Common gum-disease bug may also give cancer a boost

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What do your mouth and your behind have in common? They're linked by a bug that we thought was usually benign, but may in fact have a much darker side.

*Fusobacterium nucleatum* is a common bacterium that lives in our mouths, often without causing any ill effects, although it is also frequently the culprit in gum disease. Until recently, it was thought to be just one of many relatively harmless bacteria we carry around.

Previous work on gum disease had hinted that *F. nucleatum* interacts with natural killer cells, part of the immune system's first line of defence against infection and cancer. But when a recent study revealed high levels of the bacterium in human colorectal tumours, Gilad Bachrach at the Hebrew University of Jerusalem, Israel, and his colleagues decided to take a closer look.

First, they incubated *F. nucleatum* together with a variety of human tumour cells and natural killer cells, and found that the bacterium inhibited the killer cells' ability to attack cancer. Further work revealed that a bacterial protein called Fap2 binds to a receptor on the natural killer cells called TIGIT. "By activating this receptor, *F. nucleatum* prevents the killing of cancer cells by the natural killer cells," Bachrach says.

A handful of other bacteria are known to boost the risk of certain cancers by triggering an inflammatory response. But this is the first time a bacterium has been shown to be helping cancer develop by inhibiting the immune system.

**Coincidence or ploy?**

Whether this interaction is a coincidence or a deliberate strategy on the part of the bacterium remains unclear, but the relationship between it and cancer is probably a mutually beneficial one. *F. nucleatum* prefers anaerobic – low-oxygen – environments, and tumours are often precisely that. Once established, tumours also harness or suppress the immune system in some way themselves. But by suppressing the natural killer cells that detect and destroy cancer, *F. nucleatum* may help tumours gain a foothold.

"The purpose of this pathogen is not to kill the host; it is to survive. Maybe by preventing these tumours from being killed, the bacterium creates a sheltered niche in which to proliferate," says Yiping Han of Columbia University in New York. She recently published data suggesting that *F. nucleatum* can also stimulate the growth of colon cancer cells via a different mechanism.

Now that it's clear that the bacterium is interacting with natural killer cells, the next question is whether that link could be disrupted – possibly by developing drugs that block Fap2.

Could the bacterium be lurking in other types of tumours and influencing their growth in similar ways? Han thinks it might; the bacterium can escape the mouth and has been found in many other tissues. There are even hints that it could be associated with other diseases,
including Alzheimer's and atherosclerosis.

"I wouldn't be surprised if *F. nucleatum* was associated with other types of cancer, but I think it's premature to generalise that it is a root cause of all cancer," says Han. "For now, I think it's safe to say it's one of the causes of colon cancer, although it's probably not the exclusive cause."

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