Cancer researchers at Princess Margaret Hospital (PMH) have discovered that the ovarian hormone progesterone plays a pivotal role in altering breast stem cells, a finding that has important implications for breast cancer risk.

The findings, published online today in *Nature*, are significant because reproductive history is among the strongest risk factors for breast cancer, says principal investigator Rama Khokha, a molecular biologist at Ontario Cancer Institute and the Campbell Family Cancer Research Institute, PMH. Other major known risk factors are age, genetics and breast density.

“Our study shows how and when hormones affect breast stem cells during the natural reproductive cycle. There are well accepted links between ovarian hormones and breast cancer, and there is mounting evidence that stem cells are seeds for breast cancer. We now show a direct connection between hormones and breast stem cells.”

Lead author Purna Joshi adds: "Our research demonstrates that when progesterone peaks during the second half of the menstrual cycle, it starts a cross-talk between stem cells and neighbouring cells that propels normal breast stem cells to expand in number, and may trigger an environment where cancer can begin."

Until now, breast stem cells were thought to be generally inactive in the adult female breast, says Dr. Khokha, whose speciality is modelling human cancer in the laboratory. In this study, the research team replicated the human natural reproductive cycle in mice to determine the impact of hormones on breast stem cells.

How hormones change these stem cells opens a new pathway to understanding the cell growth that begins breast cancer, and, with further research, will open new ways of targeting stem cells.