Bacteria protect intestinal tumor model from being killed by immune cells

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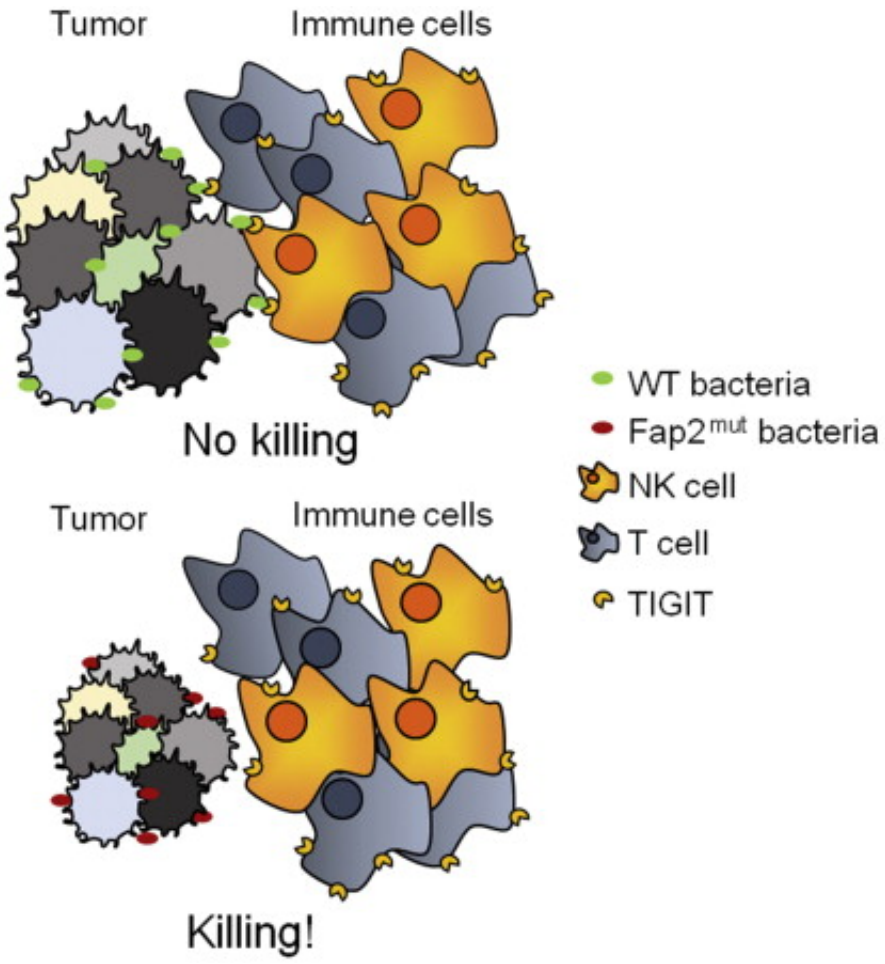

Credit: Cell Press

Bacteria that are commonly found in the mouth are often abundant in patients with colon cancer, but the potential role these microbes play in

tumor development has not been clear. A study published by Cell Press February 10th in the journal *Immunity* reveals that the oral pathogen *Fusobacterium nucleatum* protects a variety of tumor cells from being killed by immune cells. The findings could open new avenues for the treatment of cancer in human patients.

"Certain bacteria have previously been shown to fight cancer, so the surprising finding of this paper is that bacteria such as *Fusobacterium nucleatum* can grant tumors an anti-immune defense mechanism," says co-senior study author Ofer Mandelboim, PhD, of The Hebrew University Hadassah Medical School. "Blocking the interaction between these bacteria and immune cells might improve anti-tumor immunity both in general and with regard to colon cancer in particular."

Immune cells called natural killer cells defend the body against a variety of health threats, including viruses and parasites. These cells can also kill tumors, but cancer cells have evolved ways to evade this immune response. In the early 1890s, a surgeon named William Coley recognized that certain bacteria can enhance anti-tumor immunity, and he even used bacterial extracts to successfully treat cancer patients. But the relationship between bacteria and tumors is complex, and until now, it was not known whether other types of bacteria that are common in cancer patients could have the opposite effect: protecting developing tumors from immune cell attack.

To address this question, Mandelboim teamed up with co-senior author Gilad Bachrach of the Hebrew University-Hadassah School of Dental Medicine to study how the anti-cancer activity of natural killer cells might be affected by *Fusobacterium nucleatum*—an oral pathogen that has been linked to periodontal diseases and is also present in human colorectal tumors.

They found that this bacterium protects a variety of human tumor cells

from destruction by human natural killer cells. Moreover, this immune evasion depends on the binding of a bacterial protein called Fap2 to an immune cell receptor called TIGIT. "The implications are that if we either remove the *Fusobacterium nucleatum* bacteria from the tumors or inhibit TIGIT with antibodies, we might enable immune cells to kill the colon tumors more efficiently," says first author Chamutal Gur of The Hebrew University Hadassah Medical School.

The researchers now intend to test whether this bacterium is found in other types of tumors and whether additional bacteria that colonize tumors affect the activity of immune cells. They also plan to study Fap2-TIGIT interactions in more detail and develop ways to block these interactions. "Because *Fusobacterium nucleatum* specifically targets tumors, it may be possible in the future to use a Fap2-deleted *Fusobacterium nucleatum* to guide therapeutic agents to kill the tumors," Mandelboim says.

More information: *Immunity*, Gur et al.: "Binding of the Fap2 protein of Fusobacterium nucleatum to human inhibitory receptor TIGIT protects tumors from immune cell attack", www.cell.com/immunity/abstract … 1074-7613(15)00036-9

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