

New hope for therapy in heartburn-related cancer

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A new study published in the journal *Disease Models and Mechanisms* shows that DBZ, a drug currently in clinical trials for use in the treatment of Alzheimer's disease, is able in rats to stop the growth of Barrett's esophagus, a pre-cancerous condition which if unchecked can lead to esophageal (gullet) cancer. This may be a powerful new weapon in the fight against a common cancer which is hard to treat and usually fatal.

Cancer of the gullet, or oesophagus, is one of the ten most common cancers in the Western world, and there have been recent alarming increases in the number of cases each year in the US and UK. There is no good treatment, and sufferers frequently face a short, painful battle which ends all too quickly in death. Many of the cancers diagnosed are in people with a long history of heartburn.

Chronic heartburn leads to the lower parts of the gullet being bathed in a toxic acid solution, and the lining of the gullet defends itself against this by changing itself into something which looks a lot like the lining of the lower intestines. Although the damaged tissue, called Barrett's oesophagus, is not cancerous in itself, its presence warns doctors that the patient has taken the first step towards cancer, and triggers a rigorous programme of monitoring, coupled with therapy to prevent further damage.

Patients with Barrett's oesophagus can be stabilised, and most do not go on to develop cancer, but once it is there, the mutated tissue is almost

impossible to eradicate, so the risk always remains. Researchers have long been searching for new drugs able to revert Barrett's oesophagus to the healthy, normal lining of the gullet, and now, a team led by Hans Clevers of the Hubrecht Institute, Utrecht, may have a candidate. Clevers' team, whose research into colon cancer is world-renowned, reasoned that as Barrett's oesophagus cells are very similar to the cells which line the colon, they might share vital control pathways. This turns out to be true.

Clevers and his team then put this together with the fact that the anti-Alzheimer's drug DBZ, currently in [clinical trials](#), is known to have side effects on the lower gut lining. They used a rat model of oesophageal cancer to observe the effects of DBZ on Barrett's oesophagus tissue, and found that DBZ could halt the growth of Barrett's oesophagus, and in some cases completely destroyed the mutant tissue. Whilst the treatment is still a long way from being trialled in humans, it is an exciting step forward in the fight for a cure for oesophageal [cancer](#).

More information: New hope for therapy in heartburn-related cancer is presented in the Research Article entitled 'Conversion of metaplastic Barrett's epithelium into post-mitotic goblet cells by gamma-secretase inhibition', written by Vivianda Menke, Ernst Kuipers, Ron de Bruin and Johannes Kusters of the Erasmus Medical Centre, University of Rotterdam, Hans Clevers, Johan van Es, Wim de Lau and Maaïke van den Born, of the Hubrecht Institute, Utrecht, and Peter Siersema of the University Medical Centre, Utrecht. The study is published in Volume 3, Issue 1/2 of the research journal, *Disease Models & Mechanisms* (DMM), dmm.biologists.org/.

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