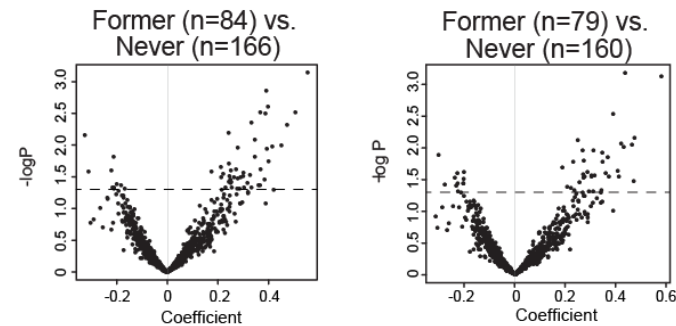
A All tumors



B HR-



C HR+

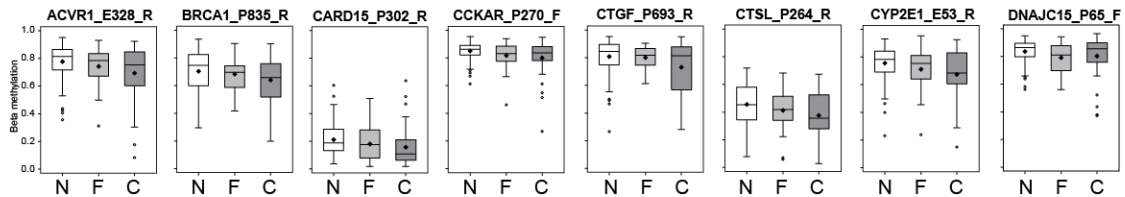


Not adjusted for stage

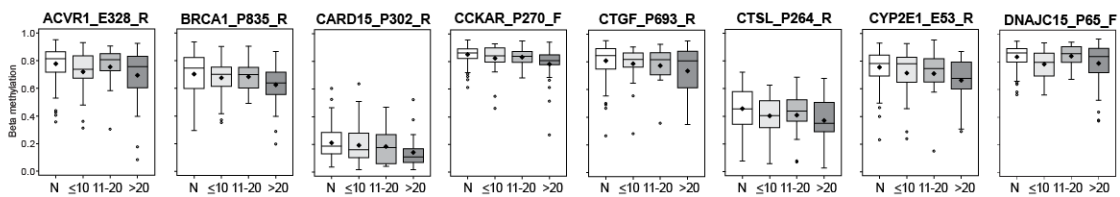
Adjusted for stage

Figure S3a. Patterns of methylation at CpGs differentially methylated at $p < 0.05$ in HR-breast tumors from current versus never smokers. Methylation differences according to (A) smoking status in current (C) ($n=37$) or former (F) ($n=34$) smokers compared with never smokers (N) ($n=92$), (B) increasing duration of smoking in years among ever smokers: N ($n=92$), ≤ 10 ($n=25$), 11-20 ($n=16$), or >20 years ($n=29$), and (C) years since quitting among former smokers: C ($n=37$), ≤ 10 ($n=18$), 11+ ($n=16$), N ($n=92$).

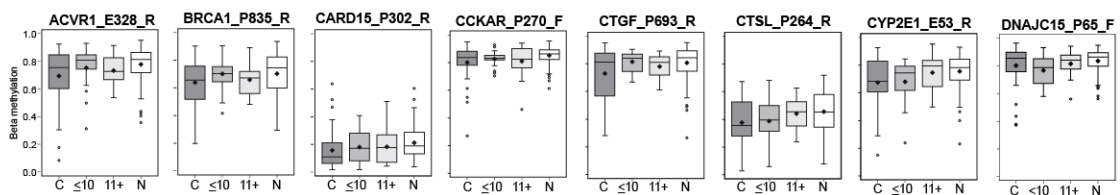
A Smoking Status



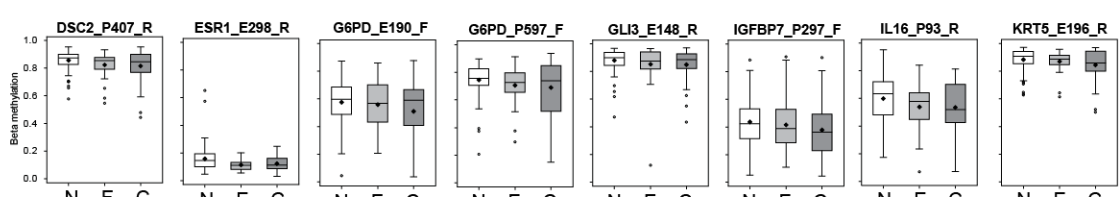
B Years Smoked (ever smokers)



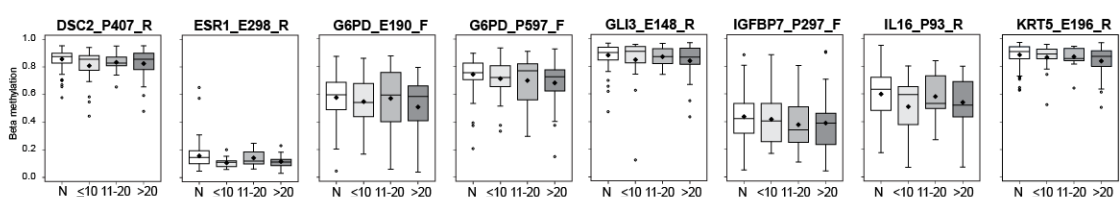
C Years Since Quitting (former smokers)



A Smoking Status



B Years Smoked (ever smokers)



C Years Since Quitting (former smokers)

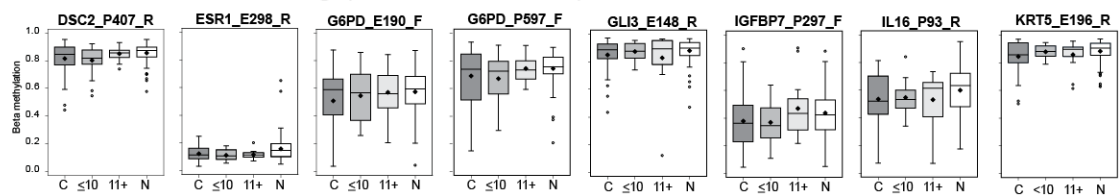


Figure S3b. Patterns of methylation at CpGs differentially methylated at $p < 0.05$ in HR-breast tumors from current versus never smokers. Methylation differences according to (A) smoking status in current (C) ($n=37$) or former (F) ($n=34$) smokers compared with never smokers (N) ($n=92$), (B) increasing duration of smoking in years among ever smokers: N ($n=92$), ≤ 10 ($n=25$), 11-20 ($n=16$), or >20 years ($n=29$), and (C) years since quitting among former smokers: C ($n=37$), ≤ 10 ($n=18$), 11+ ($n=16$), N ($n=92$).

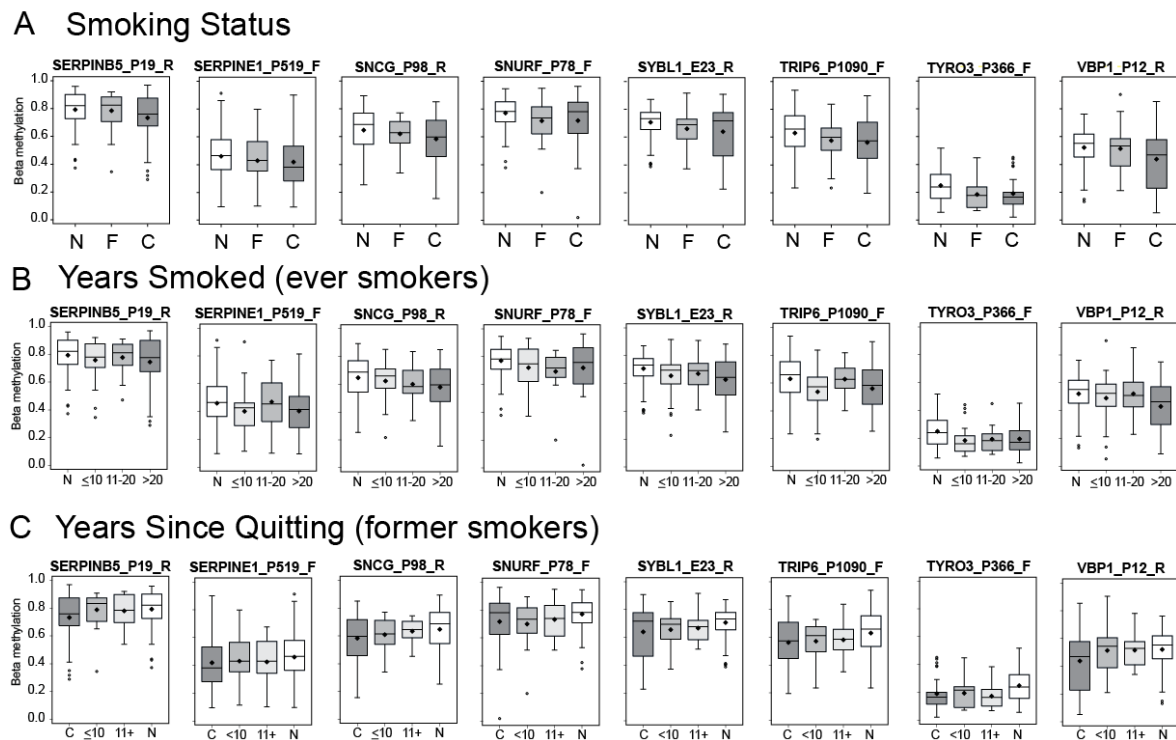
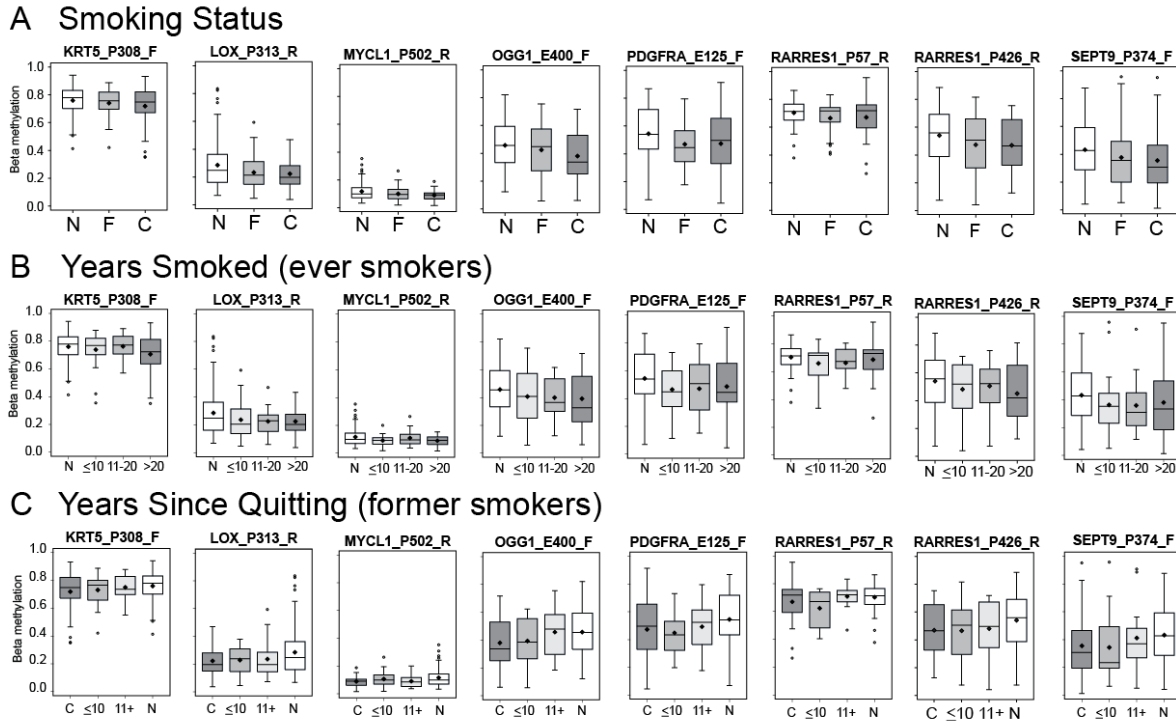
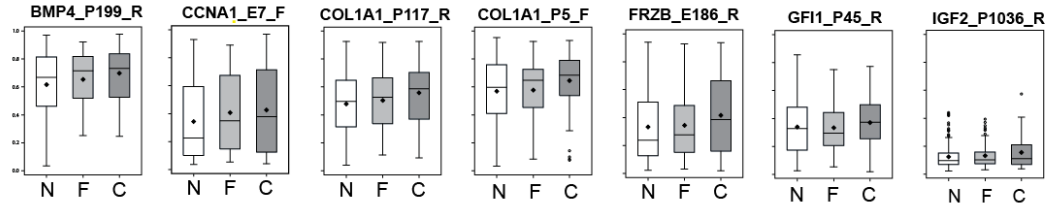
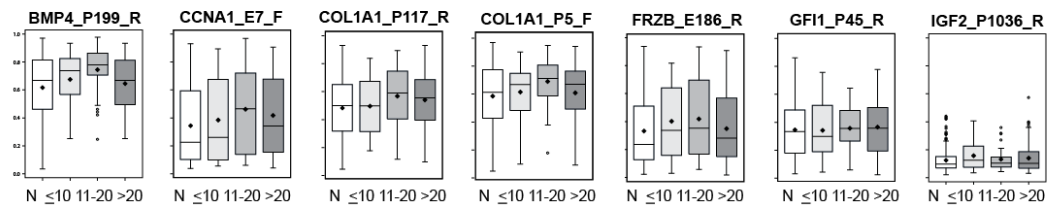


Figure S3c. Patterns of methylation at CpGs differentially methylated at $p < 0.05$ in HR+ breast tumors from current versus never smokers. Methylation differences according to (A) smoking status in current (C) ($n=82$) or former (F) ($n=86$) smokers compared with never smokers (N) ($n=170$), (B) increasing duration of smoking in years among ever smokers: N ($n=170$), ≤ 10 ($n=47$), 11-20 ($n=34$), or >20 years ($n=87$), and (C) years since quitting among former smokers: C ($n=82$), ≤ 10 ($n=40$), 11+ ($n=46$), N ($n=170$).

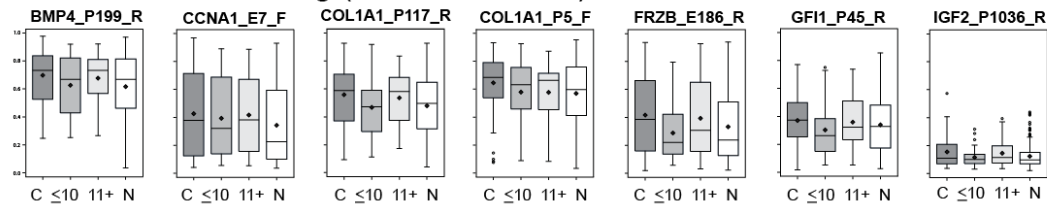
A Smoking Status



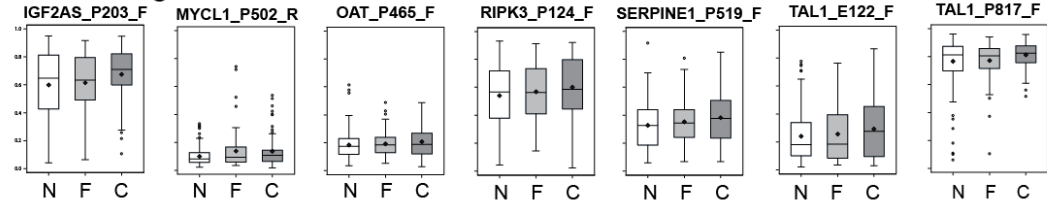
B Years Smoked (ever smokers)



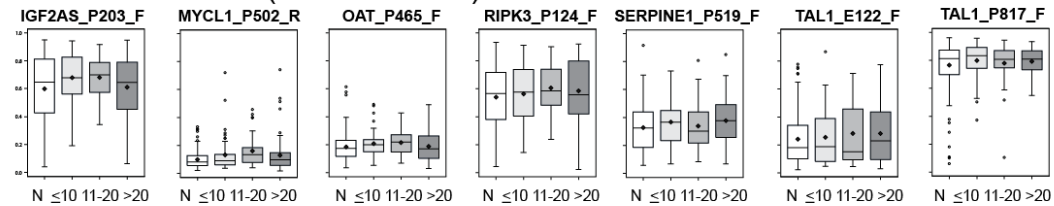
C Years Since Quitting (former smokers)



A Smoking Status



B Years Smoked (ever smokers)



C Years Since Quitting (former smokers)

