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MEDIA RELEASE

Embargoed until May 4, 2009, 9 a.m. PDT

New study identifies a protein that makes breast cancer cells more invasive

Understanding of cell behaviour offers new treatment targets

BC Cancer Agency scientists, in collaboration with international researchers, have identified the important role that a specific protein plays in breast cancer metastasis (spread of cancer cells to distant tissues or organs in the body), which may lead to new treatment targets in the future.

Published today in the journal *Cancer Cell*, the study found that high amounts of a protein called YB-1 (Y-box binding protein-1), which is present in a subset of breast cancers, causes two different reactions in tumour cells. YB-1 actually slows or stops the growth of cancer cells at the primary site. However, it simultaneously enables these cells to become more invasive and to migrate to secondary sites, thereby potentially causing a recurrence of breast cancer when the cells re-activate.

"It's disturbing that approximately 30 percent of breast cancer patients may develop metastatic disease, and that this may occur five to 10 years after their initial treatment," says Dr. Poul Sorensen, principal investigator of the study, a senior scientist at BC Cancer Agency, an agency of the Provincial Health Services Authority, and the Johal Chair in the Childhood Cancer Research Program at the Child & Family Research Institute at BC Children's Hospital. "It's unclear why this happens, but scientists have hypothesized that certain drug-resistant cells persist after treatment and resume growth after being dormant for extended periods."

"Our study has now identified that the YB-1 protein 'reprograms' certain breast cancer cells to become dormant and to gain the ability to crawl out of the primary tumour site to other parts of the body, potentially giving rise to metastatic disease."

The study was conducted using human breast cancer cells and validated using a variety of model systems.

"What is also significant about the discovery is that it suggests that conventional therapies may not work in eradicating breast cancer cells with high quantities of YB-1," adds Dr. Sorensen. "Conventional therapies are targeted at cancer cells that rapidly grow and divide, but these cells behave differently, since the YB-1 protein actually prevents cells from growing."

The next step of the research is to learn more about cancer cells with high amounts of YB-1, such as what causes them to reactivate after they have migrated to secondary sites. Now that such cells have been identified, researchers can also begin to determine what their vulnerabilities might be for specific targeting.

"We need to understand how cancer cells over-expressing YB-1 are different from other cells so that we can find ways to eradicate them before they become reactivated causing metastatic disease," says Dr. Cristina Tognon, a researcher at the BC Cancer Agency, who along with Dr. Valentina Evdokimova are co-first authors of the study.

The study is funded by the Canadian Institute of Health Research (CIHR) and the BC Cancer Foundation. The work was also supported by a Rethink Breast Cancer Career Development Award, and fellowships from CIHR, Michael Smith Foundation for Health Research and the University of British Columbia Clinician Investigator Program (Royal

College of Physicians and Surgeons of Canada) to two of the investigators. Support for this study was also provided through the BC Children's Hospital Foundation.

The BC Cancer Agency, an agency of the Provincial Health Services Authority, is committed to reducing the incidence of cancer, reducing the mortality from cancer, and improving the quality of life of those living with cancer. It provides a comprehensive cancer control program for the people of British Columbia by working with community partners to deliver a range of oncology services, including prevention, early detection, diagnosis and treatment, research, education, supportive care, rehabilitation and palliative care. The BC Cancer Foundation raises funds to support research and enhancements to patient care at the BC Cancer Agency.

The Child & Family Research Institute conducts discovery, clinical and applied research to benefit the health of children and families. It is the largest institute of its kind in Western Canada. CFRI works in close partnership with the University of British Columbia, BC Children's Hospital and Sunny Hill Health Centre for Children, BC Women's Hospital & Health Centre, agencies of the Provincial Health Services Authority, and BC Children's Hospital Foundation. CFRI has additional other important relationships with BC's five regional health authorities and with BC academic institutions Simon Fraser University, the University of Victoria, the University of Northern British Columbia, and the British Columbia Institute of Technology.