Study provides new clue to family risk for breast cancer

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An international team of researchers, led by Dr. William Foulkes of McGill University's Program in Cancer Genetics and Chief of Cancer Genetics, Jewish General Hospital Cancer Prevention Centre, has linked a particular genetic mutation to increased risk for breast cancer. The discovery, reached after more than a decade of studying two families in Montreal with particularly high rates of breast cancer, is published in this week's *Proceedings of the National Academy of Science*.

Dr. Foulkes and his team, including genetic counselor Nora Wong and Marc Tischkowitz, Assistant Professor and Medical Geneticist at the Jewish General Hospital's Segal Cancer Centre, characterized two mutations in the recently identified breast cancer susceptibility gene, PALB2, as being associated with a particular breast cancer "signature." The discovery may open new avenues for both identifying PALB2 mutation carriers and for treating women who carry these mutations with drugs that are targeted to components of the novel signature. "The door was already unlocked with the discovery of PALB2," said Dr. Foulkes. "What we've done is rearranged the furniture a bit."

With the help of collaborators at Harvard's Dana Farber Cancer Institute (including Dr. Bing Xia, who first identified PALB2 just over a year ago), Breakthrough Breast Cancer (Institute of Cancer Research, London, UK) and the Netherlands Cancer Institute, Amsterdam, they showed that these two mutations may be associated with a higher than expected risk of breast cancer, which could have implications for other PALB2 mutation carriers. In addition, unlike the situation for most other

breast cancer susceptibility genes, it now appears that inactivation of the PALB2 gene does not have to be complete for breast cancer to develop.

"This is another 'factual brick' in the ongoing construction of our understanding of breast cancer susceptibility," explained Dr. Foulkes. "Approximately 10 genes, including PALB2, have now been associated with a two-fold or greater risk for breast cancer, and carriers of mutations in these genes require special surveillance, including magnetic resonance imaging. Some may opt for preventive surgery."

As those choices are often difficult, Dr. Foulkes pointed out that the Montreal-based Hereditary Breast and Ovarian Cancer foundation, led by McGill physician Harley Eisman, has been established with the specific aim of meeting the needs of families at risk.

The clinical work for this project was carried out by members of the Medical Genetics service at the McGill University Health Centre (MUHC) and the Sir Mortimer B. Davis Institute at the Jewish General Hospital, a McGill University teaching hospital.

Source: McGill University