

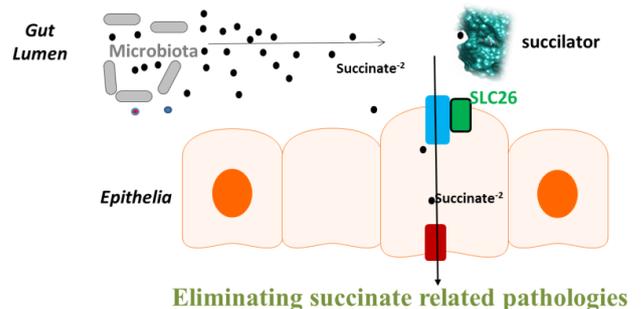
# Succinate Decoy Receptors "Succilators" as Biological Treatment for IBD and Related Extra Intestinal Symptoms

**S**uccinate is a metabolic intermediate of the tricarboxylic acid (TCA) cycle and a pivotal inflammatory and ischemia-reperfusion signaling molecule. Succinate stimulates the selective G-protein coupled receptor, SUCNR1, which is linked to Diabetes, Hypertension, Arthritis and Inflammatory bowel disease (IBD). Our research demonstrated that bio-specimens from IBD patients and IBD mouse models contain high concentrations of succinate and are enriched with succinate producing bacteria. In addition, we proved that elevated succinate absorption in the kidney leads to hypertension and is associated with kidney stone formation. Hence, high concentrations of succinate are a metabolic poison that can cause several morbidities for which the etiology remains unknown.

## The Technology

**Therapy:** Our long term goal is to utilize purified high-affinity recombinant human SUCNR1 proteins as succinate chelators ('succilators') to treat pathologies associated with high succinate concentrations, predominantly **IBD**.

**Diagnostic:** Using biochemical and mass spectrometry methods to measure succinate concentrations in biological specimens for a better diagnosis of IBD and related extra intestinal symptoms. These methods will be used as companion diagnostic tools to select the most appropriate IBD patients. To date, we have used an established enzymatic succinate assay to successfully monitor succinate concentrations in serum, urine and fecal samples of human IBD patients, human kidney stone formers, IBD mouse models and knockout mice which develop kidney stones and hypertension due to impaired succinate homeostasis.



## Advantages

- ✓ **Specificity** – the human SUCNR1 is highly specific for succinate binding.
- ✓ **Safety** - Since succilators are modified human proteins they are expected to evade immune response.
- ✓ **Efficiency** – we will modify the affinity of succilators to succinate by point mutations to generate improved and robust succinate chelators.
- ✓ Succinate assays can be used as a diagnostic tool as well as a tool for monitoring the efficiency of treatment.

## Patent Status

Patent pending

## Research Team

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