

Cross-cancer genome-wide analysis of lung, ovary, breast, prostate and colorectal cancer reveals novel pleiotropic associations

Supplementary Material: Funding, Acknowledgements, Consortia, and Bioinformatics Tools

Funding sources

TRICL (Transdisciplinary Research for Cancer of Lung): National Institute of Health U19 CA148127-01 (PI: Amos), Canadian Cancer Society Research Institute (no. 020214, PI: Hung). Harvard Lung Study: The Harvard Lung Cancer Study is supported by the US National Institutes of Health (R01 CA092824, P50 CA090578, and R01 CA074386).

DRIVE (Discovery, Biology, and Risk of Inherited Variants in Breast Cancer): National Institute of Health U19 CA148065. WHI: The Women's Health Initiative contribution to DRIVE is supported by the U.S. National Heart, Lung and Blood Institute via contract HHSN26820110046C and other contracts. BBCS: This work was funded by Cancer Research UK (C150/A5660 and C1178/A3947); Breakthrough Breast Cancer and the Institut National de Cancer. We acknowledge National Health Service funding to the NIHR Biomedical Research Centre and the National Cancer Research Network (NCRN). Funding for the project was provided by the Wellcome Trust under award 076113 and 085475. Rotterdam Study: The GWAS datasets are supported by the Netherlands Organisation of Scientific Research NWO Investments (nr. 175.010.2005.011, 911-03-012), the Genetic Laboratory of the Department of Internal Medicine, Erasmus MC, the Research Institute for Diseases in the Elderly (014-93-015; RIDE2), the Netherlands Genomics Initiative (NGI)/Netherlands Organisation for Scientific Research (NWO) Netherlands Consortium for Healthy Aging (NCHA), project nr. 050-060-810. The Rotterdam Study is funded by Erasmus Medical Center and Erasmus University, Rotterdam, Netherlands Organization for the Health Research and Development (ZonMw), the Research Institute for Diseases in the Elderly (RIDE), the Ministry of Education, Culture and Science, the Ministry for Health, Welfare and Sports, the European Commission (DG XII), and the Municipality of Rotterdam. The authors are grateful to the study participants, the staff from the Rotterdam Study and the participating general practitioners and pharmacists.

CORECT (ColoRectal Transdisciplinary Study): This work was supported in part by the GAME-ON U19 initiative for colorectal cancer (CORECT), U19 CA148107; R01 CA81488, P30 CA014089, P30 CA46592. The work of CFR was by grant UM1 CA167551 from the National Cancer Institute and through cooperative agreements with the following CCFR centers: Australasian Colorectal Cancer Family Registry (U01 CA074778 and U01/U24 CA097735), Mayo Clinic Cooperative Family Registry for Colon Cancer Studies (U01/U24 CA074800), Ontario Familial Colorectal Cancer Registry (U01/U24 CA074783), Seattle Colorectal Cancer Family Registry (U01/U24 CA074794), University of Hawaii Colorectal Cancer Family Registry (U01/U24 CA074806), USC Consortium Colorectal Cancer Family Registry U01/U24 CA074799). The Colon CFR GWAS was supported by funding from the National Cancer Institute, National Institutes of Health (U01 CA122839 and R01 CA143237 to Graham Casey). The content of this manuscript does not necessarily reflect the views or policies of the National Cancer Institute or any of the collaborating centers in the Colon Cancer Family Registry (CCFR), nor does mention of trade names, commercial products, or organizations imply endorsement by the US Government or the CCFR.

ELLIPSE (ELLIPSE, Elucidating Loci in Prostate Cancer Susceptibility): This work was supported by the GAME-ON U19 initiative for prostate cancer (ELLIPSE), U19 CA148537.

FOCI (Transdisciplinary Cancer Genetic Association and Interacting Studies): National Institutes of Health U19 CA148112-01 (PI: Sellers), R01-CA122443, P50-CA136393, P30-CA15083 (PI: Goode), Cancer Research UK (C490/A8339, C490/A16561, C490/A10119, C490/A10124 (PI: Pharoah)).

GECCO (Genetics and Epidemiology of Colorectal Cancer Consortium): National Cancer Institute, National Institutes of Health, U.S. Department of Health and Human Services (U01 CA137088; R01 CA059045). ASTERISK: a Hospital Clinical Research Program (PHRC) and supported by the Regional Council of Pays de la Loire, the Groupement des Entreprises Françaises dans la Lutte contre le Cancer (GEFLUC), the Association Anne de Bretagne Génétique and the Ligue Régionale Contre le Cancer (LRCC). DACHS: German Research Council (Deutsche Forschungsgemeinschaft, BR 1704/6-1, BR 1704/6-3, BR 1704/6-4 and CH 117/1-1), and the German Federal Ministry of Education and Research (01KH0404 and 01ER0814). DALs: National Institutes of Health (R01 CA48998 to M.L. Slattery); HPFS is supported by the National Institutes of Health (P01 CA 055075, UM1 CA167552, R01 137178, R01 CA 151993 and P50 CA 127003), NHS by the National Institutes of Health (R01 CA137178, P01 CA 087969, R01 CA151993 and P50 CA 127003,) and PHS by the National Institutes of Health (R01 CA042182). OFCCR: National Institutes of Health, through funding allocated to the Ontario Registry for Studies of Familial Colorectal Cancer (U01 CA074783);. Additional funding toward genetic analyses of OFCCR includes the Ontario Research Fund, the Canadian Institutes of Health Research, and the Ontario Institute for Cancer Research, through generous support from the Ontario Ministry of Research and Innovation. PLCO: Intramural Research Program of the Division of Cancer Epidemiology and Genetics and supported by contracts from the Division of Cancer Prevention, National Cancer Institute, NIH, DHHS. Additionally, a subset of control samples were genotyped as part of the Cancer Genetic Markers of Susceptibility (CGEMS) Prostate Cancer GWAS (Yeager, M et al. Nat Genet 2007 May;39(5):645-9), Colon CGEMS pancreatic cancer scan (PanScan) (Amundadottir, L et al. Nat Genet. 2009 Sep;41(9):986-90 and Petersen, GM et al Nat Genet. 2010 Mar;42(3):224-8), and the Lung Cancer and Smoking study (Landi, MT et al. Am J Hum Genet. 2009 Nov;85(5):679-91). The prostate and PanScan study datasets were accessed with appropriate approval through the dbGaP online resource (<http://cgems.cancer.gov/data/>) accession numbers phs000207.v1.p1 and phs000206.v3.p2, respectively, and the lung datasets were accessed from the dbGaP website (<http://www.ncbi.nlm.nih.gov/gap>) through accession number phs000093.v2.p2. Funding for the Lung Cancer and Smoking study was provided by National Institutes of Health (NIH), Genes, Environment and Health Initiative (GEI) Z01 CP 010200, NIH U01 HG004446, and NIH GEI U01 HG 004438. For the lung study, the GENEVA Coordinating Center provided assistance with genotype cleaning and general study coordination, and the Johns Hopkins University Center for Inherited Disease Research conducted genotyping. PMH: National Institutes of Health (R01 CA076366 to P.A. Newcomb). VITAL: National Institutes of Health (K05 CA154337). WHI: The WHI program is funded by the National Heart, Lung, and Blood Institute, National Institutes of Health, U.S. Department of Health and Human Services through contracts HHSN268201100046C, HHSN268201100001C, HHSN268201100002C, HHSN268201100003C, HHSN268201100004C, and HHSN271201100004C. NHS by the National Institutes of Health (UM1 CA186107, R01 CA137178, P01 CA 087969, R01 CA151993 and P50 CA 127003).

BCAC is funded by Cancer Research UK [C1287/A10118, C1287/A12014] and by the European Community's Seventh Framework Programme under grant agreement number 223175 (grant number HEALTH-F2-2009-223175) (COGS).

Lung eQTL study: The lung eQTL study at Laval University was supported by the Chaire de pneumologie de la Fondation JD Bégin de l'Université Laval, the Fondation de l'Institut universitaire de cardiologie et de pneumologie de Québec, the Respiratory Health Network of the FRQS, the Canadian Institutes of Health Research (MOP - 123369), and the Cancer Research Society and Read for the Cure. Y. Bossé is the recipient of a Junior 2 Research Scholar award from the Fonds de recherche Québec – Santé (FRQS).

Prostate eQTL study: supported by National Institute of General Medical Science grant R01GM107427

Additional Acknowledgements

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, Renate Hettler-Jensen, Utz Benschaid, 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 of 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, Wen Shao, 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>

BCAC: We thank all the individuals who took part in these studies and all the researchers, clinicians, technicians and administrative staff who have enabled this work to be carried out.

Rotterdam Study: The generation and management of GWAS genotype data for the Rotterdam Study (RS I, RS II, RS III) was executed by the Human Genotyping Facility of the Genetic Laboratory of the Department of Internal Medicine, Erasmus MC, Rotterdam, The Netherlands. We thank Pascal Arp, Mila Jhamai, Marijn Verkerk, Lizbeth Herrera, Marjolein Peters, MSc, Carolina Medina-Gomez, MSc, and Fernando Rivadeneira, PhD for their help in creating the GWAS database, and Karol Estrada, PhD, Yurii Aulchenko, PhD, and Carolina Medina-Gomez, MSc, for the creation and analysis of imputed data.

Consortia

African American Breast Cancer Consortium (AABC)

Christine B. Ambrosone, Esther M. John, Leslie Bernstein, Wei Zheng, Andrew F. Olshan, Jennifer J. Hu, Regina G. Ziegler, Sarah Nyante, Elisa V. Bandera, Sue A. Ingles, Michael F. Press, Sandra L. Deming, Jorge L. Rodriguez-Gil, Stephen J. Chanock.

African Ancestry Prostate Cancer Consortium (AAPC)

Sara S. Strom, Rick A. Kittles, Benjamin A. Rybicki, Janet L. Stanford, Phyllis J. Goodman, Sonja I. Berndt, John Carpten, Graham Casey⁹, Lisa Chu, Ryan W. Diver, Anselm JM Hennis, Eric A. Klein, Suzanne Kolb, Loic Le Marchand, M. Cristina Leske, Adam B. Murphy, Christine Neslund-Dudas, Curtis Pettaway, Susan M. Gapstur, S. Lilly Zheng, Suh-Yuh Wu, John S. Witte, Jianfeng Xu, William Isaacs, Barbara Nemesure, William J. Blot.

Colorectal Transdisciplinary (CORECT) Study

Aaron K Aragaki, Sonja I Berndt, Stéphane Bezieau, Hermann Brenner, Daniel D Buchanan, Katja Butterbach, Bette J Caan, Peter T Campbell, Christopher S Carlson, Graham Casey, Jenny Chang-Claude, Stephen J Chanock, Andrew T Chan, Gerhard A Coetzee, David V Conti, Keith R Curtis, David Duggan, Christopher K Edlund, Jane C Figueiredo, Christopher P Fischer, Barbara K Fortini, Charles S Fuchs, Manish Gala, Steven J Gallinger, W James Gauderman, Graham Giles, Edward L Giovannucci, Stephanie M Gogarten, Roger Green, Stephen B Gruber, Robert W Haile, John F Harju, Tabitha A Harrison, Richard B Hayes, Brian Henderson, Michael Hoffmeister, John L Hopper, Li Hsu, Shu-Chen Huang, Thomas J Hudson, David J Hunter, Carolyn M Hutter, Gregory E Idos, Motoki Iwasaki, Rebecca D Jackson, Eric Jacobs, Sun Ha Jee, Mark Jenkins, Wei-Hua Jia, Shuo Jiao, Amit Joshi, Laurence N Kolonel, Suminori Kono, Charles Kooperberg, Sébastien Küry, Andrea LaCroix, Cathy C Laurie, Loic Le Marchand, Flavio Lejbkowitz, Mathieu Lemire, David Levine, Li Li, Noralene M Lindor, Jing Ma, Karen W Makar, Frank J Manion, Sanford D Markowitz, Keitaro Matsuo, Kevin J McDonnell, Caroline E McNeil, Marilena Melas, Victor Moreno, Bhramar Mukherjee, Polly A Newcomb, Kenneth Offit, Ulrike Peters, John D Potter, Conghui Qu, Leon Raskin, Gad Rennert, Hedy S Rennert, Stephanie Rosse, Stephanie L Schmit, Robert E Schoen, Fredrick R Schumacher, Daniela Seminara, Gianluca Severi, Wei Shi, Xiao-Ou Shu, Martha L Slattery, Darin Taverna, Stephen N. Thibodeau, Duncan C Thomas, Shoichiro Tsugane, Cornelia M Ulrich, David J Van Den Berg, Hansong Wang, Dee W West, Emily White, Kana Wu, Yong-Bing Xiang, Brent W Zanke, Ben Zhang, Wei Zheng

Hereditary Breast and Ovarian Cancer Research Group Netherlands (HEBON)

Rookus M, Hogervorst F, van Leeuwen F, Verhoef S, Schmidt M, de Lange J, Collee J, van den Ouweland A, Hoening M, Seynaeve C, van Deurzen C, Obdeijn I, van Asperen C, Wijnen J, Tollenaar R, Devilee P, van Cronenburg TC, Kets C, Mensenkamp A, Ausems M, van der Luijt R, Aalfs C, van Os T, Gille J, Waisfisz Q, Meijers-Heijboer H, Gomez-Garcia E, Blok M, Oosterwijk J, van der Hout A, Mourits M, de Bock G, Vasen H.

Ovarian Cancer Association Consortium (OCAC)

Hoda Anton-Culver, Elisa Bandera, Susana Banerjee, Ros Glasspool, Iain McNeish, Jim Paul, Nadeem Siddiqui, Natalia Bogdanova, Thilo Dörk-Bousset, Ralf Butzow, Heli Nevanlinna, Jenny Chang-Claude, Georgia Chenevix-Trench, Penelope Webb, Linda Cook, Nhu Le, Daniel Cramer, Kathryn Terry, Thilo Dörk-Bousset, Matthias Duerst, Peter Fasching, Simon Gayther, Usha Menon, Graham Giles, Ellen Goode, Marc Goodman, Jacek Gronwald, Michelle Hildebrandt, Karen Lu, Estrid Høgdall, Claus Høgdall,

Beth Karlan, Lambertus Kiemeneij, Leon Massuger, Susanne Kruger Kjaer, Jolanta Kupryjanczyk, Diether Lambrechts, Douglas Levine, Keitaro Matsuo, Francesmary Modugno, Kirsten Moysich, Roberta Ness, Kirsten Moysich, Steven Narod, Catherine Phelan, Harvey Risch, Leigh Pearce, Anna Wu, Tanja Pejovic, Paul Pharoah, Mary Anne Rossing, Dale P. Sandler, Helga B Salvesen, Joellen Schildkraut, Weiva Sieh, Alice Whittemore, Meir Stampfer, Shelley Tworoger, Walter Willett, Soo-Hwang Teo, Yin Ling Woo, Nicolas Wentzensen, Wei Zheng.

The PRACTICAL Consortium (<http://practical.ccge.medschl.cam.ac.uk/>)

Rosalind Eeles, Doug Easton, Zsofia Kote-Jarai, Ali Amin Al Olama, Sara Benlloch, Kenneth Muir, Graham G. Giles, Fredrik Wiklund, Henrik Gronberg, Christopher A. Haiman, Johanna Schleutker, Maren Weischer, Ruth C. Travis, David Neal, Paul Pharoah, Kay-Tee Khaw, Janet L. Stanford, William J. Blot, Stephen Thibodeau, Christiane Maier, Adam S. Kibel, Cezary Cybulski, Lisa Cannon-Albright, Hermann Brenner, Jong Park, Radka Kaneva, Jyotsna Batra, Manuel R. Teixeira, Hardev Pandha.

San Francisco Study and Latino American Breast Cancer Consortium (LABC)

Elad Ziv, Esther M. John, Laura Fejerman.

Japanese American Prostate Cancer (JAPC) Consortium and Latino Prostate Cancer Consortium (LAPC)

Brian E. Henderson, Christopher A. Haiman, Loic Le Marchand.

Bioinformatics tools

<http://snpinfo.niehs.nih.gov/>

Xu, Z. & Taylor, J. A. SNPinfo: integrating GWAS and candidate gene information into functional SNP selection for genetic association studies. *Nucleic acids research* 37, W600-605, doi:10.1093/nar/gkp290 (2009).

<http://www.regulomedb.org/>

Boyle, A. P. *et al.* Annotation of functional variation in personal genomes using RegulomeDB. *Genome research* 22, 1790-1797, doi:10.1101/gr.137323.112 (2012).

<https://genome.ucsc.edu/>

Kent, W. J. *et al.* The human genome browser at UCSC. *Genome research* 12, 996-1006, doi:10.1101/gr.229102. Article published online before print in May 2002 (2002).