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**I**t was serendipity,” says Seema A. Khan, MD, when asked why she became a breast cancer specialist. But, while chance may have decided her field, her passion for it hasn’t wavered. She continues to be fascinated, rewarded and challenged by the combination of her work as a scientist and clinician.

Khan is Bluhm Family Professor of Cancer Research, Director of the Bluhm Family Program for Breast Cancer Early Detection and Prevention, and Professor of Surgery at the Feinberg School of Medicine. Growing up in Pakistan, she says her mother encouraged her children to do well in school and pursue meaningful careers. This was especially true for her daughters. A self-taught woman, Khan’s mother first became a teacher and then pursued a successful career in radio and television after the birth of her children. “She believed strongly that women should have choices and be independent,” Khan says. “So she pushed us to acquire skills that would allow us to support ourselves.”

Apart from teaching and journalism, Khan says, medicine was one of the few challenging careers available to Pakistani women at the time. With a natural affinity for science, she considered both teaching and medicine, ultimately choosing medicine because “I thought it would be more interesting.”

Co-leader of the Lurie Cancer Center’s Breast Cancer Program, Khan received her medical degree from Dow Medical College in Karachi in

1978 and went on to receive her SM degree in epidemiology from the Harvard School of Public Health. She served on the faculty of the Department of Surgery at the State University of New York (SUNY) until 2000 when she was hired by Northwestern University to develop a research program for breast cancer prevention.

#### Improving Identification of High-Risk Patients

Dr. Khan has a special interest in identifying women at high risk for breast cancer. "One of the major problems with breast cancer prevention is that we target women based on probability," says Khan. Currently, doctors assess risk by relying on factors in a woman's history, such as her age at the onset of menses, how old she was when she had her first child and when menopause occurred. "Our ability to estimate risk this way is poor, just a little better than a coin toss," Kahn believes. Early and accurate identification of those at high risk will result in better targeting of chemoprevention agents and help physicians avoid treating healthy patients unnecessarily.

Recent research suggests that the breast itself can provide important clues to a woman's risk for breast cancer. For example, scientists now agree that density is an important indicator. "Women with dense breasts on mammography are at about a four- to five-fold higher risk than women whose breasts are not dense," Khan says. Atypical hyperplasia is another reliable clue that can help identify those women who are more likely to get breast cancer. Other than a strong family history of the disease, "the best indicators are found in the breast itself," says Khan.

Dr. Khan notes that her surgical background lends itself to this research approach since surgeons tend to focus on what occurs locally. She is Principal Investigator on a study of "Nipple Fluid Hormone Levels and Breast Cancer Risk," funded by the National Institutes of Health and the National Cancer Institute, to determine whether there is a relationship between estradiol levels in breast tissue and malignancy risk. By comparing hormone levels in nipple fluid with levels in the blood, and comparing the levels between healthy women and those with cancer, the investigators hope to determine whether local hormone synthesis is an important risk factor for breast malignancy. "We think the breast tissue itself makes hormones and that hormone formation there might be more important for the development

of breast cancer than what circulates in the blood," Khan explains.

Khan is also the PI for an Avon Foundation/Prevention Research Initiative evaluating gene methylation and breast tissue estradiol concentrations. DNA methylation is of interest because it may spur uncontrolled tumor growth. When the promoter sequences of genes (those responsible for gene expression) acquire extra methyl groups, the genes are silenced. When this occurs in tumor suppressor genes, cancer is then allowed to grow unchecked. Khan says that if the investigation confirms the study's hypothesis, patients who present with hyper-methylation of tumor suppressor genes could be identified as high-risk. Doctors could then administer chemoprevention agents to these high-risk patients, targeting those who may already be in the process of tumor formation.

Khan emphasizes the valuable role breast cancer studies have played in advancing research in other cancers. "Breast cancer has always been in the vanguard of solid tumor research," she says. Advancements, such as the use of mammography as a screening tool and adjuvant chemotherapy have led to significant progress in other fields as well.

#### Rewards of Clinical Practice

Dr. Khan finds her work as a clinician complements and enhances her research. "There are so many things that turn upside down in a patient's life when she is diagnosed with breast cancer, and these women are so brave," says Khan. "It's wonderful to help them through this difficult process." She takes pleasure in watching many of her patients go on to live fulfilling lives. One of the most rewarding aspects of her work as a breast cancer clinician, she says, is "seeing my patients doing well years after treatment and watching their children grow up."

Dr. Khan and her husband, A. Vania Apkarian, a neuroscientist and Professor of Physiology at Northwestern, enjoy sharing their love of theatre, dance and travel with their own two children.