New Player in Cancer's Spread

A commonplace mouth bacterium now is tied to metastasis of some tumors

- When people hear that they might have cancer, perhaps the only thing more frightening than the C word is the M word.

- Metastatic disease—in which the malignancy has traveled beyond its primary site to other spots in the body—is responsible for nine out of every 10 cancer deaths.

- Recently an unexpected player in this process has emerged: a common bacterium.

- Fusobacterium nucleatum, which normally lives harmlessly in the gums, appears to have a role in the spread of some cancers of the colon, esophagus, pancreas and—possibly— breast.

- Laboratory studies and evidence in patients indicate that the microbe can travel through the blood and infect tumor cells by attaching to a sugar molecule on their surface.

- There it provokes a range of signals and immune responses known to cause tumor cells to migrate.

- If further confirmed, the work with F. nucleatum could add to a growing understanding of how the microbiome influences cancer progression and may even point the way to fresh approaches to treatment.

- In a healthy human mouth, F. nucleatum is a law-abiding member of the microbial community.

- With poor dental hygiene, uncontrolled diabetes and other conditions, however, it can go rogue and cause periodontitis, tonsillitis, appendicitis and even preterm labor.

- A connection to colorectal cancer was first hinted at about nine years ago, when two research groups discovered that the bacterium's DNA was overrepresented in colon tumor tissue compared with normal tissue.

- Dozens of studies have since found that the infection in tumor cells is a sign of trouble: it is linked to a poorer prognosis in patients with pancreatic, esophageal or colorectal cancer; resistance to chemotherapy in the latter two groups; and metastasis in colorectal cancer, which is the world's third most common and second most deadly malignancy.

- Still, the question remained: Is this bug merely a warning sign, or is it an active participant in cancer progression?

- This year at least three studies of colon cancer, by separate teams, pointed to an active role.

- “We reached the same conclusion through different pathways,” says biochemist Daniel Slade of Virginia Tech.

- Slade and his colleagues found that when cultured human colon tumor cells were invaded by the bacterium, they produced two inflammatory proteins called cytokines—specifically, interleukin-8 and CXCL1— that have been shown to promote the migration of malignant cells, a step in metastasis.

- A second paper reported that the bacterium induces changes in gene regulation that boost metastasis to the lungs in mice.

- A third study determined that the abundance of F. nucleatum in human colon cancer tissue correlates with the amount of metastases and, in mice, identified additional signals by which the microbe may “orchestrate” metastasis.

- Slade and others have also demonstrated that the bacterium incites a kind of cytokine storm that is aimed at controlling the infection but that ultimately exacerbates the cancer.

- “It’s like throwing gas on an already lit fire,” Slade says.

- Something similar may be going on in some breast tumors.

- In June a team led by microbiologist Gilad Bachrach of Hebrew University reported finding F. nucleatum DNA in 30 percent of the human breast cancer tissue examined; the bacterium was most common in cancer cells that expressed a lot of the surface sugar molecule Gal/GalNAc.

- Researchers also showed that the infection promotes growth of both primary tumors and metastases in mouse models of breast cancer.

- “The data imply that fusobacterium is not a cause of cancer, but it can accelerate progression,” Bachrach says.

- How much this is happening in humans is, of course, a critical question.

- “The findings are intriguing, and it makes sense,” says Joan Massagué of Memorial Sloan Kettering Cancer Center, who is a leading investigator of metastasis.

- Inflammation is invariably part of the metastatic process, he says, so an infection that incites a dramatic inflammatory reaction in a tumor will have a consequence: “it helps cancer cells engage in mobile, invasive behavior.”

- The discoveries about fusobacterium are part of a fast-moving field that is illuminating the way the microbiome both promotes and battles cancer.

- Many modern immunotherapy drugs, for instance, work best in the presence of beneficent microbes—as do some older chemotherapies.

- Some scientists envision that fusobacterium eventually could be turned into a cancer fighter.

- Given the microbe's attraction to a sugar on tumor cells, they suggest, perhaps it could be deployed as a Trojan horse, bound to cancer drugs and carrying them straight to a malignant target.