# Gut Commensal Microbes as Tumor Targeted Therapeutics

**An innovative strategy for identifying, enriching and utilizing gut commensal microbes to colonize tumors and facilitate tumor clearance.**

### Technology

The Schluter Lab at NYU Langone Health has developed a groundbreaking approach to harness the genetic adaptations of gut commensal microbes for tumor colonization and clearance. These gut commensal bacteria show great promise as vectors for anti-tumor microbial therapies because they have co-evolved with the host and have been naturally selected to avoid harming the host, unlike microbes such as *E. coli*, which can be lethal in high doses. Additionally, these bacteria have evolved unique genetic features that enable them to survive in nutrient-poor, hypoxic, and acidic environments, which closely resemble the harsh tumor micro-environment (TME) that often prevents the invasion of anti-tumor immune cells. Moreover, in the TME, cancer cells outcompete healthy tissue cells. The inventors have hypothesized that gut bacteria can be used to bypass this competition with cancer cells, and selectively enrich them by co-administering “private nutrients” that are inaccessible both to healthy tissue and cancer cells but support bacterial growth. They have identified a wide array of sugars that enable growth of candidate bacteria. The inventors have hypothesized that these unique properties of gut commensal bacteria may allow for selective epithelial tumor colonization and facilitate leveraging them for tumor clearance without the associated sickness and potential lethality observed with non-commensal microbe-based therapies. To test this hypothesis the inventors have developed and utilized a novel method for identifying candidate therapeutic bacterial strains and have observed no measurable sickness or lethality when these strains are injected into mice. Furthermore, these strains can persist within epithelial tumors for several days, emphasizing their therapeutic potential. Finally, they have identified “private” sugars for candidate gut bacteria. Further work is being done to evaluate the efficacy of these commensal microbes as anti-cancer therapies in combination with existing therapies.

### Background

Epithelial cancers, also known as carcinomas, arise from epithelial cells that line the surface of organs, glands, and tissues throughout the body. Carcinomas are the most common type of cancer, accounting for 80-90 percent of all cancer diagnoses. Epithelial cancer can affect a variety of organs, including the skin, breast, prostate, colon, and pancreas. These cancers exhibit aggressive growth, high mutation rates, and complex interactions with the TME.

The use of bacteria as anti-cancer agents was recognized over a century ago and has recently been gaining significant momentum in the field. Today, the primary strategy involves using genetically-modified, attenuated bacteria (such as *Salmonella*, *Escherichia*, and *Listeria*) to target solid tumors. While these therapies have shown promising anti-tumor activity, they must be applied carefully, as these bacteria can cause life-threatening infections or sepsis. The use of

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commensal bacteria represents a major advance, increasing the feasibility and decreasing the risk of this anti-cancer therapy.

### Applications

- Strategy for identification of candidate commensal strains that will specifically colonize epithelial tumors.
- Therapeutic strategy for tumor clearance in epithelial cancers using single or combination of commensal microbe strains with access to “private nutrients.”
- Combination of privately nutritionally supported bacteria with immune-checkpoint therapies or cell therapies to augment the anti-tumor immune response.

### Advantages

- **Selective enrichment through competitive growth advantage:** Commensal bacterial strains with access to combination therapy of “private nutrients” have a growth advantage over the tumor in harsh conditions of the tumor microenvironment, allowing them to persist at the tumor site and maintain therapeutic activity.
- **Improvement over existing microbe-based therapies:** Repurposing commensal microbes is expected to be safer than commonly used aerobic microbes like *E.coli*.
- **Modulate tumor immune environment:** Microbes can stimulate localized immune responses to make tumors more responsive to immune therapies.
- **Scale-up potential:** Naturally occurring gut microbes allow large-scale production.

### Next Development Steps

The inventors are continuing to identify new therapeutic microbial strains and quantify tumor colonization under various growth conditions.

### Intellectual Property

NYU has a pending provisional patent application covering the methods of identification and composition of anti-tumoral bacterial strains.