Dr. Danny Crohn Video #2: Intellia's Approach to CRISPR/Cas 9

00:07 – 00:16

Overall, the process by which an *in vivo* CRISPR-based therapy is believed to work may seem complicated, but it can really be broken down into 4 key steps:

00:17 – 01:02

First, the CRISPR/Cas9 components are packaged into a proprietary lipid nanoparticle delivery system and administered as a one-time IV infusion.

Then the lipid nanoparticle preferentially distributes to the liver and is taken up by hepatocytes, where the CRISPR/Cas9 complex forms and enters hepatocyte nuclei.

Next, the guide RNA targets a specific location on the gene of interest, helping Cas9 make a precise edit. It's at this point that the cell's natural DNA repair process helps the CRISPR/Cas9 complex complete the edit to the target gene.

Finally, once the edit is completed, a genetic modification should occur to change the way the gene is read and halt the production of the target protein.

01:03 – 01:27

Importantly, the reason this effect might be expected to be durable is because an edit made by CRISPR/Cas9 is passed on to daughter cells when the cell replicates, essentially propagating the edit through the cell lineage. That said, gene edits in somatic cells, such as hepatocytes, should only affect the patient being treated, and would not be expected to be passed on to the patient's children.

01:32 – 01:48

To alleviate the need for chronic therapy, investigational *in vivo* CRISPR-based therapies have been designed to be administered as a one-time treatment via IV infusion.

Animal models suggest the investigational therapy remains in circulation and in the liver for as little as 5 days.