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Killing Targeted Bacteria With CRISPR Drugs Is SNIPR BIOME's Promise

CEO Says Danish Biotech Wants To Soon Raise $100-$150m

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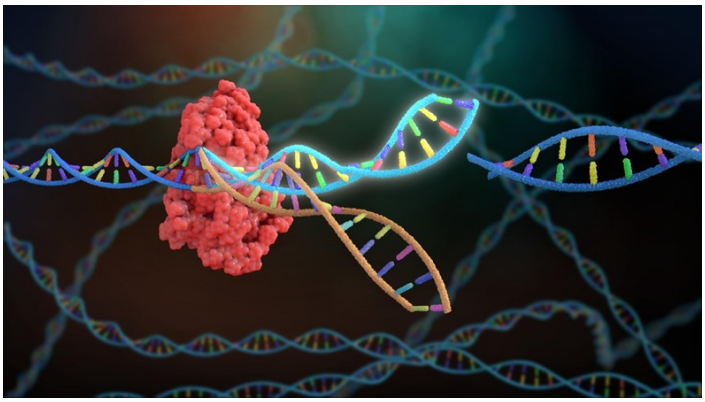
Executive Summary

SNIPR BIOME aims to be the world's top developer of CRISPR-based drugs that selectively target and kill bacteria, while leaving the rest of the patient's microbiome intact, the biotech's CEO tells *Scrip*.



SNIPR BIOME'S FIRST CANDIDATE WILL TARGET ONLY E. COLI BACTERIA IN THE GUT

Source: Alamy

Denmark-based SNIPR Biome ApS has developed a CRISPR/Cas 3 approach to precisely target bacteria like *E. coli* to prevent infections without harming the beneficial bacteria in the patient's microbiome and aims to test its first candidate therapy in humans during the first half of 2022, the biotech's CEO told *Scrip*.

The microbiome-focused start-up has a license to patented CRISPR/Cas technology and is developing therapies to selectively eradicate target bacteria based on specific DNA sequence signatures in the bacterial genome, while leaving the rest of the patient's microbiome intact.

Its recently identified lead candidate, named SNIPR001, would target only *E. coli* bacteria in the gut, preventing the translocation of the bacteria to the bloodstream and sparing the beneficial bacteria in the patient's microbiome, Christian Grøndahl said in an exclusive interview.

Precision Cellular 'Surgery'

This precision approach to killing harmful bacteria could transform the way *E. coli* infections are prevented and treated. Cancer patients today are often pre-emptively given broad-spectrum antibiotics designed to kill bacteria indiscriminately.

"This approach is increasingly ineffective. Antimicrobial resistance to many drugs means the *E. Coli* is not being killed, leading to a fatal outcome for the patients. The other big problem is that you are killing off all the good bacteria with this shotgun approach to antibiotics and harvesting your entire microbiome – this pristine and wonderful diversity that we have in our microbiome – and that has a lot of other dangerous implications," Grøndahl explained.

SNIPR's new lead candidate drug is in development for the prevention of infections in cancer patients with hematological malignancies. These patients are at increased risk of bloodstream infections due both to the disease and to chemotherapy treatment, with the pathogen *E. coli* posing a heightened risk.

"With these patients, the combination of the disease and the full body chemotherapy treatment mean the body's immune system's ability to function is grossly reduced. It also leads to damage in the gastrointestinal tract. So all the epithelial cells that would normally keep your gut fully sealed off and intact so bacteria cannot escape are damaged by the process and you get what's called 'leaky gut', allowing bacteria to escape from your GI tract and get into the blood, leading to sepsis and a potentially very life-threatening situa Grøndahl said.

The biotech plans to start testing SNIPR001 in healthy volunteers next year. "Then, once it has shown itself to be safe and efficacious, we'll move into a small group of patients with hematologic malignancies," Grøndahl added.

What the biotech hopes to accomplish is *de facto* precision surgery. With its technology, the removal of the targeted bacteria will be very precise. The CEO compared the technique to "using a surgical scalpel rather than the sledgehammer approach" currently being used with antibiotics.

"We are actually using Cas 3 in our initial therapy. But our technology allows us the possibility to use whatever Cas we choose."

"What we'll do is sequence all the *E. coli* that we want to kill, and then seek out essential genes in *E. coli* and modulate the CRISPR array so that it will recognize the *E. coli* specific gene. Then the Cas 3 actually cuts up those genes. But it's a big challenge, because we must also ensure not to kill the 'innocent bystander' healthy bacteria in the microbiome," the CEO explained.

Funding Needs

The company's developmental ambitions will become increasingly costly. That will mean fresh funding rounds soon, he added.

In March 2019, SNIPR raised $50m in a series A round, led by its seed investor, Lundbeck Inc.'s affiliated early-stage investment arm Lundbeckfonden Emerge. (Also see "Lundbeck Leads $50m Fund Raise For CRISPR Microbiome StartUp" - Scrip, 11 Mar, 2019.)

"We have now spent around half of that series A funding, raised just over two years ago, and our expenses are increasing as we advance. We will therefore start talks with investors late this year with a view to raising a larger series B round."

In May, the non-profit antibiotic-resistant initiative CARB-X said it was awarding SNIPR up to $3.9m to help it develop SNIPR001 as an innovative new drug to prevent *E. coli* infections in cancer patients.

Under the award, SNIPR may be eligible for up to $6.3m in additional funds from CARB-X if the project achieves certain milestones, subject to available funds.

“The way CARB-X works is that it will help us with some of our preclinical activities and when we decide to bring the drug into human clinical trials, they have the option to support some of those,” Grøndahl said.

“What CARB-X typically does is help with the stage immediately before a therapy goes into the clinic, and if that’s successful, again with Phase I. Of course, if that were then to be successful it would be up to us to meet the costs of advancing to Phase II and beyond. But their role is a very important part of the journey,” he added.

The Dane says he is confident that - with backers like CARB-X and Lundbeckfonden - SNIPR will be able to raise the money that it needs to move its candidate and pipeline forward at speed.

“We want to be the leading CRISPR microbiome company in the world. So, we’ll be looking to raise two or three times the amount that we raised in our series A, which was $50m,” he said.