

## Dr. Danny Crohn Video #1: Understanding CRISPR/Cas9 Components Transcript

00:07 – 00:23

Broadly speaking, investigational *in vivo* CRISPR-based gene-editing approaches aim to address the underlying mechanism of human diseases by making precise edits to certain genes that produce problematic proteins or are otherwise involved in the manifestation of a disease.

00:24 – 00:54

These approaches generally involve 2 key elements: a CRISPR/Cas9 complex, and a delivery system.

The CRISPR/Cas9 complex consists of a guide RNA, which is like a molecular “GPS” that recognizes the target gene, and a Cas9 enzyme, which makes a precise edit to the DNA at the location targeted by the guide RNA.

For *in vivo* delivery of CRISPR/Cas9 to patients, components can be packaged into either a lipid nanoparticle, also known as an LNP, or a viral vector.

00:55 – 01:18

LNPs are developed with careful consideration of lipid composition and RNA cargo to ensure specific distribution to cells of interest.

Viral vectors have tropism for a variety of tissues and can support transient expression of Cas9.

Overall, packaging CRISPR/Cas9 components into a delivery system can enable the delivery of the gene-editing therapy directly to patients.

01:23 – 01:32

A lipid nanoparticle, also known as LNP, can help to efficiently deliver the CRISPR/Cas9 complex to the specific cells underlying a disease.

01:33 – 2:09

The actual components packaged inside the LNP are a guide RNA specific to the target gene, and an mRNA sequence encoding Cas9, which is translated into the Cas9 enzyme once deposited in target cells.

LNPs are an attractive delivery vehicle in that they are generally tunable to a range of tissues. *In vitro* and *in vivo* studies suggest they yield low immunogenicity.

Additionally, certain proprietary LNP delivery systems include liver tropism (to help ensure intended cells are preferentially distributed to), and transient expression of CRISPR/Cas9 components.

02:10 – 02:16

The proprietary LNP delivery system was designed with these efficacy and safety implications in mind.