SOARNEWS
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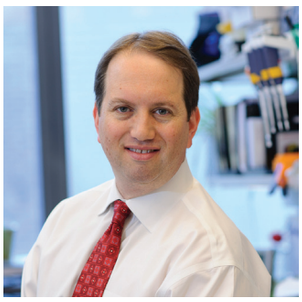
Newsletter of the Survivorship, Outcomes And Risk Program at MSKCC

Genomic Analysis Reveals Endometrial Cancer Subtypes

Study Finds Four Tumor Types with Distinct Molecular Features



Endometrial cancers can be classified into four distinct subtypes based on molecular features, according to a recent study led by SOAR investigator, Douglas Levine (Surgery). Using a variety of genomic and proteomic techniques, scientists analyzed tumor samples and germline DNA collected from 373 endometrial cancer patients at 19 centers. Their results identified four types of endometrial tumors with varying prognosis, distinguished by specific molecular characteristics.

Endometrial cancers have traditionally been classified as one of two types based on histologic features. Type I, or endometrioid, tumors are associated with excess estrogen, obesity, hormone-receptor positivity, and more favorable prognosis. Type II, or serous, tumors are more common in older, non-obese women and are associated with poorer prognosis. Endometriod tumors are usually treated with surgery and radiation, while chemotherapy is typically reserved for the more aggressive serous cancers. In their analysis, Levine and colleagues found a previously unrecognized subset of high-grade endometrioid tumors that are similar in molecular phenotype and behavior to the serous tumor type, and may therefore warrant more aggressive treatment. They also found that serous tumors shared many molecular features with high-grade serous ovarian cancers and basal-like breast cancers.

Endometrial cancer is the fourth most common cancer in US women, responsible for almost 50,000 new cases and more than 8,000 deaths each year. While most endometrial cancers are diagnosed at an early stage with a favorable prognosis, patients diagnosed with advanced disease have five-year survival rates less than 20%. Reclassification of endometrial cancers based on molecular characteristics has the potential to improve health outcomes, if it can help clinicians identify the best treatment for each patient based on her tumor type.

The study, published in *Nature*, was conducted within The Cancer Genome Atlas (TCGA) Research Network, an NCI-sponsored network of investigators across the US and Canada. Core resources of TCGA include biospecimen processing, high-throughput genome sequencing and genome characterization. Levine acknowledged the importance of multi-institutional collaborations for amassing high quality, representative specimens, noting that collaboration "is even more critical when dealing with a rare tumor or when tissue requirements are complex." He commended NCI leadership and the TCGA Biospecimen Repository for their work on behalf of the study team.

Sara Olson (Epidemiology), who was not part of the TCGA study, noted that the new molecular classification may have important implications for epidemiologic studies of endometrial cancer. Olson said, "we are hopeful that having well-described molecular subtypes that are strongly related to outcome will…enable epidemiologists to relate risk factors to specific subtypes." Such studies will advance the ultimate goals of "understanding carcinogenesis for the more lethal tumors and identifying those at increased risk," Olson said.

The four endometrial tumor subtypes identified in the recent study have been labeled *POLE* ultamutated, microsatellite instabilty (MIS) hypermutated, copy-number low and copy-number high, based on their specific molecular features. Levine said the next step is to use this new information in the design of clinical trials, and he hopes that within a few years, "we will have a better understanding of how exactly to incorporate these findings into patient care."

New Research Council Established for Minimal Risk Studies

Change Expected to Improve Quality and Speed of Reviews

The Office of Clinical Research has established a new Research Council for Minimal Risk Research. The council is a response to growing demands on the protocol review process at MSKCC and increasing recognition that different types of research pose varying levels of risk to human subjects. Like the existing council (to be known as Research Council A), the new group (Research Council B) will review research protocols for scientific merit, quality of methods, appropriateness of resource allocation and programmatic fit. The group will be chaired by SOAR investigator William Breitbart (Psychiatry).

As defined in the federal regulations governing human subjects research, minimal risk means that "the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests." Protocols that may qualify for minimal risk designation include studies involving psychosocial or behavioral interventions, patient or general population surveys, focus groups, basic biometric data collection and quality improvement interventions. MSKCC PI's will identify their protocols as minimal risk at the time of submission, and questions about qualification for this designation will be adjudicated by the new research council and the IRB.

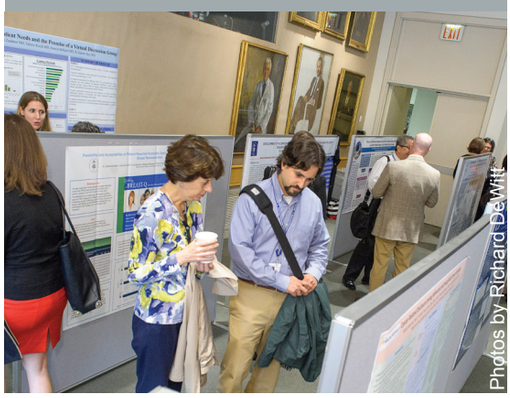
Anticipated benefits of the new dual research council structure include both improved review quality and shorter times from protocol submission to approval. Dr. Breitbart noted that the new system, "will allow for minimal risk studies to be reviewed by experts in the science of quality improvement, screening, prevention, epidemiology, and psychosocial intervention research to be reviewing the science of these studies. It will also relieve the burden on the main Research Council from having to review these types of studies and to be able to more rapidly review moderate to high risk protocols." Breitbart also commended Jose Baselga (Memorial Hospital Physician-in-Chief) and Paul Sabbatini (Deputy Physician-in-Chief for Research) for their leadership of this initiative.

In addition to Breitbart and Vice-Chair Martee Henslee, the new council includes SOAR investigators Victoria Blinder (Health Outcomes), Elena Elkin (Health Outcomes), Jennifer Ford (Behavioral Sciences), Francesca Gany (Immigrant Health and Disparities), Kevin Oeffinger (Medicine), Sara Olson (Epidemiology), Jamie Ostroff (Behavioral Sciences) and Jaya Satagopan (Biostatistics).

SURVIVORSHIP RESEARCH SYMPOSIUM

The 3rd annual Survivorship Research Symposium was held at MSKCC on Wednesday, May 15th. Several SOAR investigators and staff members shared their research in posters and oral presentations.

Photos (from top): Chaya Moskowitz (Biostatistics); Kevin Oeffinger (Survivorship); Danielle Baum (Behavioral Sciences), Sabrina Jennings (Psychiatry), Chaya Moskowitz, Anthony De La Cruz (Survivorship), Carolyn Eberle (Health Outcomes); poster session.



Photos by Richard DeWitt

SOAR NEWS

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Q&A

Yvonne Bombard

Yvonne Bombard is a health services researcher completing a postdoctoral fellowship in Clinical Genetics and Health Outcomes. She recently accepted a position at the Li Ka Shing Knowledge Institute, a research center at St. Michael's Hospital and the University of Toronto. The SOAR Newsletter spoke with her before her departure.

Q: Why did you want to come to MSKCC?
A: Working at MSKCC allowed me to apply my experience in genomics and health services research to cancer. Oncology is really the testbed for implementing personalized medicine, and it's exciting to be at the forefront of translational initiatives in cancer genomics.

Q: What have you been studying here?
A: I've been designing and launching a protocol to study the impact of disclosing incidental results of whole genome sequencing (WGS) tests. Some MSKCC patients and their relatives have donated tissue or serum samples which have been tested using WGS for research purposes. But those tests may provide information about their risks for a range of diseases and health conditions. We need to understand whether people want to know about these risks, how they respond to learning about their risks and whether the information influences their behavior.

Q: Have you had your genome sequenced?
A: No.

Q: Would you like to?
A: Not unless I had a family history of a specific disease and the incidental information could help me lower my risk for other diseases.

Q: Are there differences between the US and Canada in the demand for or use of genomic information?
A: In terms of research the environment is similar, and Canadian scientists are using the same technologies that are being used here. The difference is in clinical care. Typically, in Canada, for a new technology to be reimbursed, it must first be subjected systematic assessment of its risks, benefits and costs. That is not the same in the US.

Q: What have you enjoyed most about your time in New York?
A: Running from a concert in Brooklyn, to a show in the Theater District to a gallery opening downtown, all in the same day! My husband and I have taken our love of food, music and art to another level in this city. I've also worked with and learned from so many talented people at MSKCC who were great collaborators and mentors.

Q: What's the craziest show or concert you've seen in New York?
A: Sleep No More. I haven't been able to sleep anymore since I saw this choose-your-own-adventure Macbeth adaptation. And it's the first time I saw a show where the entire audience wore masks. Creepy and communal at the same time.

Mark your calendar

May 31- June 4	**ASCO Annual Meeting** Chicago, IL
June 7	**Citywide Colon Cancer Control Coalition (C5) Summit** Icahn School of Medicine, Mount Sinai Hospital, NY
June 23-25	**AcademyHealth Annual Research Meeting** Baltimore, MD
August 3-8	**Joint Statistical Meetings** Montreal, Quebec
August 22-23	**Advances in Statistical Methods for Cancer Genetic Epidemiology** MSKCC (abstracts due June 15th)

SOAR Honors

Jamie Ostroff (Behavioral Sciences) was invited to serve on the Cancer Prevention Committee of the American Society of Clinical Oncology. The committee leads the Society's cancer prevention efforts, including priority initiatives in the areas of familial risk assessment and management and tobacco cessation & control.