MedicalXpress

Researchers identify a gene that predicts recurrence in squamous cell carcinoma of the head and neck

April 2 2012

Squamous cell carcinoma of the head and neck—which typically arises from thin, flat cells that line moist surfaces inside the mouth, nose and throat—is the sixth most common type of cancer worldwide, and it has a relatively low five-year survival rate and a high recurrence rate. Recently, the disease has become even more prevalent among adults 40 years of age or younger. These statistics underscore the need for a greater understanding of the molecular underpinnings of this form of cancer. Toward this goal, Fox Chase Cancer Center researchers have identified a gene that predicts disease recurrence in individuals with squamous cell carcinoma of the head and neck.

The new findings, which will be presented at the AACR Annual Meeting 2012 on Monday, April 2, show that patients with one common variant of a gene which encodes the cytochrome P450 (CYP1B1) protein are likely to have a longer time-to-recurrence than those with the more typical form of the gene.

"This is the first study to look at the association between CYP1B1 variants and time-to-recurrence in head and neck cancer, and the findings could lead to personalized treatment strategies for patients with this type of cancer," says Fox Chase study author Ekaterina Shatalova, Ph.D., research associate in the lab of Margie L. Clapper, Ph.D., also senior investigator on the study.

Shatalova, Clapper and their colleagues focused on CYP1B1 because this enzyme is known to produce carcinogens by metabolizing tobacco smoke and alcohol—substances that increase the risk of squamous cell carcinoma of the head and neck. This protein is also abundant in tumor tissue from a wide range of organs, including the breast and lung.

For the study, the researchers analyzed the CYP1B1 gene using DNA samples from 155 patients with squamous cell carcinoma of the head and neck diagnosed at Fox Chase between 2001 and 2008. They found that carriers of the N453S variant of the gene had a longer time-to-recurrence than individuals carrying the more typical form of the gene. Moreover, only 16 percent of patients with the N453S variant had a recurrence, compared to 33 percent of patients with the normal version of the gene. By contrast, the other CYP1B1 gene variants known as R48G or L432V did not have any impact on time-to-recurrence.

In addition, the research team found that women with the normal form of CYP1B1 had a shorter time-to-recurrence than men with the same gene variant. This finding is consistent with CYP1B1's known ability to metabolize estrogens, the primary sex hormones in females, to carcinogenic derivatives.

"The genetic makeup of a person could have an impact on how detrimental exposure to tobacco smoke or estrogen might be, and on the time course of their cancer recurrence," says Clapper, who is co-leader of the Cancer Prevention and Control Program at Fox Chase. "This is really an exciting finding because it suggests that the CYP1B1 protein may be a target for intervention in head and neck cancer."

The researchers also tested, at the cellular level, how variants of CYP1B1 may affect time-to-recurrence and found that cells with high levels of the N453S variant proliferated five to eight times slower than did cells with the normal form of the protein.

The results could have important implications for the treatment of patients with squamous cell carcinoma of the head and neck. Clinicians could use information about variations in the CYP1B1 gene to identify individuals who are at risk for faster recurrence. That subset of patients could receive "a treatment regimen that is tailored to be more aggressive," Clapper says. "Using a personalized medicine approach, we could impact the duration of the disease-free interval for these individuals if we knew ahead of time which ones were more likely to experience recurrence at a faster rate."

Moving forward, Shatalova and her colleagues plan to define the mechanism by which the variant alters recurrence and expand the study to a larger group of head and neck cancer patients.

Provided by Fox Chase Cancer Center