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Small viruses could accelerate cell and gene therapy research

Novartis collaborates with Homology Medicines to adapt and refine genome editing technology.

By Alyssa Kneller | Nov 13, 2017

Interest in the field of genome editing continues to heat up, fueled by technological advances and the first approval of a gene therapy in the United States. The latest development in this exciting frontier of science involves small viruses called AAVs (short for adeno-associated viruses) that have the power to overwrite DNA in human cells.

“AAV biology is one of the most febrile areas of basic research, and we’re planning to explore its therapeutic potential through a new collaboration,” says Craig Mickanin, who focuses on new tools and technologies as a director at the Novartis Institutes for BioMedical Research (NIBR).

Novartis will work with Homology Medicines, a biotech company with a proprietary AAV platform, to adapt and refine the technology for the treatment of a blood disorder and certain eye diseases. Novartis biologists with expertise in these conditions will work side-by-side with Homology scientists over the course of the collaboration – announced November 13 – to move projects toward clinical testing.

The collaboration is designed to accelerate an initiative at NIBR that engages researchers across the company who are involved in projects with a common denominator: the genetic reprogramming of cells. Homology’s AAV technology may aid their work.

“It is our hope that this collaboration will help advance our Cell and Gene Therapy initiative,” says Susan Stevenson, an executive director at NIBR who leads the initiative.

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The AAV advantage

AAVs are unusual in one key respect. In contrast to larger viruses, they don’t seem to cause illness. This built-in safety feature makes AAVs attractive tools for genome editing.

The benign viruses can be engineered to carry a specific genetic sequence, and they can be programmed to home in on a target site in the genome. When they arrive, AAVs trigger a process called homologous recombination, which overwrites a particular portion of a gene or even replaces an entire gene. In this way, AAVs can be used to correct genetic defects.

Homologous recombination may give AAVs an edge over other genome editing tools such as CRISPR in certain contexts.

Unlike AAVs, CRISPR employs molecular scissors to generate double-stranded breaks in DNA. The breaks

can be repaired one of two ways. The repair mechanism that tends to dominate – called non-homologous end joining – results in the insertion or deletion of short DNA sequences, which typically break the original gene. As a result, it's relatively easy for researchers to disrupt a gene with CRISPR, but it's harder for them to fix an error in a gene.

"We aim to select the right tool for the right project," says Mickanin, the technology specialist. "In some cases, that will mean using AAVs to correct a genetic defect rather than disabling a gene."

Testing the technology

The collaboration with Homology includes three work streams. The first focuses on a blood disorder. The Novartis-Homology team hopes to design a single AAV reagent that can be injected directly into the bloodstream of any patient with a defective gene to cure the disease. "We want to figure out if these AAVs are safe enough to inject directly into the bloodstream – and if we can use them to fix a defective gene once and for all," says Stevenson, the cell and gene therapy expert.

The second work stream involves diseases of the eye, a testing ground for gene editing therapies because such therapies can be delivered locally. Gene editing agents can be injected directly under the retina, for example, where researchers hope they will work without affecting the rest of the body. "The fact that we can directly observe the treatment and its effects in the eye gives us an important opportunity for assessing gene editing efficacy and helping patients with eye disease," explains Cynthia Grosskreutz, Global Head of Ophthalmology at NIBR.

The final work stream is exploratory. Researchers from across NIBR will be able to nominate projects that could benefit from Homology's AAV technology. Homology's viruses will be tested on a variety of cell types and model systems, potentially exposing new opportunities for therapeutic applications.

"This technology could be applied to many different diseases," Mickanin says. "We're excited to work with the Homology team to explore the possibilities."

In addition to collaborating with Homology Medicines, Novartis has made an equity investment in the company.

New Novartis collaboration aims to advance cell and gene therapy research

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