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EMERGING COMPANY PROFILE

SNIPR: Turning CRISPR into a microbiome suicide

BY MARK ZIPKIN, STAFF WRITER

SNIPR is using CRISPR to target specific bacteria to fight infection or modulate the immune system.

Growing interest in CRISPR for mammalian cells and microbiome-focused therapeutics led the company's co-founders, Christian Grøndahl, Morten Sommer and Jasper Clube, to explore the possibility of using bacteria's own endogenous CRISPR-associated (Cas) proteins to cut its DNA, CEO Grøndahl told BioCentury.

The company was incubated at the Novo Nordisk Foundation Center for Biosustainability at Technical University of Denmark (DTU), where SNIPR Chair of Research Sommer is scientific director.

For infectious diseases, the company uses a CRISPR screen to identify guide RNAs (gRNAs) that induce a pathogen's endogenous Cas system to cut 10-20 of its own genes, then encodes the gRNAs in plasmid-like DNA vectors. This therapeutic strategy acts as a suicide switch within the bacteria and poses no risk of off-target effects in human cells, according to Grøndahl.

To modulate the microbiome for autoimmune diseases or to enhance responses to cancer immunotherapies, SNIPR uses bioinformatics to identify which species of commensal bacteria occupy microbiome niches that prevent more beneficial bacteria from thriving or colonizing, then triggers their endogenous CRISPR machinery with gRNAs encoded in the vectors.

Grøndahl said that compared with targeting a single pathogen to combat infection, targeting multiple gut microbes for immunomodulatory purposes is trickier but achievable. "What you want to do is much more refined: dial down maybe four or five bacteria and also dial up others," which can include transplanting bacteria once a niche has been carved out.

Through commissioned research at DTU, SNIPR confirmed its technology could modify bacterial population growth *in vitro*. Grøndahl added that the company and its collaborators at Statens Serum Institut have proof-of-concept mouse data showing the gRNA-encoding vectors can be delivered in multiple ways, such as via carrier bacteria or microparticles. Details are not disclosed.

He said SNIPR has two lead programs for undisclosed indications: one for a difficult-to-treat infection, the other for immune modulation.

Because its system is modular, SNIPR can quickly personalize a therapy based on an individual's gut composition, giving it much needed flexibility, said Grøndahl, because "there will be many versions of a healthy microbiome."

SNIPR is seeking to partner its platform with other microbiome companies outside its target areas, and with cancer companies that need a more robust immune response for their immunotherapeutics. The company is also open to collaborating on a CRISPR-based microbiome therapy in other disease areas with well established microbiome links, including metabolic and CNS diseases.

SNIPR BIOME APS
Copenhagen, Denmark

Technology: CRISPR-guided vectors to activate endogenous Cas-mediated killing of specific bacteria within the gut microbiome

Disease focus: Infectious, autoimmune, cancer

Clinical status: Preclinical

Founded: 2017 by Christian Grøndahl, Morten Sommer and Jasper Clube

University collaborators: Statens Serum Institut

Corporate partners: NA

Number of employees: 18

Funds raised: $53.4 million

Investors: Lundbeckfonden Emerge, LSP, North-East Family Office and Wellington Partners

CEO: Christian Grøndahl

Patents: 2 issued patents covering methods to alter microbial populations for infectious and immune modulation

Locus Biosciences Inc., Eligo Biosciences S.A.S. and Nemesis Bioscience Ltd. all use CRISPR technology to kill bacteria or cut out resistance mechanisms, but utilize larger exogenous CRISPR systems delivered by bacteriophages.

Locus' system can also deliver a gRNA targeting endogenous Cas3 system. But Locus CEO Paul Garofolo said less than half of all bacteria species have an endogenous Cas system, and Locus' exogenous technology allows it to target bacteria with or without their own Cas proteins.

Grøndahl said SNIPR would deliver exogenous Cas to target bacteria lacking the enzymes, but declined to say how.

Multiple companies are developing non-CRISPR, microbiome-based cancer therapies and microbiome therapies for autoimmune diseases that deliver therapeutic microbes or their antigens to the gut to produce disease modifying effects.

The co-founding team tapped Clube's expertise as a patent attorney to carve out an early IP position and secure its first issued patent in July 2017 covering the use of endogenous CRISPR system to engineer the microbiome. The company raised €3 million ($3.4 million) in seed funding from Lundbeckfonden Emerge and officially launched a month later.

In March, Lundbeckfonden Emerge and LSP led a $50 million series A round for SNIPR. Grøndahl expects the funding to support the infection and immune-modulating programs for four years, plus a Phase I trial for one of them in 2021.

COMPANIES AND INSTITUTIONS MENTIONED

Eligo Bioscience S.A.S., Paris, France
Locus Biosciences Inc., Morrisville, N.C.
Nemesis Bioscience Ltd., Cambridge, U.K.
Technical University of Denmark, Copenhagen, Denmark
SNIPR Biome ApS, Copenhagen, Denmark
Statens Serum Institut, Copenhagen, Denmark

TARGETS

Cas3 - CRISPR-associated helicase Cas3

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