



Engineered Probiotics as Systemic Therapeutic Delivery Platform

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The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in lactic acid bacteria engineered to express therapeutic molecules and achieve systemic delivery following oral administration.

This approach could be used to deliver new or existing therapies for a wide variety of medical indications at dramatically reduced cost. In mice studies the method has been used to deliver IL-22 and reverse many effects associated with metabolic syndrome.

Overview

Polypeptides, such as enzymes, antibodies, hormones and cytokines, are useful therapeutic agents. However, routes for systemically introducing such polypeptides to a subject are limited. Oral administration typically is not feasible, as the polypeptides are either degraded in the gastrointestinal tract or are blocked from reaching the bloodstream. Direct intravenous administration is therefore the major route by which polypeptides are systemically introduced.

Certain types of genetically engineered bacteria have been used as vehicles for locally delivering polypeptides to various tissues and even tumors. However, systemic distribution is potentially deleterious in certain subject populations such as immunocompromised patients.

Needed are engineered bacteria capable of being administered into the gastrointestinal tract and delivering polypeptides into the bloodstream – *without* systemic levels of the bacteria themselves being increased.

The Invention

UW–Madison researchers have developed bacteria engineered to systemically deliver a therapeutic polypeptide into a subject without the bacteria being substantially introduced into the bloodstream. This platform could be used to non-invasively increase systemic levels of hormones, peptides and potentially single-chain antibodies.

Using this new approach, the researchers engineered a lactic acid bacteria, *Lactobacillus reuteri*, to systemically deliver interleukin-22 (IL-22) in mice. The method is not limited to IL-22; other potential polypeptides include IL-35, insulin, leptin, a peptide inhibitor of PCSK9 and endolysin.

Applications

- Diseases and conditions that may be targeted include metabolic syndrome (e.g., obesity and type-2 diabetes), atherosclerosis, type-1 diabetes and cardiovascular disease.

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- Non-invasive and effective

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- Inexpensive approach to increase systemic levels of proteins that would otherwise be cost-prohibitive

Stage of Development

Since IL-22 has been shown to alleviate metabolic disorders and provide other therapeutic effects in diabetic subjects, the researchers tested whether administering IL-22-secreting *L. reuteri* to mice with diet-induced obesity could recapitulate these effects.

Results show that oral administration of recombinant *L. reuteri* engineered to secrete IL-22 are capable of delivering IL-22 in a manner that results in systemic physiological effects including an increase in growth, increase in growth hormone in plasma, and reduction in BMI and liver weight. In sum, the administration reversed many effects associated with metabolic syndrome.

The researchers predict that systemic delivery of IL-22 will also reverse many of the metabolic symptoms of diabetic subjects, including hyperglycemia and insulin resistance, and will improve insulin sensitivity, preserve gut mucosal barrier and endocrine functions, decrease endotoxemia and chronic inflammation, and reverse the dysregulation of lipid metabolism in liver and adipose tissues.

Additional Information

For More Information About the Inventors

- [Jan Peter Van Pijkeren](#)

Related Technologies

- [For information about phage-cured *Lactobacillus* strains developed by the researchers for therapeutic delivery, see WARF reference number P170020US01.](#)

Tech Fields

- [Drug Delivery : Other drug delivery technologies](#)
- [Therapeutics & Vaccines : Metabolic disorders](#)

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