Researchers use sugar to halt esophageal cancer in its tracks

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Scientists working at the Medical Research Council have identified changes in the patterns of sugar molecules that line pre-cancerous cells in the esophagus, a condition called Barrett's dysplasia, making it much easier to detect and remove these cells before they develop into esophageal cancer. These findings, reported in the journal *Nature Medicine*, have important implications for patients and may help to monitor their condition and prevent the development of cancer.

Oesophageal cancer is the fifth biggest cause of cancer death in the United Kingdom and the eighth leading cause of cancer deaths for men in the United States. Moreover, the number of people diagnosed with this disease is increasing rapidly. Individuals with a pre-cancerous condition known as Barrett's oesophagus are at an increased risk of developing esophageal cancer, and need to be closely monitored to make sure that the disease is not progressing.

Dysplasia offers a stage at which cancer can be prevented by removing these cells. However correctly identifying these areas has proved to be problematic, as they can easily be missed during endoscopy and biopsy, which only take samples from a small part of the esophagus. This can result in false reassurance for patients in whom their dysplasia has been missed, and conversely those without dysplasia having to undergo further unnecessary treatments.

The team, based at the MRC Cancer Cell Unit in Cambridge, was led by Dr. Rebecca Fitzgerald and included New York University's Lara Mahal,

an associate professor of chemistry, and William Eng, a laboratory technician.

The researchers discovered a new mechanism for identifying Barrett's dysplasia cells by spraying on a fluorescent probe that sticks to sugars and lights up any abnormal areas during endoscopy. By analyzing the sugars present in human tissue samples taken from different stages on the pathway to cancer—using microarray technology developed by NYU's Mahal—they found that there were different sugar molecules present on the surface of the pre-cancerous cells. This technology uses sugar binding proteins, known as lectins, to identify changes in sugars and pinpointed carbohydrate binding wheat germ proteins as a potential diagnostic. When the wheat germ proteins, attached to a fluorescent tag that glows under a specific type of light, were sprayed onto tissue samples, it showed decreased binding in areas of dysplasia, and these cells were clearly marked compared with the glowing green background.

"The rise in cases of oesophageal cancer both in the UK and throughout the Western world means that it is increasingly important to find ways of detecting it as early as possible," Fitzgerald said. "Our work has many potential benefits for those with Barrett's esophagus who have an increased risk of developing esophageal cancer."

"We have demonstrated that binding of a wheat germ protein, which is cheap and non-toxic, can identify differences in surface sugars on pre-cancerous cells," she added. "And when coupled with fluorescence imaging using an endoscopic camera, this technique offers a promising new way of finding and then treating patients with the highest risk of developing esophageal cancer, at the earliest stage."

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