

Newsletter of the Survivorship, Outcomes And Risk Program at MSKCC

MSK Symposium Addresses Challenges in Genetic Epidemiology

Experts Discuss Novel Statistical Methods

In August MSKCC hosted a special symposium, *Advances in Statistical Methods for Cancer Genetic Epidemiology*, chaired by SOAR investigator, **Jaya Satagopan** (Biostatistics), and Sanjay Shete of MD Anderson Cancer Center. The two-day meeting attracted participants from across the country to discuss theoretical approaches and practical applications of analytic methods in cancer genetic epidemiology. The symposium was supported by a grant from the National Cancer Institute.

Nineteen experts spoke on topics within several general categories: the use of “omics” data, sampling design parameters, sequencing data analysis, models for high throughput data, risk modeling and gene-environment interactions, incorporation of biological data, and software packages for data analysis. Throughout the meeting researchers discussed the broader goals of developing and applying novel statistical methods to reduce false discovery rates and the effects of confounding in genetic epidemiology studies in cancer.



Photo by Rick Dewitt

Jaya Satagopan welcomes symposium participants

Advances in technology have increased the breadth and depth of genomic data, but also challenged statisticians to develop new bioinformatic and computational tools. Dr. Satagopan said that she and many of her colleagues have puzzled over analytic techniques. “Our general consensus over numerous discussions was that while technology-specific analytic developments may be warranted in some

cases, perhaps the time is ripe for us to change the way we reason, interrogate, and integrate these data by making innovative use of...principles of statistical sciences to address clinically relevant hypotheses about the stochastic evolution of cancer,” Satagopan said.

Shrinking research budgets have prompted interest in the use of publicly available datasets for genetic epidemiology studies. In her overview of the Epidemiology and Genomics Research Program at the NCI, Carolyn Hutter (NCI) described some of the institute’s resources and datasets, including the database of Genotypes and Phenotypes (dbGaP), an archive of studies on the interaction of genotype and phenotype, and Genetic Simulation Resources,

a catalog of computer applications for simulating genetic data. Dr. Hutter emphasized the need to reduce barriers that researchers often face by standardizing databases and simplifying the process for distributing or accessing publicly available datasets. Hutter and other speakers also noted the need to develop novel analytic techniques for increasing statistical power in rare subtype analyses and for replicating research findings.

In addition to Dr. Satagopan, MSKCC presenters included **Colin Begg** (Biostatistics), who discussed strategies for investigating etiologic heterogeneity, and **Marinela Capanu** (Biostatistics), who presented her work on controlling false discovery rates when testing for rare genetic variants. Capanu and other participants commended the symposium chairs, noting the range of topics covered, the inclusion of both junior and senior scientists, and the size and format of the meeting, which facilitated meaningful discussions and close professional networking. Selected papers from the symposium will be submitted for publication.



Photo by Rick Dewitt

Xuefeng Wang, of Harvard University, speaking with colleagues.

Mark your calendar

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| October 3
12:30PM
M-107 | SOAR Seminar
Christopher Amos, PhD
Geisel School of Medicine at Dartmouth |
| October 18-23 | Society for Medical Decision Making Annual Meeting
Baltimore |
| October 31
11:30AM
RRL-116 | SOAR Seminar
Ross Prentice, PhD
Fred Hutchinson Cancer Research Center |
| November 1-2 | ASCO Quality of Care Symposium
San Diego |
| November 2-6 | American Public Health Association Annual Meeting
Boston |

MSKCC Amends Institutional Biospecimen Protocol

Changes Address New Tests and Incidental Findings

The MSKCC Institutional Review Board approved an amendment to the Center’s human biospecimen protocol (IRB #06-107). The protocol now includes next-generation sequencing of tumor specimens and normal tissue samples; allows, by verbal consent, collection of additional samples of routinely biopsied tissue if there is no additional risk to the patient; explicitly states that patients will not receive results of tests done solely for research purposes; and provides a standardized procedure for re-contacting patients regarding incidental genetic findings.

The amendment addresses issues raised by the use of next-generation sequencing (NGS) technologies, which yield information about thousands or millions of gene sequences at the same time. Commenting on the importance of these changes, **Mark Robson** (Clinical Genetics) said, “MSK has crafted an approach that protects the human subjects participating in studies at our institution, without

unnecessarily restricting potentially ground-breaking genomics research.”

A particular concern with NGS is the discovery of gene sequences or mutations that indicate a specific, known health risk, but are unrelated to the research question at hand. The amended consent form for protocol 06-107 asks participants for permission to re-contact them if their samples are used in a research study and an incidental finding is made that may be critical to their preventive care. Notification of incidental findings will be made following review by the IRB.

Participants will not be told of a specific test result, but told that their tissue sample was used in a research study and a potential risk was uncovered. Participants notified of an incidental finding will be asked to come to MSKCC’s Clinical Genetics Service for counseling and subsequent genetic testing.

SOAR Grants

Colin Begg (Epidemiology and Biostatistics) was awarded a grant from the MSKCC Metastasis Research Center. The study, “*Contralateral Breast Cancers: Independent Cancers or Metastases?*”, will use next-generation sequencing technology and specialized statistical models to analyze archival breast cancer specimens. Co-investigators include **Jonine Bernstein** and **Tari King**.

Matthew Matasar (Medicine) was awarded a Translational Research Program grant from the Leukemia and Lymphoma Society for his study, “*Tissue and Functional Assessment of Myocardial Injury in Hodgkin Lymphoma Survivors*”. Treatment-related heart disease is a leading of death and comorbidity in Hodgkin lymphoma (HL) survivors. The study will compare novel magnetic resonance techniques with echocardiography to evaluate cardiac injury in HL survivors. Co-investigators include **Kevin Oeffinger**, **Emily Tonorezos**, **Kenneth Offit**, **Steve Horwitz** and **Chaya Moskowitz**.

SOAR Investigator Brings MSK Program to Qatar



Carma Bylund (Psychiatry and Behavioral Sciences), has accepted a position at Hamad Medical Corporation (HMC) in Qatar, where she will be Associate Director of Medical Education. Dr. Bylund is an Associate Attending

at MSKCC and Director of the Communication Skills Research and Training Lab (Comskil).

Dr. Bylund began her career at MSKCC in 2005, and with Richard Brown, created the Comskil Training Program to provide communications skills training to physicians, fellows, residents and nurses throughout the Center. In 2009, a group of HMC faculty members visited MSKCC to participate in the Comskil Training Program, and subsequently invited Dr. Bylund to Qatar for a week-long training of HMC faculty. She was later recruited to a full-time faculty position in Qatar.

HMC manages eight hospitals in Qatar and is accredited by the Joint Commission International (JCI). In 2012 it became the first institution in the Middle East and the second outside the US to be accredited by the Accreditation Council for Graduate Medical Education International (ACGME-I). Commenting on this achievement, Dr. Bylund said, “communication is one of the big skills ACGME looks for and it was important for Hamad to develop [the Comskil] program.”

When asked how she feels about moving to Qatar, Dr. Bylund said, “It’s a really interesting area of the world. The cultural issues there and how they affect healthcare are so profound. It’s exciting to work with them to develop the first real communications training program in the Middle East. The people are wonderful.” Dr. Bylund added, “Qatar is a large urban area similar to New York. I’ll miss Broadway shows though.”

SOARNEWS EDITORIAL STAFF

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Q&A

Jada Hamilton

Jada Hamilton is an Assistant Attending Psychologist who joined the Behavioral Sciences Service at MSKCC in July, after finishing a Cancer Prevention fellowship at the NCI. She recently spoke with the SOAR Newsletter about her training and research.

Welcome to MSKCC. How did you get here?

I grew up in a small town in Ohio and went to Ohio Wesleyan University to be a genetics major, I realized I really liked psychology too. I was interested in studying patient motivations and understanding of genetic information. That’s what led me to a PhD in Health Psychology at Stony Brook University on Long Island.

Did you plan to focus on cancer?

I didn’t. I started working in pregnancy and women’s health, looking at prenatal maternal stress. I always had interests in genetic testing, genetic counseling, and risk information. I think cancer is a natural environment for that because we’ve had so much progress in the context of BRCA testing and genetic testing related to colon cancer risk. Going to cancer made a lot of sense, but it was not something I knew I was going to do. I had the opportunity to meet Bob Croyle, Director of Cancer Control and Population Sciences at NCI, and learned about the NCI fellowship.

What did you study at the NCI?

I worked on a project looking at decision making and uncertainty in Fanconi anemia, a rare inherited bone marrow syndrome associated with cancer risk. It’s a really challenging decision-making context for parents to try to decide if and when an affected child will have a stem cell transplant.

What did you find?

Parents who perceived more uncertainty were less likely to choose a transplant, and they had more difficulty making that decision. It seems like the uncertainty made them very worried about the outcome. As scientists we’re sort of comfortable with uncertainty. But that space can be difficult for patients and their family members dealing with a treatment decision.

You also studied genetic testing for breast cancer risk.

I had done a meta-analysis looking at emotional distress following BRCA testing and found that across 21 different studies, women who learned they were a carrier of a mutation did experience an increase in their distress but it went back to baseline over time. Women who did not carry the mutation, their distress just decreased over time. For women who had an inconclusive result, their distress looked similar to the non-carriers. I think it’s interesting because these women could still be at high risk of developing a future cancer so it raises the questions - what are they thinking this result means; are they not adopting appropriate cancer prevention behaviors.

How are you hoping to answer those questions at MSKCC?

The Clinical Genetics service has helped identify a panel of gene variants that appear to more accurately predict breast cancer risk in women who have a *BRCA2* mutation. If a woman has a *BRCA2* mutation, her risk of breast cancer is 40% to 85%, a pretty big window. Research shows that it’s challenging to decide what you want to do then to manage your risk - be screened more regularly, take a drug or have prophylactic surgery. We’re thinking about how we can give women results from this panel and be able to more accurately predict their risk. I’m interested in how we can communicate those test results to women in a way that is informative, understandable and trustworthy.

What do you think about Angelina Jolie’s decision to have a prophylactic double mastectomy?

It’s fascinating how much media coverage it got, and I think it will be really interesting to see what this does for public awareness, not only BRCA testing but risk reducing strategies. Also to see if it has an impact on what patients who are not Angelina Jolie decide to do.

You have four degrees – BA, MA, MPH, and a PhD. You’ve spent a lot of time studying. What do you do outside of your professional life?

I’m kind of a homebody. I love baking. Baking is my stress reliever. I love trying new recipes and then tweaking them. I’m kind of vigorous, I do it once by the book and then I start playing with it. My husband and I are foodies, and New York is a great place to be a foodie.

MEET THE REPORTER

Meghan Woods, Research Project Manager in Epidemiology, works with Jonine Bernstein on the Women’s Environmental, Cancer, and Radiation Epidemiology (WECARE) Study. When she’s not at work,



Meghan enjoys year-round outdoor adventures - from hiking and camping in the warm months to skiing when the conditions are right. Meghan reported this issue’s story on the recent genetic epidemiology statistical methods symposium at MSKCC.