Estrogen may help precancerous cells spread in oral cavity

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Head and neck cancer is the sixth most common type of cancer and is on the rise in some demographic groups, including young women without any known risk factors. Now, researchers at Fox Chase Cancer Center report that estrogen may increase the movement of precancerous cells in the mouth and thus promote the spread of the disease within the oral cavity.

The new results, published in the January issue of *Cancer Prevention Research*, a journal of the American Association for Cancer Research, may lead to novel chemoprevention strategies in the future.

Margie Clapper, Ph.D., co-leader of the Cancer Prevention and Control Program at Fox Chase Cancer Center and Cancer Prevention Research editorial board member, and colleagues had previously reported that estrogen metabolism changes following smoke exposure in the lungs and may contribute to lung cancer. This study on estrogen and lung cancer first appeared in the June 3, 2010, issue of Cancer Prevention Research.

To find out if this female hormone influences development of head and neck cancer, Ekaterina Shatalova, Ph.D., a postdoctoral fellow at Fox Chase Cancer Center and researcher on this study, examined the impact of estrogen on precancerous and cancerous cells.

They found that estrogen induces the expression of an enzyme called cytochrome P450 1B1 (CYP1B1), which is responsible for breaking down toxins and metabolizing estrogen. Interestingly, CYP1B1 induction

occurred only in precancerous cells, which are neither totally normal nor cancerous. Surprisingly, estrogen did not induce CYP1B1 in cancer cells.

With closer investigation, the researchers found that depleting the expression of CYP1B1 diminished the ability of precancerous cells to move and divide, as compared to similar cells with normal levels of CYP1B1. Estrogen also reduced cell death in the precancerous cells, irrespective of the amount of CYP1B1 present.

"In the future, we would like to find a natural or dietary agent to deplete the CYP1B1 enzyme and see if we can prevent oral cancer at the precancerous stage," said Shatalova.

"Our previous studies showed that the CYP1B1 enzyme sits at the hub of changes that occur in the lungs after smoke exposure. We were now able to look at its role in a more direct fashion by removing it from precancerous cells of the oral cavity," Clapper said. "We found that cells lacking it move slower. CYP1B1 could be a wonderful target in precancerous lesions of the head and neck, because by attacking it, we might stop these lesions from progressing or moving to a more advanced stage."

In addition, patients diagnosed with head and neck cancer are at a high risk of developing a second primary tumor, which is associated with poorer overall survival. Finding a way to reduce these subsequent tumors could improve patients' survival.

These results may help researchers to "understand factors that cause head and neck cancer, in addition to the traditional risk factors of tobacco and alcohol exposure," said Jennifer R. Grandis, M.D., professor and director of the Head and Neck Cancer Program at the University of Pittsburgh School of Medicine, and an editorial board member for Cancer Prevention Research.

However, because these results are limited to a single premalignant cell line, said Grandis, further studies are needed to validate these findings in head and neck cancer in a human population.

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