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GENETICALLY ENGINEERED YEAST STRAIN FOR THE TREATMENT OF GASTROINTESTINAL TUMORS WITH IMMUNE CHECKPOINT INHIBITOR THERAPY

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Value Proposition: *Genetically engineered yeast used to treat gastrointestinal tumors through the delivery of immune checkpoint inhibitor (ICI) proteins.*

Technology Description

Researchers at Washington University in St. Louis have developed a genetically engineered strain of Saccharomyces cerevisiae var. boulardii (Sb) that enables non-invasive and direct treatment of gastrointestinal (GI) tumors with immune checkpoint inhibitor (ICI) protein therapy. Conventional therapies are administered systemically, are frequently associated with off-target toxicities, are costly and labor-intensive to produce, and have limited efficacy in treating GI cancers.

The engineered yeast strain used in this technology has been transformed with a modified plasmid OGS539 that enables it to secrete a high-affinity programmed cell death 1 ectodomain protein (haPD-1), which can be administered orally allowing it to survive the gastrointestinal tract while maintaining its ability to secrete haPD-1. This may increase exposure and specificity of ICI therapy to tumors of the gastrointestinal tract, while limiting off-target exposures that provoke toxicity.

Stage of Research

Demonstrated that Sb_haPD-1 produces and secretes a functional haPD-1 product that can bind mouse and human PD-L1 and block the PD-1/PD-L1 axis. Demonstrated reduction of intestinal tumor burdens in a mouse model following a multi-day oral gavage regimen of Sb_haPD-1 with associated shifts to the gut microbiome and immune cell landscape. This same mouse model was not responsive to conventional therapy comprised of systemic injection of an anti-PD-L1 IgG antibody.

Applications

- Treatment of gastrointestinal tumors

Key Advantages

- Less treatment-associated toxicity
- Increases exposure and specificity of ICI therapy to tumors of the gastrointestinal tract

- Can be administered orally, while surviving the GI tract

Patents

Patent application filed. The inventors have another Sb-based technology that selectively senses or targets gut microorganisms, with a patent recently granted in Q4 2024.

Related Web Links – Gautam Dantas Profile; Dantas Lab