enGene
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Pioneering gene therapies for mucosal tissues

enGene has developed a proprietary nonviral gene delivery platform and Gene Pill technology to deliver gene therapies to mucosal tissues, creating new opportunities for treating hard-to-reach tissues across many indications.

Mucosal tissues, such as the gastrointestinal tract (GIT), bladder, lungs and female reproductive organs are challenging to treat using current delivery approaches for protein therapies. It is difficult to achieve sufficient concentration of therapeutic protein at the intended target site without systemic toxicities. enGene is taking a radically different approach to overcome this problem; by turning mucosal tissue cells into bioreactors of therapeutic effectors, such as proteins and antibodies, the company aims to concentrate biologics exactly where they are needed.

"We have built a robust nonviral gene delivery platform, which can penetrate mucosal tissues and deliver a nucleic acid (NA) payload encoding a specific therapeutic protein, and we have developed a solid dosage form for oral delivery with our Gene Pill technology," said Anthony Cheung, CTO and cofounder of enGene. "To the best of our knowledge, this is the most advanced platform for oral delivery of gene therapies."

Unlike virus-based gene therapies, the dosing of enGene's nonviral delivery nanoparticle vehicle is transient, owing to the rapid turnover of epithelial cells in mucosal tissues. It is also repeatable, titratable and does not require systemic injections or infusions. No immunogenicity has been observed to date. The approach overcomes the capacity limitations typical of viral vectors, as it enables large and/or multiple genes to be delivered simultaneously. Reimbursement challenges are also expected to be significantly lower than for virus-based gene therapies. Importantly, enGene has successfully formulated its novel nonviral gene delivery vector into an oral solid dosage form without compromising its stability and potency.

Based in Montreal, Canada, and Boston, Massachusetts, enGene has a world-class leadership team and board. The company has been highly capital efficient and strategically focused in order to advance its proprietary mucosal gene delivery platform, including the development of a robust, scalable manufacturing process with a low cost of goods. With the ability to deliver payloads to several tissues, and with proof-of-efficacy in multiple disease models, enGene is open to partnering opportunities to advance the development of its assets.

Robust nonviral delivery vehicle

enGene has built a scalable plug-and-play gene therapy platform with the flexibility to deliver a wide range of NA payloads. The platform comprises a proprietary DDX polymer that is coupled with high efficiency to a plasmid payload before undergoing a proprietary manufacturing process to create a dose-ready nanoparticle suspension.

With its DDX polymer, enGene has demonstrated the capability to deliver nucleotide sequences encoding therapeutic proteins. The platform is also amenable to carrying RNA and oligo-NA payloads, thereby facilitating the delivery of messenger RNA, long noncoding RNA, small interfering RNA, microRNA and aptamers. Additionally, the technology can be leveraged in partnerships with companies advancing gene-editing approaches.

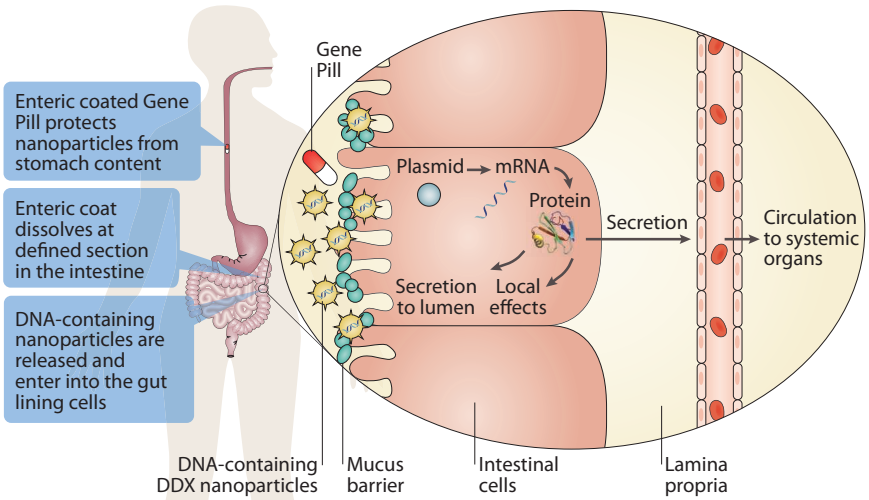

Fig. 1 | The Gene Pill. This system turns intestinal cells into 'bioreactors' that produce therapeutic proteins for local or systemic effects. The mucus-penetrating mechanism of DDX is consistent across all target tissues.

The DDX nanoparticle suspension can be converted readily into a Gene Pill for oral delivery via a second proprietary manufacturing process. Gene therapy companies that use viral vectors are unable to create solid dosage forms in this way, as viral vectors are not able to withstand the process of generating an amenable solid dosage form.

Pipeline programs

enGene is developing a powder-in-bottle DDX formulation designed to be rehydrated in the clinic for intravesical administration to patients with non-muscle-invasive bladder cancer (NMIBC). Intravesical administration is consistent with clinical practice in NMIBC for the administration of bacillus Calmette–Guérin, the current standard of care. Importantly, enGene's approach circumscribes immunomodulating gene therapies to the bladder, thereby delivering robust efficacy while mitigating systemic exposure.

Following its lead program, enGene is developing gene therapies for two gastrointestinal indications—inflammatory bowel disease and short bowel syndrome. These programs leverage enGene's Gene Pill technology to coax the epithelial cells of the GIT to produce protein drugs locally in the intestine, thereby concentrating therapeutic proteins at the intended site of action. By using defined enteric coatings for the Gene Pill, it is possible to deliver NA payloads to specific sections of the GIT. Once the Gene Pill has dissolved in the targeted section of the GIT, it releases DDX nanoparticles, which are designed to overcome the challenging mucosal barrier. The nanoparticles are only ~100 nm in diameter, and can therefore pass through mucus layer pores, and a hydrophilic surface prevents them from becoming trapped in mucin (unlike hydrophobic lipid nanoparticles).

The target epithelial cells are then coaxed into becoming bioreactors to produce therapeutic protein for local effects or to potentially secrete protein into the systemic circulation to treat peripheral tissues (**Fig. 1**).

Partnering opportunities

enGene is advancing its pipeline of candidates to the clinic with an investigational new drug (IND) filing for its NMIBC program in mid-2020 and IND filings for its gastrointestinal programs at the end of 2020

"We have only scratched the surface of possibilities for our platform," said José Lora, the company's CSO. "We can effectively formulate DDX to express any therapeutic protein in any accessible mucosal tissue. Recent efforts have demonstrated proof-of-concept for inhalable delivery to the lungs, enabling treatments for various pulmonary diseases such as cystic fibrosis and asthma, among many others."

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