

Using 'Succilators' as potential treatment for IBD and other GI diseases

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Technology

Prof. Ohana is developing polypeptides, named 'Succilators', and a method of treating (possibly also preventing) a succinate-associated disease or condition, such as inflammatory bowel disease (IBD), urolithiasis, rheumatoid arthritis, cardiac hypertrophy, inflammation, kidney stones and hypertension. Various recombinant Succilators polypeptides are being developed among them Slc26a6 STAS domain and IRBIT that binds soluble NaDC-1, a transport of succinate and recombinant succinate receptor 1 (SUCNR1). Additional and improved Succilators are also being developed.

Succinate 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 IBD. Intriguingly, several studies show that intracellular succinate reprograms macrophages (M ϕ) to the pro inflammatory M1 state. Recent appreciation of M ϕ heterogeneity, with respect to both development and metabolism, indicates that different lineages of tissue-resident M ϕ respond divergently to microbial, environmental and immunological stimuli. Hence, trans epithelial absorption of succinate, which is produced by several bacterial strains of the gut microbiota, may potentially stimulate M ϕ polarization causing chronic inflammation. Research done in Dr. Ohana's lab demonstrated that bio-specimens from IBD patients and IBD mouse models contain high concentrations of succinate and are enriched with succinate producing bacteria. Dr. Ohana and his team have used an established enzymatic succinate assay to successfully monitor succinate concentrations in human IBD and kidney stone patients, IBD mouse models, and knockout mice which developed kidney stones and hypertension. In parallel, biochemical and mass spectrometry methods were used to measure succinate concentrations from human biological specimens for a better diagnosis of IBD and related additional intestinal symptoms.

Application

- Treatment for IBD and other diseases associated with high succinate concentrations
- Novel improved diagnostic method of IBD and intestinal symptoms
- Ability to monitor the efficiency of succinate treatment

Advantages

- Specificity – The human SUCNR1 is highly specific for succinate binding
- Safety - Since succilators are modified human proteins they are expected to evade immune responses
- Efficiency – Ability to modify the affinity of succilators to succinate by point mutations to generate improve and robust succinate chelators

Patent

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