Rani Therapeutics
www.ranitherapeutics.com

Cracking the oral drug delivery code

Google Ventures-backed Rani Therapeutics has developed a swallowable pill that injects biologic drugs directly into the intestine without degrading the drug in the stomach or gastrointestinal tract.

Therapeutic biologics have changed the treatment of chronic diseases such as diabetes and arthritis and now account for ~$200 billion in annual sales. Yet currently biologics can be effectively delivered only by injection, and the associated pain can reduce patient quality of life and compliance. Although the goal of delivering biologics orally is something of a holy grail, dozens of attempts using protective coatings or other methods have failed. So far the low bioavailability of orally delivered biologics—mainly due to degradation by digestive enzymes in the gut—has precluded their commercialization. No orally delivered biologic has come close to matching the bioavailability of subcutaneous (SC) injections.

Startup Rani Therapeutics believes it has cracked the code, with a novel platform technology to enable oral delivery of biologics that leverages insights into biology, engineering and material science. The resulting Rani capsule is a 'pill' engineered to inject biologic drugs directly into the upper intestine (jejunum). The Rani team decided on this approach because it takes advantage of a quirk of gut biology: unlike the body's surface, the intestine lacks sharp-pain receptors, making intestinal injection painless. The upper intestine is also highly vascularized, making it an ideal site for drug absorption. These characteristics supported the idea that an intestinal injection delivered by a Rani capsule could deliver biologics painlessly and overcome the hurdle of low bioavailability.

Oral delivery coupled with an intestinal injection is an entirely new and unprecedented solution to the problem of enzymatic destruction of protein drugs as they move through the digestive tract. To create the capsule, the Rani team had to solve several engineering challenges: ensuring safe transit through the stomach and duodenum and into the intestine; identifying appropriate biodegradable materials for the capsule and needle; generating the energy required to propel the needle into the intestinal wall; and delivering the drug without causing intestinal obstruction or harm.

Preclinical studies (**Fig. 1**) showed that the Rani capsule was able to achieve bioavailability levels similar to those observed with SC injection, which, if replicated in humans, would be a game changer for biologics. The advantages of orally delivered biologics are compelling. Given a choice, most people would prefer to swallow medication than face a needle. Shifting from painful SC injections to oral pills could have multiple advantages, including increased patient compliance and quality of life. In addition, different biologics could be combined into a single pill.

Rani Therapeutics CEO Mir Imran is also the founder of InCube Labs, a multi-disciplinary applied research incubator with a 20-year track record of tackling difficult medical problems. Imran holds over 400 US patents and has founded 22 companies, including Rani. According to Imran, the Rani capsule technology could "change the market landscape for biologics." The fact that the capsule relies on a dry drug formulation has important implications, as it could potentially reduce the need for refrigeration, increase shelf life and even decrease the cost of goods.

The promise of the Rani capsule has attracted backers including Google Ventures and VentureHealth, as well as biopharmaceutical partners such as Novartis and AstraZeneca, both of which are currently collaborating with Rani on feasibility studies. Rani has raised more than $70 million so far and is currently expanding manufacturing capabilities to support preclinical and clinical studies. If the work moves ahead as expected, the Rani capsule could enter clinical trials in 2017.

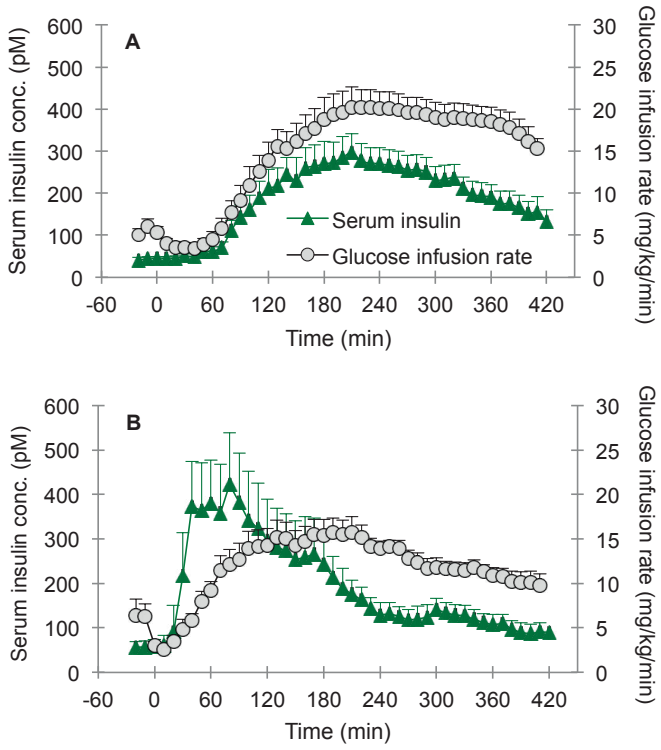

Figure 1: Pharmacokinetic-pharmacodynamic (PK-PD) profiles of insulin delivered subcutaneously (SC) or via Rani capsule. Anesthetized, age- and weight-matched juvenile Yorkshire pigs under a euglycemic glucose clamp received (at t=0) 20 units of fast-acting human insulin either SC (A, N=9) or intra-jejunally via autonomously deployed Rani capsules (B, N=8). Each panel shows the time course of changes in PK (serum insulin concentrations, determined using a sensitive ELISA) and PD (glucose infusion rate). The faster rise in serum insulin in the Rani group is likely due to the rapid uptake of the peptide from the highly vascularized intestinal wall. All data are means ± SEM.

> **"The Rani capsule technology could change the market landscape for biologics"**
>
> Mir Imran, CEO

contact
Stephanie McGrory,
Vice President, Business Development
Rani Therapeutics
San Jose, California, USA
Tel: +1-408-457-3730
Email: stephanie@incubelabs.com