

Pregnancy may help protect against bladder cancer

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Pregnancy seems to confer some protection against bladder cancer in mice, scientists have found. Female mice that had never become pregnant had approximately 15 times as much cancer in their bladders as their counterparts that had become pregnant, according to new findings by investigators at the University of Rochester Medical Center.

Their work appears online as a rapid communication in the journal *Urology*. The researchers led by Jay Reeder, Ph.D., are focusing on a fact that has puzzled doctors and scientists for decades: Why does bladder cancer, the fifth most common malignancy in the nation, affect about three times as many men as women? Scientists long blamed men's historically higher rates of smoking and greater exposure to dangers in the workplace, but the gap has persisted even as women swelled the workforce and took up smoking in greater numbers.

"While some researchers have asked why men are more vulnerable to bladder cancer, perhaps we should be asking why women have more protection," said Reeder, a research assistant professor in the departments of Pathology and Laboratory Medicine, Urology, and Imaging Sciences. "When it comes to bladder cancer, being female is a very good thing."

First author Aimee Johnson was investigating ways in which hormones might make males more vulnerable to bladder cancer. She was comparing rates of bladder cancer in male and female mice when she took a closer look at the females. She found an unexpected, marked



difference in cancer rates and volumes among the female mice.

Female mice that had gotten pregnant repeatedly had far fewer bladder cancers than both their normal male counterparts and their female counterparts that had never gotten pregnant. On average, the total tumor volume was about 15 times greater in female mice that had never gotten pregnant compared to mice that had gotten pregnant.

"We were shocked at the differences between the two groups," said Reeder. "These mice were specially susceptible to bladder cancer, yet we saw virtually no cancer in the females that had become pregnant.

"The mice that were pregnant nursed their offspring, and a protective effect could be related to pregnancy, lactation, or both. Additional studies are needed to identify the specific mechanism."

While scientists do know that early onset of menopause increases a woman's risk of getting bladder cancer, pregnancy hasn't generally been considered a possible factor in determining one's risk for bladder cancer, said Reeder.

Reeder's team used a sophisticated imaging instrument known as a conebeam CT scanner to take some of the most detailed images ever of a developing cancer in mice with the disease. Cancers of the bladder grow into the hollow space from the lining of the bladder, somewhat resembling tiny heads of sprouting broccoli.

The imaging was done thanks to a collaboration with scientists at Koning Inc., a Rochester-based start-up company based on technology developed by Ruola Ning, Ph.D. Koning scientist David Conover worked closely with Reeder's team to customize the technology to evaluate bladder cancer as it develops.



The results highlight a possible role for hormones in bladder cancer, perhaps like the known role hormones have in the development of breast cancer. Most hormone research in bladder cancer has focused on male hormones such as testosterone and their capability of boosting the cancer process.

In April, Reeder's team published an article in BMC Urology showing one way male hormones might boost bladder cancer risk. The team demonstrated a link between testosterone and the ability of new tissue to form new blood vessels, a crucial ability for cancerous tissue as it seeks to grow.

Scientists showed that male mice with a normal amount of testosterone have less of a protein known as thrombospondin-1 (TSP1), which helps to stop new blood vessels from forming. When Reeder's team cut off the supply of testosterone, TSP1 levels were boosted in male mice, and they had fewer bladder tumors, perhaps because their blood supply had been cut off.

The team made a similar finding in people with bladder cancer. In an analysis of human bladder tissue done together with colleagues at the University's James P. Wilmot Cancer Center, cancerous tissue had lower levels of TSP1 than normal tissue.

Source: University of Rochester Medical Center

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