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Additional Acknowledgement

GECCO: The authors would like to thank all those at the GECCO Coordinating Center for helping bring together the data and people that made this project possible. The authors acknowledge Dave Duggan and team members at TGEN (Translational Genomics Research Institute), the Broad Institute, and the Génome Québec Innovation Center for genotyping DNA samples of cases and controls, and for scientific input for GECCO.
ASTERISK: We are very grateful to Dr. Bruno Buecher without whom this project would not have existed. We also thank all those who agreed to participate in this study, including the patients and the healthy control persons, as well as all the physicians, technicians and students.
DACHS: We thank all participants and cooperating clinicians, and Ute Handte-Daub, Utz Benscheid, Muhabbet Celik and Ursula Eilber for excellent technical assistance.
HPFS, **NHS** and **PHS**: We would like to acknowledge Patrice Soule and Hardeep Ranu of the Dana Farber Harvard Cancer Center High-Throughput Polymorphism Core who assisted in the genotyping for NHS, HPFS, and PHS under the supervision of Dr. Immaculata Devivo and Dr. David Hunter, Qin (Carolyn) Guo and Lixue Zhu who assisted in programming for NHS and HPFS, and Haiyan Zhang who assisted in programming for the PHS. We would like to thank the participants and staff of the Nurses' Health Study and the Health Professionals Follow-Up Study, for their valuable contributions as well as the following state cancer registries for their help: AL, AZ, AR, CA, CO, CT, DE, FL, GA, ID, IL, IN, IA, KY, LA, ME, MD, MA, MI, NE, NH, NJ, NY, NC, ND, OH, OK, OR, PA, RI, SC, TN, TX, VA, WA, WY. The authors assume full responsibility for analyses and interpretation of these data.
PLCO: The authors thank Drs. Christine Berg and Philip Prorok, Division of Cancer Prevention, National Cancer Institute, the Screening Center investigators and staff or the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial, Mr. Tom Riley and staff, Information Management Services, Inc., Ms. Barbara O'Brien and staff, Westat, Inc., and Drs. Bill Kopp and staff, SAIC-Frederick. Most importantly, we acknowledge the study participants for their contributions to making this study possible. The statements contained herein are solely those of the authors and do not represent or imply concurrence or endorsement by NCI.
PMH: The authors would like to thank the study participants and staff of the Hormones and Colon Cancer study.

WHI: The authors thank the WHI investigators and staff for their dedication, and the study participants for making the program possible. A full listing of WHI investigators can be found at: http://www.whi.org/researchers/Documents%20%20Write%20a%20Paper/WHI%20Investigator%20Short%20List.pdf

Supplementary Table 1. Population and design of each contributed study

Cancer	Study	Locations	Design
Initial analytical data in GAME-ON			
Colon & Rectum	MECC	US	Cohort
(CORECT)	CFR	US	Cohort
	Kentucky	US	Pop. CC
	CPS-II/ACS	US	Cohort
	Melbourne	Australia	Cohort
	Newfoundland	Canada	Pop. CC
Lung	MDACC	US	Hospital CC
(TRICL)	ICR	UK	Hospital CC
	Toronto	Canada	Clinic CC
	IARC	Europe	Hospital CC
	GLC	German	Pop. CC
	NCI	US	Pop. CC and nested CC
Ovary	UKGWAS	UK	CC
(FOCI)	USGWAS	US, Canada, Poland	CC
	U19	US	CC
Prostate	BPC3	US	CC, nested CC
(ELLIPSE)	CRUK1	UK	CC
	CRUK2	UK	CC
	CAPS1	Sweden	CC
	CAPS2	Sweden	CC
Replication data			
Prostate (PLCO)	PLCO	US	Nested CC
Colon & Rectum			

(GECCO)	ASTERISK	France	Hospital CC
	COLO23	US	Pop. CC
	DACHS1	Germany	Pop. CC
	DACHS2	Germany	Pop. CC
	DALS1	US	Pop. CC
	DALS2	US	Pop. CC
	HPFS1	US	Nested CC
	HPFS2	US	Nested CC
	HPFSad	US	Nested CC
	MEC	US	Nested CC
	NHS1	US	Nested CC
	NHS2	US	Nested CC
	NHSad	US	Nested CC
	OFCCR	Canada	Pop.CC
	PHS1P2	US	Nested CC
	PLCO1	US	Nested CC
	PLCO2	US	Nested CC
	PMH	US	Pop. CC
	VITAL	US	Nested CC
	WHI1	US	Nested CC
	WHI2	US	Nested CC

CC: case-control

Supplementary table 2. Gene- and pathway-based p-values for overall and aggressive prostate cancer

		Combined results (14818 cases, 14227 controls)		Aggressive prostate (up to 4446 cases, 12724 controls)	
Gene	Chr	N.SNPs	P-value	N.SNPs	P-value
Circadian rhythm pathway					
ARNTL	11	80	0.29	80	0.54
CK1E	22	48	0.30	48	0.58
CLOCK	4	24	**0.021**	24	0.093
CRYI	12	35	0.55	35	0.87
CRY2	11	20	**0.043**	20	0.57
NPAS2	2	167	**0.0062**	167	0.18
PER1	17	30	0.063	30	0.70
PER2	2	50	0.060	50	0.23
PER3	1	67	0.24	67	**0.030**
Pathway-level		521	**0.0016***	521	0.29
Melanotin pathway					
AANAT	17	38	**0.00078***	38	0.47
DDC	7	84	**0.050**	84	0.49
MTNR1A	4	35	0.35	35	0.22
MTNR1B	11	23	0.96	23	0.32
TPH1	11	18	0.15	18	0.96
TPH2	12	65	0.21	65	0.35
Pathway-level		263	**0.0060***	263	0.66

*Statistically significant after Bonferroni correction ($p < 0.05/8=0.00625$ at pathway level; $p < 0.05/60=0.00083$ at gene level)

P<0.05 in bold

Supplementary Table 3. Comparison of SNP-based results between overall and aggressive prostate cancer*

		Allele		Overall			Aggressive		
Gene	SNP*	Ref**	Eff**	log(OR)	SE	P-value	log(OR)	SE	P-value
Circadian rhythm pathway									
CLOCK	rs62309758	T	C	-0.09	0.03	1.45E-03	-0.09	0.04	7.57E-03
CRY2	rs7108730	T	C	0.08	0.03	3.66E-03	0.06	0.04	1.05E-01
NPAS2	rs2305160	A	G	0.08	0.02	3.47E-05	0.06	0.03	3.00E-02
Melatonin pathway									
AANAT	rs150316415	G	A	0.28	0.07	3.41E-05	0.16	0.08	6.49E-02
DDC	rs12718611	G	A	-0.11	0.04	1.72E-03	-0.07	0.05	1.12E-01

*SNPs with the smallest p-value in the genes with $P_{gene} \leq 0.05$, based on association with overall prostate cancer.

**reference and effect alleles

Supplementary table 4. Gene- and pathway-based p-values for colorectal cancer in GAME-ON and replication samples

		Game-ON (CORECT) (5100 cases, 4831 controls)		GECCO (10738 cases, 13328 controls)		Combined results (15838 cases, 18159 controls)	
Gene	Chr	N.SNPs	P-value	N.SNPs	P-value	N.SNPs	P-value
Circadian rhythm pathway							
ARNTL	11	114	**0.0044**	113	0.78	140	**0.028**
CK1E	22	38	0.14	55	0.18	68	0.24
CLOCK	4	47	0.18	35	0.34	53	0.11
CRYI	12	56	0.81	47	0.83	73	0.95
CRY2	11	35	0.64	32	0.85	41	0.91
NPAS2	2	202	**0.011**	212	0.82	245	0.51
PER1	17	47	0.60	38	0.44	53	0.55
PER2	2	54	0.63	54	0.40	68	0.59
PER3	1	60	0.68	84	0.15	101	**0.047**
Pathway-level		653	**0.021**	670	0.76	842	0.17
Melatonin pathway							
AANAT	17	53	0.59	52	0.85	61	0.91
DDC	7	119	0.89	115	0.58	147	0.74
MTNR1A	4	60	0.18	61	0.86	72	0.30
MTNR1B	11	33	0.92	34	0.87	45	0.96
TPH1	11	20	**0.029**	22	0.27	27	0.068
TPH2	12	67	0.77	92	**0.0064**	107	**0.013**
Pathway-level		352	0.24	376	0.066	459	0.091

P<0.05 in bold. None of gene based or pathway based p values reached Bonferroni corrected significance

Supplementary table 5. Gene- and pathway-based p-values for lung and ovarian cancers in GAME-ON

		Lung cancer (12537 cases, 17285 controls)		Ovarian cancer (4369 cases, 9123 controls)	
Gene	Chr	N.SNP*	P-value	N.SNP*	P-value
Circadian rhythm pathway					
ARNTL	11	78	0.18	80	0.58
CK1E	22	47	0.35	48	**0.024**
CLOCK	4	24	0.19	24	0.20
CRYI	12	33	0.40	35	0.29
CRY2	11	18	0.52	20	0.13
NPAS2	2	165	0.56	167	**0.046**
PER1	17	29	0.35	30	0.87
PER2	2	50	0.87	50	0.54
PER3	1	66	0.90	67	0.68
Pathway-level		510	0.71	521	0.14
Melatonin pathway					
AANAT	17	30	0.63	38	0.14
DDC	7	82	0.089	84	0.10
MTNR1A	4	35	0.93	35	0.20
MTNR1B	11	21	0.85	23	0.64
TPH1	11	17	0.23	18	0.21
TPH2	12	58	**0.048**	65	0.75
Pathway-level		243	0.22	263	0.26

*SNP numbers after the LD pruning, using $r^2>0.95$

P<0.05 in bold. None of gene- or pathway-level p-values reached the Bonferroni correction threshold of significance.