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MouseLine

Inherited Factors Play an Important Role in Breast Cancer Progression According to New Study in Mice

New research in mice and five independent collections of human breast tumors has enabled National Cancer Institute (NCI) scientists to confirm that genes for factors contributing to susceptibility for breast cancer metastasis can be inherited. The new findings support earlier results from the same laboratory and appear in the Jan. 1, 2009, issue of Cancer Research.

The study results also show that gene activities in tumor cells and immune cells that infiltrate, or invade, tumors can contribute to the development of expression profiles, called gene signatures, that are predictive of cancer progression. The analysis of normal mouse tissue as well as tumors transplanted into mice suggests that predictive, or prognostic, gene signatures that point to a tumor's potential for spreading throughout the body can be the result of both inherited and non-inherited factors, with inherited factors being more consistently predictive. The research team that reported these findings is from the Center for Cancer Research at NCI, which is part of the National Institutes of Health.

The researchers were able to perform their analyses by using advances in microarray technology, which allows scientists to scan vast amounts of genetic information and identify gene signatures that can be used to predict cancer outcomes. Many scientists had assumed that metastatic ability is primarily determined by somatic, or non-inherited, gene mutations in tumor tissue. "Our earlier studies clearly established that inherited factors also play an important role in metastatic progression and can help distinguish which tumors have a propensity to metastasize," said author Kent W. Hunter, Ph.D., head of NCI's Metastasis Susceptibility Section in the Laboratory of Cancer Biology and Genetics. "Hopefully in the future we will be able to determine which women are more likely to have a tumor that would metastasize, and we could then tailor therapy specifically for them, avoiding the use of harsh treatments for those with a low probability of metastasis."

To determine whether mouse tumor gene expression profiles could be used to predict outcomes in human breast cancer, the investigators identified a gene expression signature that allowed them to distinguish between the tumors of mice that have a high or a low inherited susceptibility to tumor metastasis (a 20-fold difference). They then converted the mouse gene signature to the corresponding human gene signature and analyzed five pre-existing sets of human breast tumors. This signature successfully predicted outcomes (either relapse or disease-free survival) in four of the five sets of human breast tumors.

Because other studies have suggested that gene expression patterns in the nearby tissue, or stroma, are altered in tumors that are prone to metastasis, the investigators conducted transplant experiments by putting highly metastatic tumor cells into the mammary fat pads of mice that have either a high or a low susceptibility to tumor metastasis. These transplants resulted in tumors that had identical tumor cells but different stroma and immune cells that infiltrated the tumor. No significant differences were seen in tumor weight or metastasis to the lung in the two types of mice after 28 days, suggesting that metastatic differences between individual mice in this experiment were possibly due to genes in the outer layer of tissue that surrounds the tumor (the epithelium) rather than in the stroma. However, differences in gene signatures were still seen in mice with either high or low potential to develop metastases, and the corresponding human genes signatures were predictive of relapse or survival in patients. The researchers concluded that both the tumor epithelium and the stroma probably contributed to the development of the prognostic gene profiles.

"Our study provides additional evidence of the role of inherited genes in human breast cancer progression. Therefore our next step is to improve our current understanding of the role of the epithelium and stroma in tumor progression and develop more effective therapeutic strategies based on our new knowledge," said Hunter.

Source: http://www.cancer.gov/newscenter/pressreleases/BreastProgressionGene

Publication: Lukes L, Crawford NPS, Walker R, and Hunter KW. The origins of breast cancer prognostic gene expression profiles. *Cancer Research*. January 1, 2009. Vol. 69, No. 1.

Meetings

February 7 – 10, 2009
AACR-Translation of the Cancer Genome
Boston, Massachusetts
Meeting Information: http://www.aacr.org/home/scientists/meetings--workshops/special-conferences/translation-of-the-cancer-genome.aspx

February 8 – 11, 2009
AACR-Chemistry in Cancer Research: A Vital Partnership in Cancer Drug Discovery and Development
A Joint Conference Presented by the AACR and American Chemical Society
New Orleans, Louisiana
Meeting Information: http://www.aacr.org/home/scientists/meetings--workshops/meetings--workshops-calendar.aspx

February 25 – 27, 2009
CHI's-6th Annual Molecular Diagnostics: Next Wave of Personalized Medicine
San Francisco, California
Meeting Information: http://www.tri-conference.com/09_mdx.asp

March 17 - 19, 2009
CHI's-3rd Annual Next Generation Sequencing: Platforms and Progress
San Diego, California
Meeting Information: http://www.healthtech.com/seq/overview.aspx?c=693

Notices and Funding Opportunities

NIH Announces the Availability of Adobe-Based Grant Application Forms
NOT-OD-09-026
National Institutes of Health
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-026.html

Impact of NIH Transition to Adobe Forms on Appointed Members of NIH Chartered Study Sections
NOT-OD-09-028
National Institutes of Health
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-028.html

Innovative and Applied Emerging Technologies in Biospecimen Science (R21 and R33)
RFA-CA-09-004 and RFA-CA-09-005
National Cancer Institute
http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-09-004.html
http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-09-005.html

Application and Use of Transformative Emerging Technologies in Cancer Research (R21, R33)
RFA-CA-09-006 and RFA-CA-09-007
National Cancer Institute
http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-09-006.html
http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-09-007.html

Innovative Technology Development for Cancer Research (R21)
RFA-CA-09-008
National Cancer Institute
http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-09-008.html

Midcareer Investigator Award in Mouse Pathobiology Research (K26)
PAR-09-053
National Center for Research Resources
National Institute on Aging
http://grants.nih.gov/grants/guide/pa-files/PAR-09-053.html

caBIG™ Tools

caMOD 2.5 released

caMOD 2.5 includes many improvements that facilitate searching for cancer models in caMOD as well as for submitting new models to the database. It can be accessed at http://cancermodels.nci.nih.gov

Search enhancements:

- Significantly enhanced Search to better accommodate the increasing volume of data in caMOD
- Broadened keyword search
- Improved search for transgenes and targeted modifications
- Addition of the PubMed publication identifier as a search criterion to the Advanced Search page
- Enhanced customization of the Search Results list

Submission enhancements:

- Customization of the publication page for rat models
- Improved PubMed data retrieval script
- More flexible designation of URLs for associated microarray and image data

A caGrid data service for caMOD 2.5 will be available in the coming weeks and will be announced via this listserv. For more information about caGrid, please see https://cabig.nci.nih.gov/workspaces/Architecture/caGrid/.

For questions or suggestions, contact the NCICB application support team at http://ncicb.nci.nih.gov/NCICB/support.