New test follows the molecular footsteps that lead to oesophageal cancer

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(Medical Xpress)—A new diagnostic test may be around the corner thanks to the discovery of a gene mutation that marks the progression from a harmless oesophageal condition to cancer, according to research published in *Nature Genetics*.

Scientists funded by Cancer Research UK's Catalyst Club, and working as part of the International Cancer Genome Consortium (ICGC), have identified the faults that signal the early onset of oesophageal cancer.

Over time, frequent acid reflux – often called heartburn – damages the cells in the oesophagus. If left untreated, this can lead to a condition called Barrett's oesophagus, which in turn can be a precursor of oesophageal cancer. But most people with Barrett's oesophagus won't develop oesophageal cancer – highlighting the need for a test to identify people at risk.

By sequencing DNA in patients with Barrett's oesophagus and those with oesophageal cancer, the researchers have been able to map out the genetic similarities and differences between the two. They found mutations in the gene TP53 in oesophageal cells that were progressing into cancer, offering a way of spotting patients who could be treated to stop the disease before it starts.

Barrett's oesophagus often goes undiagnosed, making it difficult to identify those people who are at higher risk of going on to develop oesophageal cancer.

The cytosponge, or 'sponge-on-a-string', test involves swallowing a capsule attached to a piece of thread. Inside the capsule is a sponge and, when the capsule reaches the stomach, the outer covering of the capsule dissolves. A nurse then pulls the sponge out, which collects cells for testing as it passes up the oesophagus.

The Cytosponge test, which is still under development, could be used to look for mutations in TP53 as a way of identifying patients whose cells show changes that are likely to develop into oesophageal cancer.

Study author Professor Rebecca Fitzgerald, based at the MRC Cancer Unit at the University of Cambridge, said: "There's been a lot of research into the molecular changes responsible for cancer, but the actual timing of these faults and the series of events that lead to the disease is much less understood. We've revealed how the genetic

landscape changes as patients progress from Barrett's oesophagus to oesophageal cancer.

"We developed the sponge-on-a-string test as an easy way of getting a sample of the cells that line the oesophagus. When combined with powerful gene sequencing technology, this will help us to quickly identify which patients have Barrett's and which have started to develop oesophageal cancer, and we hope the test will soon be routinely available in hospitals.

"By recognising the point when cancer first starts to develop we can increase the chances of diagnosing the disease in its earlier stages, when treatment is much more effective."

Oesophageal cancer is the thirteenth most common cancer in the UK. Around 5,600 men in the UK develop oesophageal cancer every year compared with 2,750 women.

Nell Barrie, head of science information at Cancer Research UK, said: "As we learn more about the development of oesophageal cancer we can engineer better ways to detect and treat the disease. The Cytosponge test could be a simple and cheap way to help diagnose the disease earlier, when there's a greater chance treatment will be effective.

"If you notice food getting stuck when you swallow, persistent heartburn, or other unusual symptoms, you should see your GP. It probably won't be cancer, but it's essential to get it checked out."

More information: Weaver, J. M. J. et al, 'Ordering of mutations in preinvasive disease stages of esophageal carcinogenesis'. *Nature Genetics*, 2014. DOI: 10.1038/ng.3013

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