Presence of fetal cells in women lowers risk of breast cancer but raises risk of colon cancer

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For the first time, scientists have found what could be a causative link between the concentration of circulating Y-chromosome fetal cells in women who gave birth to children of either sex and their risk of later developing breast cancer and colon cancer. The findings show that the presence of fetal cells is a double-edged sword: Women with the lowest concentration of fetal cells were 70 percent less likely to have breast cancer, while women with the highest concentration of fetal cells had a four-fold increased risk for colon cancer when compared with healthy controls.

The how and why of this contradictory role of fetal microchimerism is not known and requires more study, according to Vijayakrishna K. (V.K.) Gadi, M.D., Ph.D, an assistant member of the Clinical Research Division at Fred Hutchinson Cancer Research Center and senior author of a study that appears online in the *European Journal of Cancer*.

Scientists at the University of Copenhagen, Denmark, led the research, which was based on data from 428 Danish women whose blood was drawn in the mid-1990s when they were cancer free. Ten years later, the cancer status of these women was determined based on an examination of Danish breast and colon cancer registries. Molecular analysis of the blood samples was done at the Hutchinson Center to measure how much microchimerism they had. Male fetal microchimerism was detected in 40 percent of 89 women who had developed breast cancer, and 90

percent of the 67 women who had developed colon cancer. Residual male fetal cells were also found in 70 percent of the 272 women who remained cancer free.

The colon cancer finding was unexpected; no prior studies had ever associated that cancer with fetal microchimerism, Gadi said. The researchers chose to measure microchimerism in women who later developed colon cancer to determine whether the possible beneficial effect of microchimerism is specific to breast cancer, as past studies have shown.

Previous studies, including research by Gadi and colleagues, found associative links between concentrations of fetal microchimerism and a decreased risk of breast cancer as well as a heightened risk of some autoimmune diseases. However, those studies were based on blood drawn from women after the onset of their disease.

"Fetal microchimerism may be highly relevant to later cancer development. However, the study does not allow us to identify the underlying biological mechanisms," Gadi said.

Gadi has a hypothesis (not contained in the study) that the fetal cells could be producing a naturally occurring graft-versus-tumor effect but the effect may be having different impacts based on the cancer type. "There are diseases of the GI tract that are associated with chronic inflammation and it is entirely possible that fetal cells are driving, seeding or initiating that inflammation or are involved in the process," he said regarding the link to colon cancer.

Detection of Y-chromosome fetal cells, thought to originate from previous pregnancies with a male fetus, is common in women. During pregnancy, fetal cells naturally pass into the mother where they can persist in small numbers in the blood and tissues for decades after

childbirth.

Interestingly, this latest study also found no obvious association between the number of live-born sons and testing positive for male microchimerism. Overall, 65 percent of women with no live-born sons tested positive for Y-chromosome fetal cells, according to the study.

"A source of Y chromosomes in women with no sons could be unrecognized pregnancies with a male fetus that terminated early," Gadi said regarding a possible explanation.

Provided by Fred Hutchinson Cancer Research Center

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