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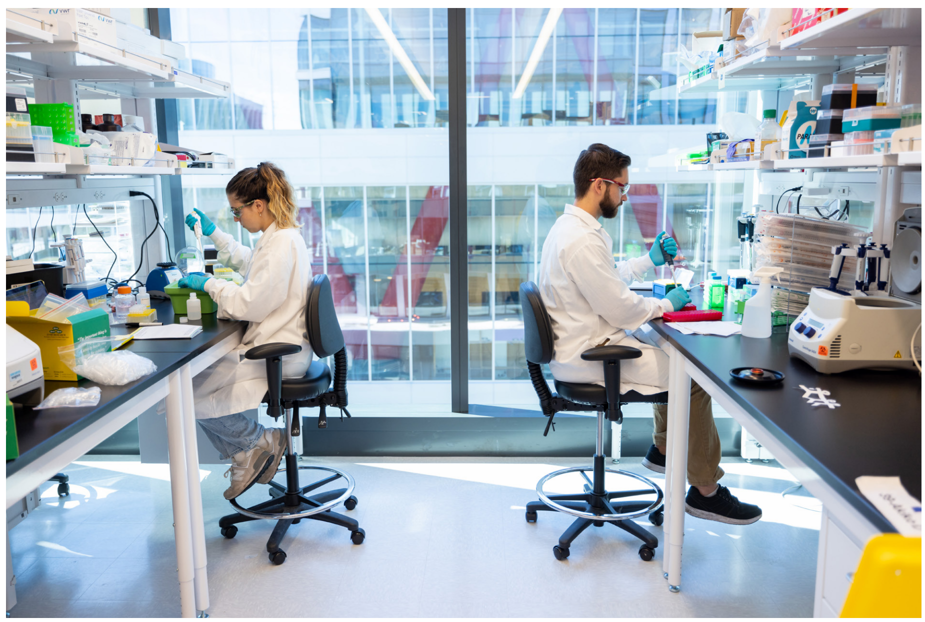
Business

Boston startup Ascidian Therapeutics charts vision for therapies that ‘rewrite RNA’

The new biotech company raised $50 million for its unique take on RNA editing therapies.

By Ryan Cross
Globe Staff



KEVIN TRIMMER

Ascidian Therapeutics scientists Julia Meredith and Sean Murphy work in the company’s new laboratory at 80 Guest Street in Boston, Massachusetts.

Competition is heating up among biotech startups building technologies that improve or expand upon what gene editing can do. While most of these firms are devising therapies that permanently modify DNA to treat, and potentially cure, genetic diseases, a growing number think that tinkering with RNA — the shorter-lived cousin to DNA — might be a safer and more effective strategy for some conditions.

Ascidian Therapeutics, the latest entrant to the budding RNA editing field, emerged from stealth on Tuesday backed with $50 million to develop therapies that “rewrite RNA.” The Boston-based startup already has its sights set on developing an RNA-altering medicine for an inherited form of vision loss called Stargardt disease, for which there is no treatment.

As with DNA editing technologies like CRISPR, the goal of RNA editing is to make a genetic change that treats a disease, sometimes by directly fixing a mutation that causes the condition. Changes to DNA are lifelong, and DNA editing technologies are too nascent to know if they will cause long-term problems. Some companies are hoping that editing these intermediary bits of genetic code could have the same benefits as DNA editing without the potential problems, since we make new RNA molecules all the time.

At least three Cambridge firms — EdiGene, Korro Bio, and Wave Life Sciences — are developing their own RNA editing therapies. Two major pharma firms are investing in RNA editing technologies as well. Eli Lilly and Company is partnering with the Dutch biotech ProQR Therapeutics to develop treatments for liver and nervous system diseases. And Roche is working with the Seattle-based Shape Therapeutics — which has a lab in Boston — on RNA editing therapies for Alzheimer’s and Parkinson’s disease.

All of these companies are developing RNA editing therapies that change a single letter of the RNA genetic code into another letter — analogous to the DNA editing technology known as base editing, which the Cambridge firm Verve recently began testing in humans with a genetic condition that predisposes them to heart disease. RNA editing therapies have not been tested in humans yet.

Ascidian is developing a unique twist on RNA editing. Rather than swapping

out single letters of the RNA code one at a time, Ascidian's technology is designed to replace whole swathes of code known as exons. Chief executive Romesh Subramanian said this so-called exon-editing will be ideal for genetic conditions that have many different causes, including Stargardt disease, which affects about 30,000 people in the US.

There are more than 900 mutations in a single gene linked to Stargardt disease, and developing a different therapy to correct each of those mutations is impractical, Subramanian said. In theory, giving patients an entirely new copy of that gene would work, but that gene is simply too big to fit into the engineered viruses commonly employed by gene therapy companies for shuttling new copies of DNA into the body.

Ascidian plans to apply its exon editing to additional eye diseases, neurological and neuromuscular conditions, and rare diseases. Subramanian said that the company has already tested the approach in monkeys, but he wouldn't disclose a timeline for when clinical trials might start.

The company's name is borrowed from the eponymous sea creatures, ascidians, which are also known as tunicates or sea squirts. These tubular animals are masters of rewriting their own RNA, and studies of their odd genetics inspired efforts to harness natural forms of exon editing for use as a therapy.

Some of Ascidian's technology came from Limelight Bio, a gene therapy company launched by the New York-based life science venture capital firm Apple Tree Partners, or ATP, in 2019. Limelight has since dissolved, but some of the firm's programs, namely RNA editing, live on at Ascidian, which ATP also founded and funded. Ascidian has a little over 30 people in its labs at 80 Guest St. by the Warrior Ice Arena.

Dr. Michael Ehlers, founding chief executive of Ascidian and chief scientific officer of ATP, is confident that there will be more investments in the RNA editing field to come. "We're at the tip of the iceberg on this," he said.

Ryan Cross can be reached at ryan.cross@globe.com. Follow him on Twitter @RLCscienceboss.