Experts Discuss Challenges in Triple-Negative Breast Cancer
Symposium Addresses Personalized Medicine in Underserved Communities

In April, MSK hosted a Translational Research Symposium focusing on scientific, clinical and societal aspects of triple-negative breast cancer. The event brought together experts in basic science, engineering, clinical genetics and community engagement from MSKCC, City College of New York (CCNY) and other local organizations.

As of 2011, triple-negative breast cancers (those that are ER-negative, PR-negative, and HER2-negative) represented almost 73% of all invasive breast cancers. But the age-specific incidence of these cancers varied from more than 90 per 100,000 in some states (including New York) to less than 80 per 100,000 in other states. Compared with other subtypes, these cancers have fewer effective treatment options than other breast cancers and patients generally have a poorer prognosis.

In her keynote address, Dr. Debra Auguste, Associate Professor of Biomedical Engineering at CCNY, described molecular mechanisms of targeted therapy and emphasized the distinction between targeted and personalized medicine. Summarizing her comments, Auguste said, “targeted therapy refers to a drug delivery vehicle recognizing an overexpressed receptor present on a diseased cell. In contrast, a personalized therapy refers to a therapy that would benefit a subset of a patient population due to specific traits of that group.”

Auguste also described a novel potential therapeutic target in triple-negative breast cancer, the intercellular adhesion molecule-1 or ICAM-1. In a discussion following the keynote speech, experts addressed other issues related to triple-negative breast cancer, in particular, the need of minority women and underserved communities. These issues are critical to improving outcomes in triple-negative disease, which represents 15-20% of all breast cancers in the US, but disproportionately affects African-American women, women under age 50, and those with a BRCA1 gene mutation.

Panelist Michael Berger (Pathology) discussed the use of genetic testing to personalize therapies and the importance of including individuals of different races and ethnicities in clinical research. Mark Robson (Medicine) spoke about ways to improve access to genetic testing and personalized therapies in underserved communities, and invited audience members to share their ideas with the group. Eileen Fuentes, founder of SPEACH (Self Promotion Empowerment Advocacy and Care Haven), related her own experience as a breast cancer survivor, and emphasized the importance of linguistic and cultural competence when treating diverse populations.

The symposium, sponsored by a partnership between CCNY and MSKCC, concluded with poster presentations from partnership-funded investigators. Symposium organizers Francesca Gany (Immigrant Health & Cancer Disparities), Tim Ahles (Psychiatry & Behavioral Sciences) and Karen Hubbard (CCNY) hope the event will lead to action plans for collaborative research in the areas of risk education, early detection and targeted treatment for triple-negative breast cancer and other diseases.

National Study Highlights Breast Cancer Heterogeneity
Report Finds Geographic and Racial Variation in Tumor Subtypes

For the first time in its seventeen-year history, the Annual Report to the Nation on the Status of Cancer addressed etiologic subtypes of breast cancer. The report, published online in March in JNCI, found substantial variation in the prevalence of different breast cancer subtypes among women of varying age, race and geographic region.

In addition to stage classification based on tumor size, lymph node involvement and distant metastases, breast cancers are typically characterized by specific tumor markers; levels of estrogen and progesterone receptors (ER and PR) and overexpression or amplification of the HER2 protein or gene. The recent report analyzed information from breast cancers diagnosed in 2011 in 42 states and the District of Columbia in women younger than 85 years.

Across racial and ethnic groups, hormone receptor (ER or PR)-positive, HER2-negative cancers were the most common, representing almost 73% of all invasive breast cancers. But the age-specific incidence of these cancers varied from more than 90 per 100,000 in some states (including New York) to less than 80 per 100,000 in other states. Consistent with prior studies, the report found that triple-negative cancers – those that are ER-negative, PR-negative and HER2-negative – were most common in non-Hispanic black women, with an incidence of 27 per 100,000, nearly double the incidence in non-Hispanic white women (14 per 100,000). Compared with other subtypes, these cancers have a poorer prognosis and fewer effective treatment options (see article above). The incidence of triple-negative cancers was greatest in the Southeastern US.

The immunohistochemical characteristics of breast tumors correspond roughly to subtype categories based on gene cluster analyses, first described in 2000. The four intrinsic subtypes – luminal A, luminal B, HER2-related, and basal-like – vary in their prognostic and therapeutic sensitivity and prognosis. According to Mark Robson (Medicine), "one value of tumor subtyping is that it allows us to look for epidemiologic risk factors that may play a role in specific types of breast cancer." Robson also noted that there is substantial heterogeneity within the four intrinsic subtypes.

The Annual Report to the Nation on the Status of Cancer is a collaboration of the American Cancer Society, US Centers for Disease Control and Prevention, the National Cancer Institute and the North American Association of Central Cancer Registries.
Predicting Late Effects of Cancer Treatment
Review Finds Few Models to Aid Risk Stratification

Long-term cancer survivors may experience side effects years after completing treatment, but the risk and severity of late effects vary considerably. In light of this variability, recent recommendations call for risk-stratified approaches to follow-up care in cancer survivors. However, according to a systematic review led by Talya Salz (Health Outcomes), there are few tools available to help clinicians predict which cancer survivors are at greatest risk of late effects.

Salz and her colleagues identified 14 studies that described prediction models for nine different adverse effects occurring or persisting at least one year after cancer treatment. Among these, the most commonly studied population was prostate cancer survivors, and the most frequently studied late effect was erectile dysfunction. Other studies evaluated prediction models for lymphedema, cardiac events and psychosocial morbidity in breast cancer survivors; swallowing dysfunction in head and neck cancer survivors; and second cancers in Hodgkin lymphoma and other childhood cancer survivors. Only two of the prediction models were externally validated.

Asked about strengths and weaknesses of the prediction models she and her colleagues reviewed, Salz emphasized the importance of clinical utility. Models that require only readily accessible information are the most useful to survivorship care providers, who often were not involved in a survivor’s original cancer treatment. She also noted that the value of a prediction model depends on the modifiability of risk for the late effect. For example, cancer survivors with a high predicted risk of cardiovascular disease may benefit from risk-reducing behavior change or medication.

A multidisciplinary group of scientists and clinicians worked with Salz on the systematic review, including several other SOAR investigators: Shrujal Baxi (Medicine), Chaya Moskowitz (Biostatistics), Kevin Oeffinger (Medicine) and Andrew Vickers (Health Outcomes). The paper was published online in the European Journal of Cancer in February.

Germline Testing Approved for MSK Patients
Protocol Expanded to Include Multi-Gene Panel

The institutional protocol for tumor genetic profiling was recently amended to include germline genetic testing in eligible MSK patients. Part C of protocol 12-245 now allows germline DNA analysis using the multi-gene IMPACT (Integrated Mutational Profiling for Actionable Cancer Targets) panel. Patients who consent to Part A for cancer tissue profiling will now have an opportunity to consent to Part C for germline testing using normal serum DNA.

Only patients seen in the breast, gynecology and prostate cancer clinics are currently eligible to participate in Part C for germline genetic testing. Prior to consent, these patients must view an educational video that explains germline testing. The video features Dr. David Hyman (Gynecology) and fulfills a New York state law requiring informed consent for germline genetic testing. Patients will also be offered genetic counseling prior to consent.

The MSK IMPACT panel is a genomic profiling assay of 410 genes. Only pathogenic mutations in 76 genes associated with inherited cancer susceptibility or high clinical utility will be reported to patients, consistent with recommendations of the American College of Medical Genetics and Genomics. Variants of unknown significance and mutations that do not have implications for the health of the carrier will not be reported. MSK-IMPACT results will be recorded in the electronic medical record and communicated to the patient’s primary MSK physician. Patients and their family members may be offered post-test counseling as appropriate.

Investigators interested in using protocol 12-245 for profiling in a research setting must submit a project plan to Dr. Hyman and the protocol’s clinical research manager. The protocol currently does not allow investigators to re-contact participants for research purposes.

Mark your calendar

May 29–June 2
ASCO Annual Meeting
Chicago, IL

June 14–15
AcademyHealth Annual Research Meeting
Minneapolis, MN

June 16
4:00PM
SOAR Seminar
Immaculata De Vivo, PhD
Harvard School of Public Health

August 8–13
Joint Statistical Meetings
Seattle, WA