SOUTHWESTERN NEWS

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BARD1 GENE LINKED TO BREAST, OVARIAN, UTERINE CANCERS

DALLAS – March 2, 1998 – Alterations in a gene discovered last year by UT Southwestern Medical Center at Dallas scientists have been linked to breast, ovarian and uterine cancers, the researchers reported in the February issue of *Human Molecular Genetics*.

Last year, Dr. Anne Bowcock and Dr. Richard Baer uncovered the *BARD1* gene and found that its protein interacted with the protein of the breast-cancer gene 1 (*BRCA1*), which is mutated in 40 percent to 50 percent of inherited cases of breast cancer.

"If *BARD1* is mutated in tumors, even if only infrequently, the normal gene probably has an important function biologically," said Bowcock, associate professor of pediatrics. She and Baer, professor of microbiology, are the lead investigators of the new findings. Baer holds the Sherry Wigley Crow Cancer Research Endowed Chair, in Honor of Robert Lewis Kirby, M.D., and the H. Lloyd and Willye V. Skaggs Professorship in Medical Research.

Of the 50 breast, 58 ovarian and 60 uterine tumors analyzed, scientists found one *BARD1* mutation in each group. The three different mutations occurred in the same region of the gene, which suggests that this gene, like *BRCA1*, may be involved in controlling cell division in response to deoxyribonucleic acid (DNA) damage. This "checkpoint" type of control normally allows a cell to repair damage to its DNA before replicating. If this mechanism is absent, there is an increased risk of tumor formation.

The researchers believe that *BARD1* mutations may play a role in spontaneous as well as hereditary tumor development. The breast and uterine tumors with *BARD1* mutations arose from new noninheritable mutations found only in the tumor cells, but the *BARD1* mutations found in

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the ovarian tumors were inherited mutations.

"We believe that the product of the *BARD1* gene may have a very broad function and belongs to a group of proteins called genome caretakers — proteins that maintain the integrity of the genome. Mutations in such proteins lead to tumors, and this is what we believe happens when there are mutations in *BARD1*," Bowcock said.

To conduct this research, Bowcock and Baer had to uncover the *BARD1* gene structure and design small pieces (primers) of corresponding DNA to look for genetic alterations. The primers now are available for others to use in tracking the possible causes of breast, ovarian and uterine cancers.

Other UT Southwestern investigators who collaborated on this research included To Hoa Thai, research associate in pediatrics; Dr. Fenghe Du, research fellow in pediatrics; Julia Tsou Tsan, research scientist in microbiology; Dr.Ying Jin, research fellow in microbiology; Anne Phung, research assistant in pediatrics; Monique Spillman, graduate student; Dr. Carolyn Muller, assistant professor of obstetrics and gynecology; Dr. Raheela Ashfaq, assistant professor of pathology; Dr. David Scott Miller, associate professor of obstetrics and gynecology and holder of the Dallas Foundation Chair in Gynecologic Oncology; and former faculty member Dr. Michael Mathis.

The Department of Molecular Biotechnology at the University of Washington School of Medicine also participated in the study.

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