



## Report of Activities – 2009

The CGACT is a Type I center founded in 2006 and housed within the Center for Clinical Epidemiology and Biostatistics (CCEB). The mission of the Center for Genetics and Complex Traits (CGACT) is to be a leading center for statistical genetics and molecular epidemiology research. Specifically, the CGACT: 1) develops epidemiological and statistical methods for the study of complex genetic traits, 2) develops applications of these methods in multidisciplinary collaborative research, and 3) supports educational opportunities related to molecular epidemiology and statistical genetics. The CGACT is directed by Dr. Timothy Rebbeck, and includes a Statistical Genetics group led by Dr. Hongzhe Li, and a Molecular Epidemiology Group led by Dr. Timothy Rebbeck. Core CGACT faculty conduct investigator-initiated and collaborative research and contribute to the educational mission of the CGACT by teaching in relevant courses.

### Space

In January 2009, the CGACT moved into space on 2 Blockley Hall that was newly renovated thanks to a grant from the NIH. This new space has facilitated the interactions among CGACT investigators. The allotment of space to those who are doing genetics research has been made a priority for the CGACT, and a plan for space usage in the context of CCEB is being developed.



*The CGACT "Genome Café"*

### Faculty Recruitment

To enhance the development and application of genetics research at Penn, the CCEB and CGACT have emphasized the recruitment of Statistical Genetics and Molecular Epidemiology Core Faculty. To date, the center consists of five core Statistical Genetics faculty members and eight Molecular Epidemiology faculty. Among these, Dr. Rui Feng was recruited in the past year. Future recruitment plans include the identification of a molecular epidemiologist to complement the current faculty.

## Symposium

The CGACT held its Inaugural Symposium entitled "APPROACHING DISEASE GENOMICS IN THE 21ST CENTURY" on April 3, 2009. This Symposium brought world leaders in the field of statistical genetics, genetic epidemiology, and molecular epidemiology to present about current approaches in their respective fields. These speakers included:

Speaker	Institution	Title
David Hunter	Harvard University	Genome-wide association studies of breast and prostate cancer
Alice Whittemore	Stanford University	Personalizing Cancer Prevention in the Genome Era
Richard Spielman	University of Pennsylvania	Gene Expression Responses to Cellular Stress
Nan Laird	Harvard University	Generalizing the Transmission/Disequilibrium Test
Goncalo Abecasis	University of Michigan	After the Genome Wide Association Studies: Further Dissection of Complex Trait Genetics
Mark Shriver	Pennsylvania State University	The Face: Ancestry, Admixture Mapping and Ethics



Participants at the Inaugural Symposium (left to right): Richard Spielman, Peter Kanetsky, Hongzhe Li, Alice Whittemore, Mark Shriver, David Hunter, Nan Laird, Nandita Mitra.

## Visiting Scholars Program

in conjunction with the goal to identify gaps in research methodology, collaborative activities, and other research needs of the centers, the Steering Committee will identify outside faculty who may be able to advise or contribute to the areas of need, and invite them as "Visiting Scholars". These Visiting Scholars spend a short amount of time at the CGACT to discuss their research and identify ways that the CGACT can meet its research needs. In the past year, we have hosted the following Visiting Scholars:

- July 21, 2009: Mike Weedon PhD, Peninsula Medical School, Exeter, U.K. "'Genome Wide Association Study meta-analysis of 133,000 individuals identifies hundreds of new loci influencing human height: Insights into the genetic architecture of a highly polygenic complex trait"
- November 6, 2009: Vanessa Hayes, PhD, Children's Cancer Institute of Australia. "SNPing away at prostate cancer - what can Africa offer?"

We anticipate inviting 2-3 Visiting Scholars in 2010.

## Journal Clubs

Beginning in the Fall of 2009, the CGACT initiated a monthly journal club series. These journal club sessions are led by CGACT faculty members. Each session focuses on a topic of broad methodological interest to all CGACT affiliates. The sessions held in 2009 are:

Date	Discussion Leader	Topic
October 1	Peter Kanetsky	Genome-wide Association Studies
November 5	Tim Rebbeck	Ancestry Informative Markers
December 3	Bao-Li Chang	Cancer Risk Prediction Models

We anticipate that these sessions will continue on a monthly basis in the future.

## Statistical Genetics Working Group

The existing statistical genetics working group allows students and postdoctoral fellows to present their ongoing research for critique by faculty. These meetings have been held weekly on Friday mornings, and led by Dr. Hongzhe Li. This is an ongoing group meeting that will continue in the future. This semester, we have covered topics related to methods for next generation sequencing data, epigenetics and eQTLs and have identified several statistical problems that can require new methods development.

## Research Papers

An important aspect of the CGACT is to develop and apply methods for the study of genetics and complex disease. Selected research developments by core CGACT members include the following papers, with an emphasis on those that appear in high profile journals, represent methodological developments, or highlight interactions with consortia and among CGACT and other Penn faculty members:

- Bishop DT, Demenais F, Iles MM, Harland M, Taylor JC, Corda E, Randerson-Moor J, Aitken JF, Avril MF, Azizi E, Bakker B, Bianchi-Scarrà G, Bressac-de Paillerets B, Calista D, Cannon-Albright LA, Chin-A-Woeng T, Debniak T, Galore-Haskel G, Ghorzo P, Gut I, Hansson J, Hocevar M, Höiom V, Hopper JL, Ingvar C, **Kanetsky PA**, Kefford RF, Landi MT, Lang J, Lubiński J, Mackie R, Malvey J, Mann GJ, Martin NG, Montgomery GW, van Nieuwpoort FA, Novakovic S, Olsson H, Puig S, Weiss M, van Workum W, Zelenika D, Brown KM, Goldstein AM, Gillanders EM, Boland A, Galan P, Elder DE, Gruis NA, Hayward NK, Lathrop GM, Barrett JH, Bishop JA. Genome-wide

association study identifies three loci associated with melanoma risk. *Nature Genetics*;41(8):920-5, 2009.

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- **Chen J**, Zheng H, Wilson ML, Kraft P: Testing Hardy-Weinberg equilibrium using mother-child case-control samples. *Genetic Epidemiology* 33(6):539-48, 2009.
- **Chen J**, Zheng H, Wilson ML: Likelihood ratio tests for maternal and fetal genetic effects on obstetric complications. *Genetic Epidemiology* Feb, 2009.
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- Eeles RA, Kote-Jarai Z, Al Olama AA, Giles GG, Guy M, Severi G, Muir K, Hopper JL, Henderson BE, Haiman CA, Schleutker J, Hamdy FC, Neal DE, Donovan JL, Stanford JL, Ostrander EA, Ingles SA, John EM, Thibodeau SN, Schaid D, Park JY, Spurdle A, Clements J, Dickinson JL, Maier C, Vogel W, Dörk T, **Rebbeck TR**, Cooney KA, Cannon-Albright L, Chappuis PO, Hutter P, Zeegers M, Kaneva R, Zhang HW, Lu YJ, Foulkes WD, English DR, Leongamornlert DA, Tymrakiewicz M, Morrison J, Ardern-Jones AT, Hall AL, O'Brien LT, Wilkinson RA, Saunders EJ, Page EC, Sawyer EJ, Edwards SM, Dearnaley DP, Horwich A, Huddart RA, Khoo VS, Parker CC, Van As N, Woodhouse CJ, Thompson A, Christmas T, Ogden C, Cooper CS, Southey MC, Lophatananon A, Liu JF, Kolonel LN, Le Marchand L, Wahlfors T, Tammela TL, Auvinen A, Lewis SJ, Cox A, FitzGerald LM, Koopmeiners JS, Karyadi DM, Kwon EM, Stern MC, Corral R, Joshi AD, Shahabi A, McDonnell SK, Sellers TA, Pow-Sang J, Chambers S, Aitken J, Gardiner RA, Batra J, Kedda MA, Lose F, Polanowski A, Patterson B, Serth J, Meyer A, Luedeke M, Stefflova K, Ray AM, Lange EM, Farnham J, Khan H, Slavov C, Mitkova A, Cao G; UK Genetic Prostate Cancer Study Collaborators/British Association of Urological Surgeons' Section of Oncology; UK ProtecT Study Collaborators; PRACTICAL Consortium, Easton DF. Identification of seven new prostate cancer susceptibility loci through a genome-wide association study. *Nature Genetics*.41(10):1116-21, 2009.
- **Kanetsky PA**, **Mitra N**, Vardhanabhuti S, **Li M**, Vaughn DJ, Letrero R, Ciosek SL, Doody DR, Smith LM, Weaver J, Albano A, Chen C, Starr JR, Rader DJ, Godwin AK, Reilly MP, Hakonarson H, Schwartz SM, **Nathanson KL**. Common variation in KITLG and at 5q31.3 predisposes to testicular germ cell cancer. *Nature Genetics*. 41(7):811-5, 2009.
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- **Li, H**, Wei Z and Maris J. A hidden Markov random field model for genome-wide association studies. *Biostatistics*, In Press, 2009.
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## Research Funding

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CGACT core faculty have been successful in obtaining research funding. As of December 2009, CGACT core faculty were PI of 24 extramural grants totaling \$7,716,582, primarily from NIH.

## Training

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Development of Educational Programs, including courses, seminar series, visiting scholar series, and degree granting educational programs is a key area for CGACT activities. These activities include Human Genetics Concentration and coursework in the Human Genetics concentration in the MSCE program. Genetics Courses offered in the Biostatistics and Epidemiology Graduate Group include the following:

Course #	Title (Course Director)
EP575	Introduction to Genetic and Molecular Epidemiology (Rebeck/Devoto)
EP775	Special Topics in Genetic and Molecular Epidemiology (Rebeck)
BSTA785	Statistical Methods for Genomic Data Analysis (H. Li)
BSTA787	Methods for Statistical Genetics in Complex Human Disease (M. Li)

An additional course entitled “Statistical Methods in Human Genetics” is being developed that introduces statistical procedures for investigating the inheritance of human characteristics through studies of families and populations. The main focus is on segregation, linkage and DNA sequence analysis.

## In Memoriam

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Dr. Richard Spielman, the Butterworth Professor of Genetics in the School of Medicine, passed away suddenly on April 25, 2009, only three weeks after presenting at the CGACT Inaugural Symposium. He was 63 years old. Dr. Spielman joined the Penn faculty in 1974, was a world-renowned expert in the fields of human genetics and genomics. His seminal work with Warren Ewens on family-based genetic association studies, the Transmission Disequilibrium Test (TDT), has been cited more than 2,400 times to date and has had a major impact on the field. His more recent studies with Dr. Vivian Cheung of Children's Hospital, were the first to investigate the genetics of natural variation of gene expression in humans. Dr. Spielman was an active participant in the CGACT as a collaborator, mentor, and valued advisor. He was committed to teaching both graduate students and medical students. He was the founding Chair of the Genomics and Computational Biology graduate group, which has become the model for similar programs elsewhere.

(Modified from: <http://www.med.upenn.edu/genetics/RichardSpielman.shtml>)