

## CHAIR'S MESSAGE



Charis Eng, M.D., Ph.D.

I am delighted to present to you our second newsletter of this year highlighting GMI's pivotal role in providing genetics-enabled healthcare not just at the Cleveland Clinic, but also across North East Ohio.

November is Family History month and we are being highlighted both on the Clinic's walkway as well as displaying our own interactive poster in the Lerner Research Institute during November through December. Our clinical services keep expanding and because of our research expertise, our involvement in the Clinic's strategic planning initiatives like the "-omics based" research project are just a few ways that we are actualizing our goal of obtaining genomic medicine data to be translated to personalized patient care. Our research continues to thrive as well. In addition to our various high impact publications and grant funding, you will learn more about the recently R01-funded research in Dr. Angela Ting's laboratory and the state-funded clinical and education grant led by Dr. Rocio Moran, the first of this type for the Clinic. Thank you for your continued engagement and hard work to achieve our mission. Onward & upward!

## UNDER THE SCOPE



Angela Ting, PhD was recently awarded an NCI grant to study changes in DNA methylation that might account for differences in the aggressiveness of prostate cancer.

In prostate cancer, DNA methylation can prevent caretaker genes and tumor suppressors from being manufactured in a cell. The goal of this project is to identify DNA methylation marks that distinguish between indolent and aggressive prostate cancer so as to help clinicians decide whether a patient actually needs treatment for prostate cancer.



"Through our objective discovery, we hope to identify molecular targets for biological studies to enhance our understanding of prostate cancer." Currently, there are no non-invasive techniques that can distinguish between indolent and aggressive forms of prostate cancer and many men diagnosed with prostate cancer undergo invasive treatments with highly undesirable side effects even if there is no certainty that the cancer they harbor will ultimately cause them harm.



These funds have allowed Dr. Ting to recruit new people in the lab and build a cohesive, productive research team to carry out this project. Maggie Taylor has already taken on a significant role in the lab with sample preparation, cell culture studies, and protocol optimization.

Dr. Ting is very excited that this project was funded by the NCI. "This is an area that deserves our attention because the outcome can directly benefit patient care in the near future through improving clinical diagnosis and decision making... (and) I get to continue doing what I love."

### congratulations to:

**Kylie Drake, PhD**, postdoctoral fellow in the Aldred Lab, for winning a Travel Award to the 2011 American Thoracic Society meeting, two years in a row.

**Hui Hui Liu, PhD**, postdoctoral fellow in the Zhang lab, for being selected as a Bumpus Award finalist.

**Brandie Leach, MS, CGC**, genetic counselor in CPGH, for being elected a member of the Council-at-Large of the Collaborative Group of the Americas on Inherited Colorectal Cancers (CGA-ICC).

**Joanne Ngeow, MD**, clinical cancer genetics fellow in the Eng lab, for winning the National Medical Research Council of Singapore Research Training Fellowship.



## GMI Employee of the Quarter Recipients



**Quarter 2, 2011  
Brandie Leach**



**Quarter 3, 2011  
Nicole Achkar**

*GMI's Mission:  
To provide a work culture that enables us to bring genetics and genomics, through our research and clinics, into all subspecialties of the Cleveland Clinic's Healthcare System*



Maureen May  
Genetic Counselor, CPGH

## IN THE CLINIC

### *Family History: a closer look*

While advances in genomic medicine continue to enhance efforts to personalize healthcare, many people are unaware that the best tool for understanding their genetic risk for disease is simple, free, and even fun! In honor of the Surgeon General's designation of Thanksgiving as National Family History Day, the Center for Personalized Genetic Healthcare (CPGH) is working to promote awareness of family health history.

Family history is one of the best indicators of an individual's risk for conditions such as cancer, heart disease, and diabetes. Sharing your complete family health history with healthcare providers can help them to be alert to early warning signs of these and other diseases so that you get the care you need faster. Family history assessment may also allow your provider to make important recommendations for prevention of diseases you're at an increased risk for, such as helping you to identify and modify lifestyle factors related to diabetes. Watch for great CPGH

tips, information, and tools to help you gather your family health history along the Skyway all month! Are you ready to explore your own family's health history? Visit the Surgeon General's My Family Health Portrait

***“Family history is one of the best indicators of an individual's risk for conditions such as cancer, heart disease, and diabetes.”***

web tool at <https://familyhistory.hhs.gov/fhh-web/home.action> to get the conversation started.

Of course, family healthy history is important all year long so with the support and guidance of Dr. Charis Eng, Chair of the Genomic Medicine Institute (GMI) and Dr. Kathryn Teng, Director of the Center for Personalized Healthcare (CPH) the CPGH has an ongoing effort to engage patients and physicians in awareness of hereditary disease risk. By inviting patients to

enter family health history data via the web-based “MyFamilyHealthHistory” (MyFHH) tool, this initiative has been able to provide clinicians with a wealth of information including an electronic pedigree to allow for more personalized, patient-centered care.

Building on the success of the MyFHH tool, the CPGH and the CPH have launched an exciting initiative to fully integrate patient-entered family history data into clinical care. This innovative project will draw on the expertise of genetic counselors, physician leaders, computer programmers, project implementation experts, and graphic designers to collect and assess family health history using a set of disease-specific algorithms, and it doesn't stop there. The tool will also provide current, evidence-based, personalized guidance to primary care physicians and give patient-specific recommendations for referrals, screening, and preventative care. The CPGH and CPH staff are proud of their part in the Cleveland Clinic's mission to shape the future of personalized healthcare.



*The Surgeon General's "My Family Health Portrait" is an internet-based tool that makes it easy for you to record your family health history. The tool is easy to access on the web and simple to fill out. It assembles your information and makes a "pedigree" family tree that you can download. It is private-it does not keep your information. It gives you a health history that you can share with family members or send to your health care practitioner.*

## SNP-bits New Personnel ...Farewells ...Congrats

### New/Returning Personnel (since April 2011):

Fusong Chen (Senior Research Technologist, Eng lab)  
 Deepa Radhakrishnan (Visiting Scientist, Eng lab)  
 Maureen May (Genetic Counselor, CPGH)  
 Maggie Taylor (Research Technician, Ting lab)  
 Erika Hanson (Research Technician, Genomics Core)  
 Rebecca Cook (Genetic Counselor, CPGH)  
 Matt Cannon (Postdoc, Serre lab)  
 Janice Blount (Dept Coordinator, Dr. Eng)  
 Giovanna Grandinetti (Postdoc, Ting lab)  
 Junying Lei (Senior Research Technologist, Eng lab)  
 Robert Shields (Programmer Analyst, Eng lab)  
 Charlene Mitchell (Genetics Education Coordinator, CPGH)

### Farewells & All the Best:

Hadley Miller (Serre lab)	Gina Keeler (CPGH)
Stephanie Fritz (CPGH)	Hongli Yan (Ting lab)
Nichole Prescott (GMB)	Pieter Faber (Genomics Core)
Patty Arscott (CPGH)	Min-Han Tan (Eng lab)

### Service Anniversaries at Cleveland Clinic

#### 15 years

Pam Price (Nov, 2011)  
 Phyllis Harbor (June, 2011)

#### 10 years

Peter Balint (Oct, 2011)

#### 5 years

Rocio Moran (Sept, 2011)  
 Effie Sehayek (Sept, 2011)  
 Petra Platzer (Aug, 2011)  
 Brandie Leach (July, 2011)

### Promotions

Chunlei Zhen	Research Associate
Kylie Drake	Research Associate
Yu Wang	Research Associate
Jessica Schweitzer	Research Technologist

### Annual Meetings (multiple posters)

#### NATIONAL SOCIETY OF GENETIC COUNSELORS (NSGC)

October, 2011  
 Plenary Session: Jessi Mester (and "Best Abstract for an NSGC Full Member" Award)  
 Educational Breakout Session: Meg Doerr  
 Presentations: Brandie Leach, Jessi Moline, Jill Polk, Amy Shealy, Marissa Smith  
 Posters: Patty Arscott, Rebecca Cook (2 posters), Christina Rigelsky, Allison Schreiber

#### AMERICAN SOCIETY OF HUMAN GENETICS (ASHG)

November, 2011  
 First Author Posters: Joanne Ngeow, Ying Ni, Jessi Mester, Emily Pontzer

### Invited Keynote and Plenary Talks

Charis Eng, MD, PhD, FACP, presented at AACC Morning Symposium on Direct-to-Consumer Genomic Testing: Opening Pandora's Box chaired by KT Jerry Yeo, PhD from the University of Chicago. Dr. Eng presented the "Bioethical and Clinical Dilemmas of Direct-to-Consumer Genomic Testing"; and Dr. Jeff Gulcher, MD, PhD, CMO of DeCode Genetics, presented "Genetic Risk Tests for Common Diseases: for Physician Eyes Only?" After the talks, a lively scholarly panel discussion ensued.

Charis Eng, MD, PhD, FACP, took a one-day break from her vacation to present at a by-invitation-only Colloquium of Leaders of Genomic Medicine Institutes hosted by NHGRI and the NIH. The goal of this day-long Colloquium is to do an as-is assessment on and discuss opportunities, challenges and solutions to integrating genetic and genomic processes and services into routine clinical care. Dr. Eng presented how the Genomic Medicine Institute collaborated with the Digestive Disease Institute and Pathology and Lab Medicine Institute to successfully integrate microsatellite testing and mismatch repair protein immunohistochemistry into pathology routine for all colorectal carcinomas resected on Cleveland Clinic main campus. This has led to an uptake of 80% of test-positive individuals reaching GMI's Center for Personalized Genetic Healthcare, and an effective strategy for identifying the majority of adult-onset heritable colon cancer (Lynch syndrome).

Charis Eng, MD, PhD, FACP, delivered a plenary lecture to 2011 Healthsmart Forum on reform legislation and the future of integrated self-funded healthcare. She spoke about genetics and genomics-enabled disease risk assessment, prediction and tailored medical management. She provided compelling evidence that this type of strategy will ensure value-based delivery of healthcare for the 21st century.

## GMI Summer Picnic

### Edgewater Park



## Publications since April 2011

**Chan ER, Hester J**, Kalady M, Xiao H, Li X, **Serre D**. A novel method for determining microflora composition using dynamic phylogenetic analysis of 16S ribosomal RNA deep sequencing data. *Genomics*. 2011 Oct;98(4):253-9. Epub 2011 Apr 15. PMID:21515358

**Wang Y, Romigh T, He X, Tan MH, Orloff MS**, Silverman RH, Heston WD, **Eng C**. Differential regulation of PTEN expression by androgen receptor in prostate and breast cancers. *Oncogene*. 2011 May 2. [Epub ahead of print] PMID:21532617

Burkardt DD, Rosenfeld JA, Helgeson ML, Angle B, Banks V, Smith WE, Gripp KW, **Moline J, Moran RT**, Niyazov DM, Stevens CA, Zackai E, Lebel RR, Ashley DG, Kramer N, Lachman RS, Graham JM Jr. Distinctive phenotype in 9 patients with deletion of chromosome 1q24-q25. *Am J Med Genet A*. 2011 Jun;155A(6):1336-51. doi: 10.1002/ajmg.a.34049. Epub 2011 May 5. PMID:21548129

**Bennett KL, Campbell R, Ganapathi S, Zhou M**, Rini B, **Ganapathi R**, Neumann HP, **Eng C**. Germline and somatic DNA methylation and epigenetic regulation of KILLIN in renal cell carcinoma. *Genes Chromosomes Cancer*. 2011 Aug;50(8):654-61. doi: 10.1002/gcc.20887. Epub 2011 May 16. PMID:21584899

**Yan H, Choi AJ, Lee BH, Ting AH**. Identification and functional analysis of epigenetically silenced microRNAs in colorectal cancer cells. *PLoS One*. 2011;6(6):e20628. Epub 2011 Jun 16. PMID:21698188

**Orloff M, Peterson C, He X, Ganapathi S, Heald B, Yang YR, Bebek G, Romigh T**, Song JH, Wu W, David S, Cheng Y, Meltzer SJ, **Eng C**. Germline mutations in MSR1, ASCC1, and CTHRC1 in patients with Barrett esophagus and esophageal adenocarcinoma. *JAMA*. 2011 Jul 27;306(4):410-9. PMID:21791690

**Bebek G, Orloff M, Eng C**. Microenvironmental genomic alterations reveal signaling networks for head and neck squamous cell carcinoma. *J Clin Bioinforma*. 2011 Aug 2;1(1):21. PMID:21884569

Sullivan M, Rybicki LA, Winter A, Hoffmann MM, Reiermann S, Linke H, Arbeiter K, Patzer L, Budde K, Hoppe B, Zeier M, Lhotta K, Bock A, Wiech T, Gaspert A, Fehr T, Woznowski M, Berisha G, Malinoc A, Goek ON, **Eng C**, Neumann HP. Age-Related Penetrance of Hereditary Atypical Hemolytic Uremic Syndrome. *Ann Hum Genet*. 2011 Nov;75(6):639-647. doi: 10.1111/j.1469-1809.2011.00671.x. Epub 2011 Sep 12. PMID:21906045

**Moline J, Eng C**. Multiple endocrine neoplasia type 2: an overview. *Genet Med*. 2011 Sep;13(9):755-64. PMID:21552134

**Drake KM, Zygmunt D**, Mavrakis L, **Harbor P**, Wang L, Comhair SA, Erzurum SC, **Aldred MA**. Altered microRNA Processing in Heritable Pulmonary Arterial Hypertension: an Important Role for Smad-8. *Am J Respir Crit Care Med*. 2011 Sep 15. [Epub ahead of print] PMID:21920918

**Ngeow J, Mester J**, Rybicki LA, **Ni Y**, Milas M, **Eng C**. Incidence and Clinical Characteristics of Thyroid Cancer in Prospective Series of Individuals with Cowden and Cowden-Like Syndrome Characterized by Germline PTEN, SDH, or KLLN Alterations. *J Clin Endocrinol Metab*. 2011 Sep 28. [Epub ahead of print] PMID:21956414

**Ni Y, He X, Chen J, Moline J, Mester J, Orloff MS**, Ringel MD, **Eng C**. Germline SDHx Variants Modify Breast and Thyroid Cancer Risks in Cowden and Cowden-like Syndrome via FAD/NAD-dependant Destabilization of p53. *Hum Mol Genet*. 2011 Oct 6. [Epub ahead of print] PMID: 21979946

Xu Y, Hu B, **Choi AJ, Gopalan B**, Lee BH, Kalady MF, Church JM, **Ting AH**. Unique DNA methylome profiles in CpG island methylator phenotype colon cancers. *Genome Res*. 2011 Oct 11. [Epub ahead of print] PMID:21990380

## Genetics Education



The Center for Personalized Genetic Healthcare is pleased to announce receipt of an Ohio Department of Health (ODH) grant in July.

The award will enhance their mission to provide exceptional clinical care, groundbreaking research, and accessible genetic education. Over a four year period, the ODH grant will support the CPGH's designated "Regional Comprehensive Genetic Center" in the provision of educational and

clinical genetic services for patients and providers.

The grant will allow the CPGH to pursue their vision of extending cancer and cardiovascular genetic services to previously overlooked populations. Outreach to high risk and underserved communities will identify families who have historically had limited or no access to assessment for hereditary cancer and heart disease, providing a potentially life-saving connection for at-risk individuals. In the spirit of this goal, the cancer genetics service area will explore options for expansion to Lake and Lorain counties, while the cardiovascular genetics service plans to provide new services to Women's Preventative Cardiology.

The CPGH team has also hit the ground running in the genetic education arena, involving four genetic counselors with a range of clinical expertise in the Universal Sisters conference in October. This conference addresses the unique health needs of women of color and strives to educate them about crucial preventive health care. With ODH grant support, the CPGH was able to provide information, referral, and screening services to hundreds of minority women concerned about their family history of diabetes, cancer, heart disease, and more. Stay tuned for more genetic education events from CPGH!

### RECENT GMI GRANTS

7/1/11 **Micheala Aldred**, 3 years, \$210,000 Cardiovascular Med Research and Educ Fund: Mutation analysis of Pulmonary Hypertension Break-through Initiative cases

7/1/11 **Rocio Moran**, 4 year, \$451,000 ODH: ODH Genetics Grant

9/1/11 **Angela Ting, PhD**, Genomic Medicine Institute, 5-year \$1.6M R01 from NIH/National Cancer Institute (NCI): "Characterizing the DNA methylomes of indolent and aggressive prostate cancers"

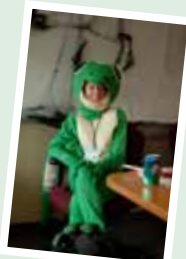
9/1/11 **Ephraim Sehayek**, 2 year, \$130,000 Merck & Co: Ezetimibe stimulates Liver Abcg5/Abcg8 Expression through the Fgf15-Fgfr4 Signaling Pathway: Coupling of Bile Acid Metabolism to Reverse Cholesterol Transport from Peripheral Tissue Macrophages"

9/1/11 **David Serre**, 1 year \$50,000 Case GI Cancers SPORE pilot award: "Molecular Analysis of the Microflora Associated with Colorectal Cancers

9/6/11 **Charis Eng**, 2 year, \$249,000 Harvard University subcontract funded through NIH: Molecular and Genetic Analysis of Neuroendocrine Tumor Risk and Survival

9/23/11 **Micheala Aldred**, 2 year, \$157,000 NIH/NHLBI: Role of the X-chromosome in Pulmonary Arterial Hypertension  
Title: Genes that Affect Mitochondrial Function as Novel Mediators of Breast Cancer Susceptibility

10/1/11. **Charis Eng** 1 Year, \$224,940: Breast Cancer Research Foundation



### GMI Halloween Party