What is CRISPR?

A guide to what CRISPR is and its far-reaching applications in healthcare, agriculture, & more.

CBINSIGHTS

WITHIN 24 HOURS

Briefing recording will be distributed

The presentation will also be sent to you. Feel free to share with colleagues. The resolution of some slides may be suboptimal due to the webinar software. Those slides will look fine in the presentation that we send you.

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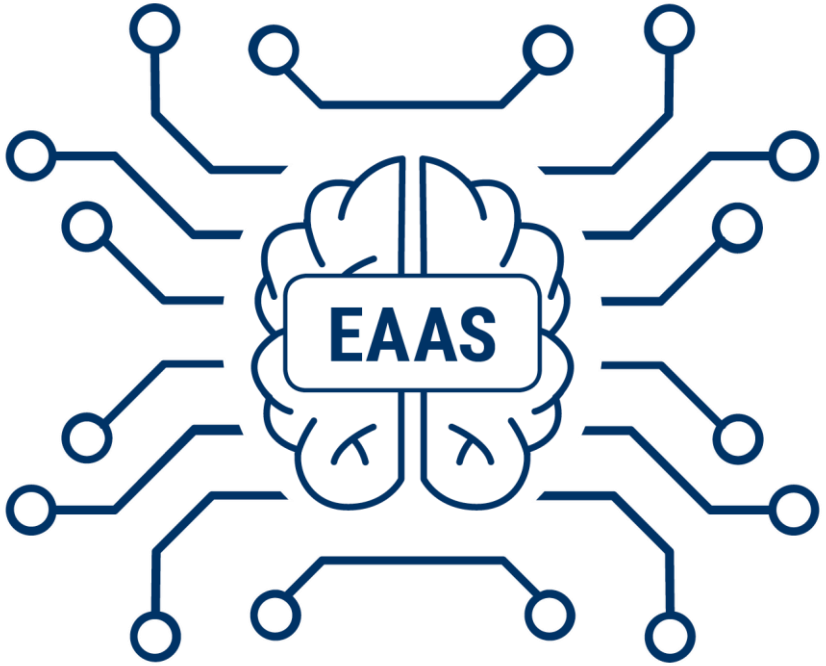
#WhatIsCRISPR

WHO WE ARE

The technology market intelligence platform.

CB Insights software lets you predict, discuss, and communicate emerging technology trends using data in ways that are beyond human cognition. We are a leader in the Expert Automation & Augmentation Software (EAAS) space.



TRUSTED BY THE WORLD'S LEADING COMPANIES

BARRICK citi F-PRIME FIRSTMARK GE IBM NORWEST VENTURE PARTNERS Riviera SEQUOIA

"We use CB Insights to find emerging trends and interesting companies that might signal a shift in technology or require us to reallocate resources."

Beti Cung, Corporate Strategy, Microsoft

Microsoft

CBINSIGHTS

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CBI Councils bring together experienced executives to accelerate their success through the sharing of experience-based insights that inform business decisions and help solve complex strategic, organizational, and growth challenges.

If you are an EVP, SVP, or C-level executive at a company doing $1B+ in revenue, request an invite by emailing councils@cbsinghts.com.

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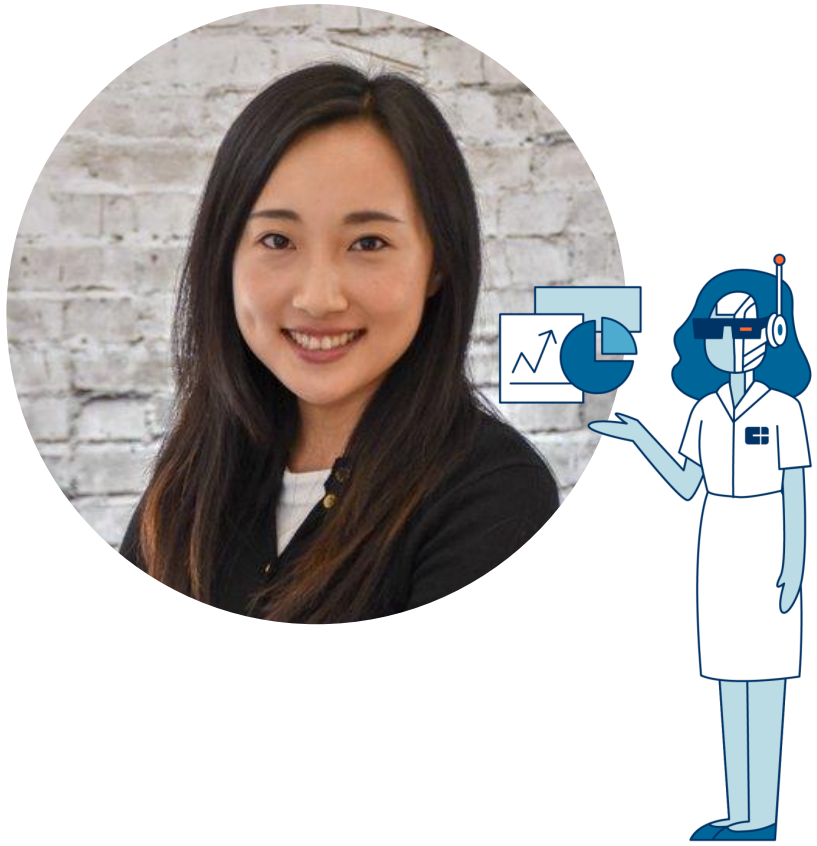
ABOUT THE ANALYST

Ja Lee



Intelligence Analyst

@Ja_Lee2 | jlee@cbinsights.com

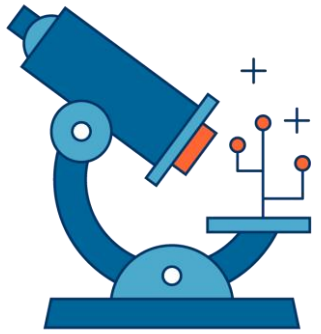
Ja Lee is an intelligence analyst at CB Insights, where she produces data-driven analysis and research reports on trends in biotechnology and medical devices.

Prior to joining CB Insights, Ja worked with clinical trials at Children's National Medical Center. She is a graduate of the University of North Carolina at Chapel Hill with majors in Biology and Spanish. She received her Master's degree in Physiology from North Carolina State University.

Contents

GENE EDITING 2.0

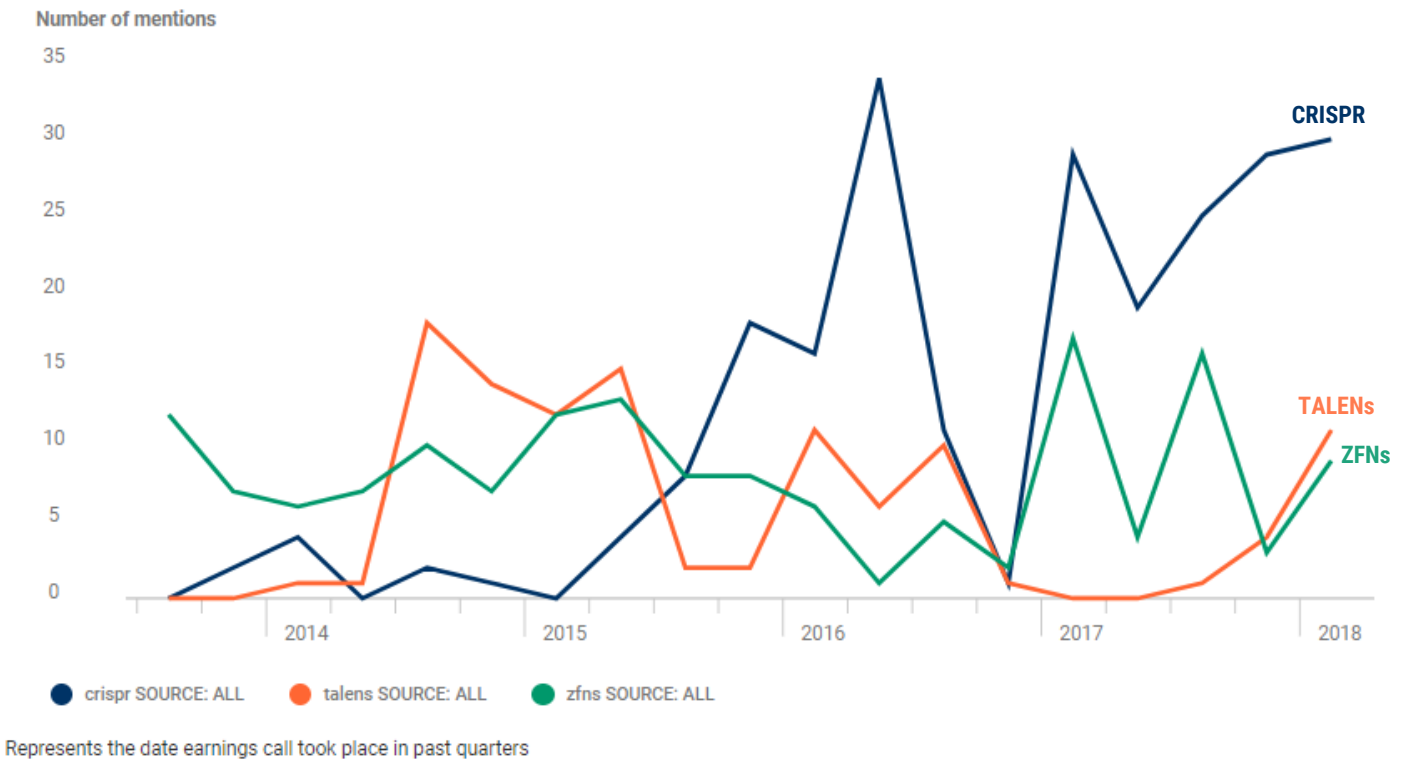
CRISPR ushers in a new wave of gene editing



CRISPR gene editing technology leads against older methods.

Before there was CRISPR, there were other gene-editing techniques known as **Zinc Finger Nucleases** (ZFNs) and **Transcription Activator-Like Effector Nucleases** (TALENs).

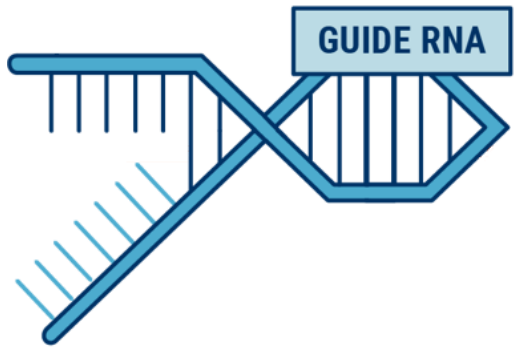
CRISPR leads among other gene editing techniques



Represents the date earnings call took place in past quarters

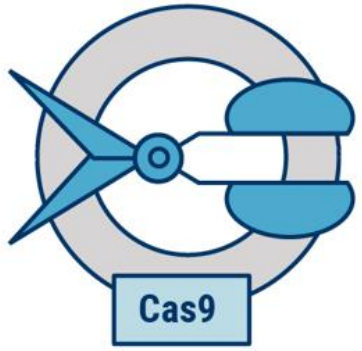
CRISPR = CLUSTERED REGULARLY INTERSPACED SHORT PALINDROME REPEATS

CRISPR-Cas9 system has 3 main players



1 **Guide RNA**

aka “GPS coordinates”



2 **Cas9 protein**

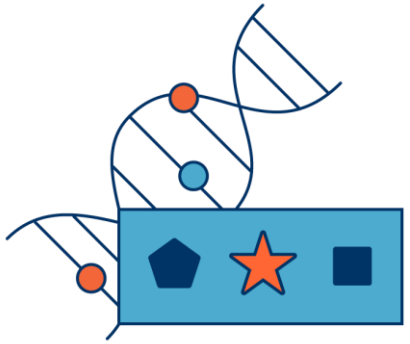
aka “molecular scissors”

3 **DNA**

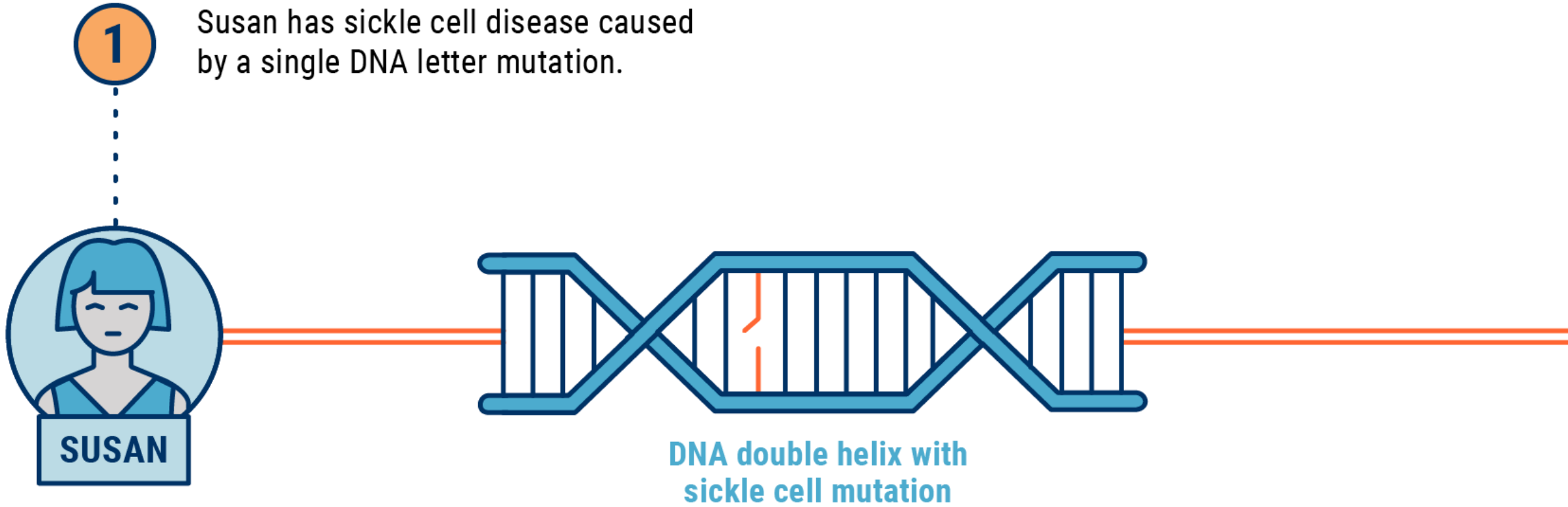
containing the sequence we want to insert

BREAKING CRISPR DOWN

How does CRISPR work?

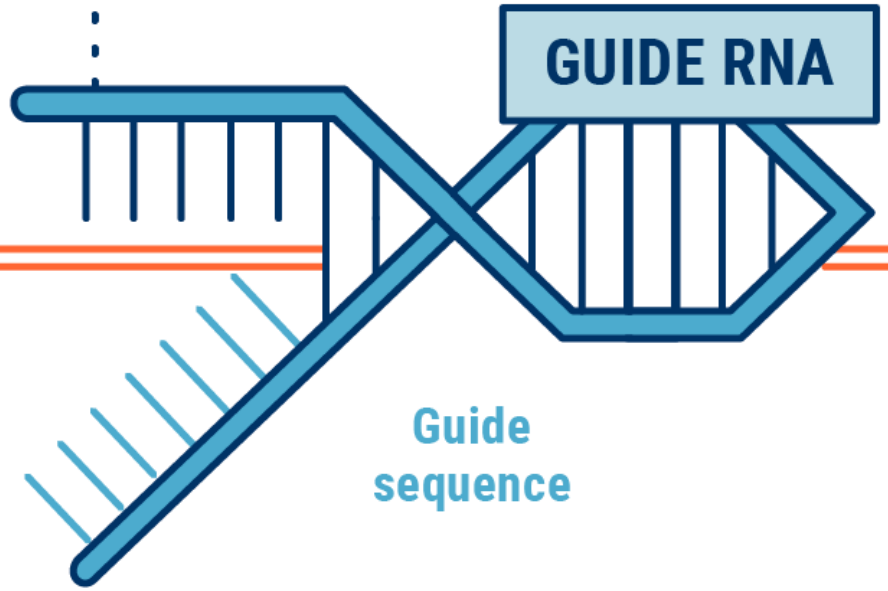


Understanding How The CRISPR Gene-editing Process Works

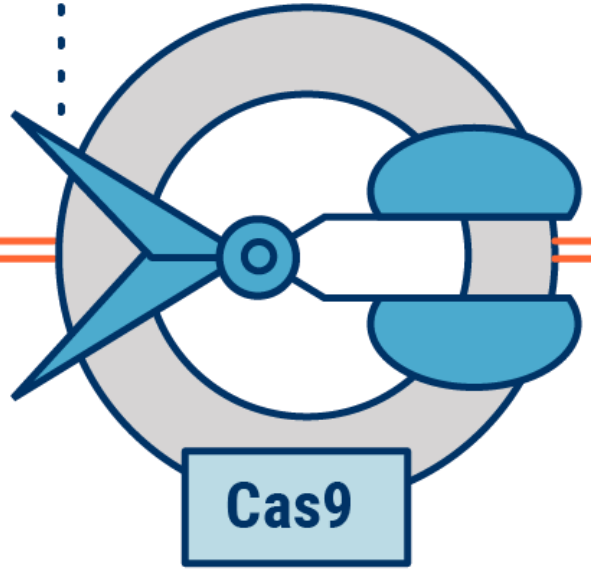


Understanding How The CRISPR Gene-editing Process Works

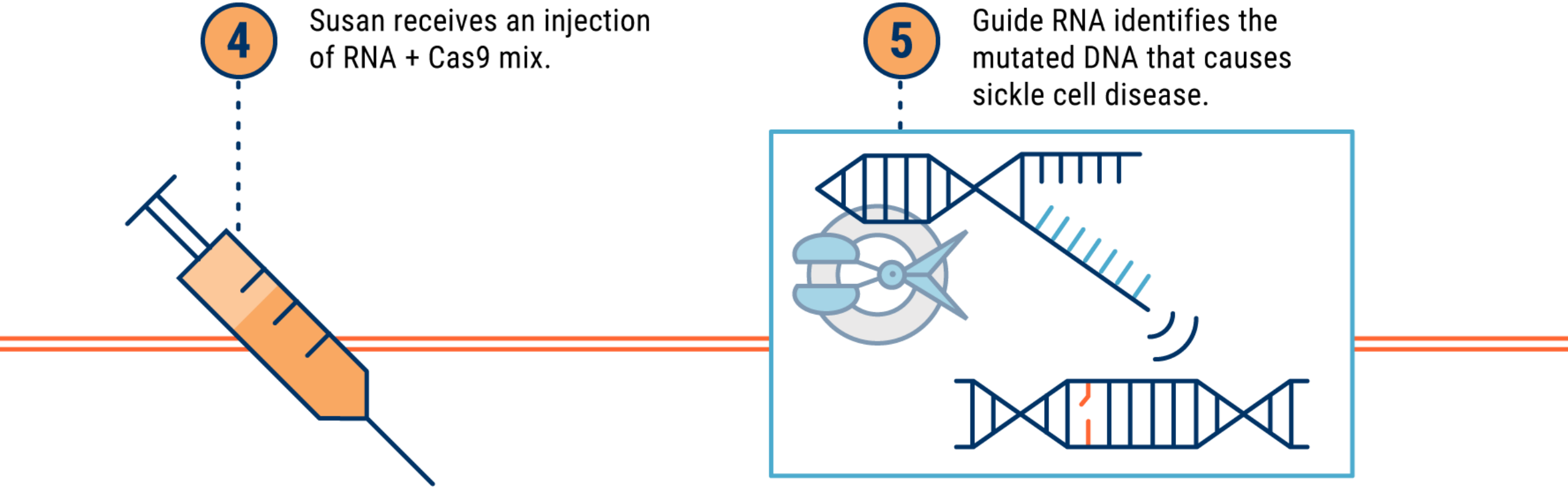
2 In the lab, scientists create a strand of **GUIDE RNA** that matches the mutated DNA sequence.



3 **Cas9,** AKA molecular scissors, is added to the RNA mix.

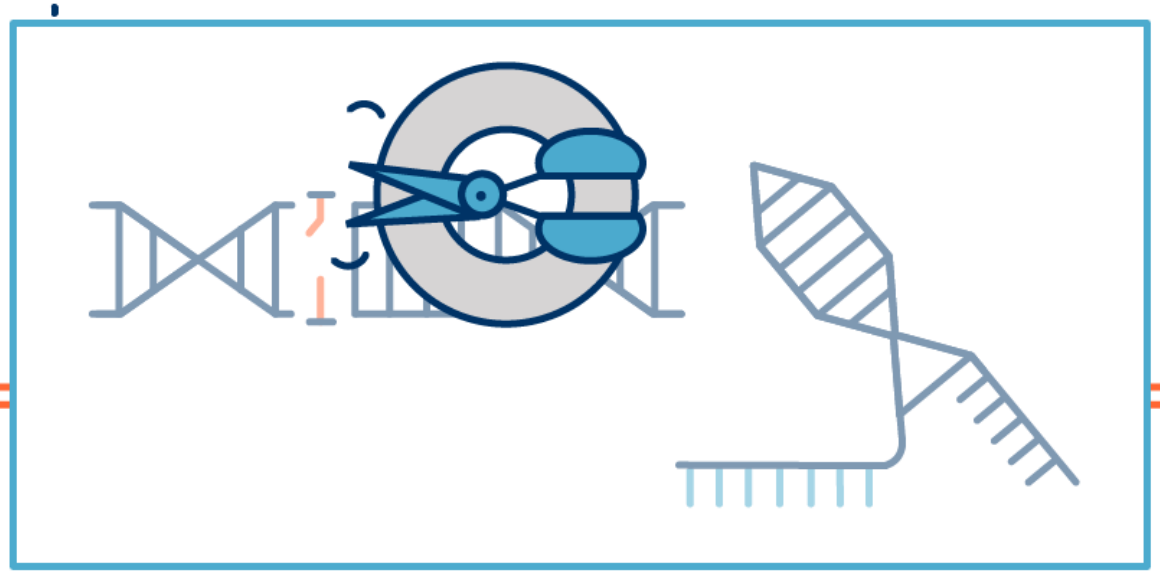


Understanding How The CRISPR Gene-editing Process Works



Understanding How The CRISPR Gene-editing Process Works

6 Cas9 cuts out the affected sequence.

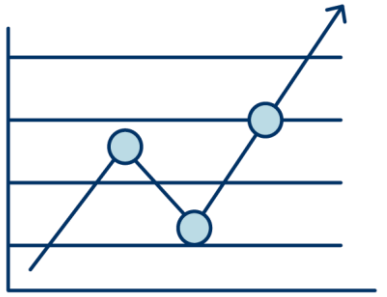


7 Scientists insert a healthy DNA sequence to replace the clipped sequence.

Understanding How The CRISPR Gene-editing Process Works

KEY STARTUPS

More CRISPR startups are on the horizon



TOP 3 PUBLIC COMPANIES

Incumbents begin CRISPR clinical trials in 2018

editas MEDICINE

Funding: $163M

Select investors: Google Ventures, Khosla Ventures, Third Rock Ventures

Clinical trial focus: Genetic eye disease – Leber Congenital Amaurosis type 10 – phase 1

CRISPR THERAPEUTICS

Funding: $162M

Select investors: Versant Ventures, Celgene, Bayer

Clinical trial focus: Beta-thalassemia (Europe) & sickle cell disease (US) phase 1/2 trials

Intellia THERAPEUTICS

Funding: $85M

Select investors: Atlas Venture, Novartis Venture Funds, OrbiMed Advisors

Clinical trial focus: Transthyretin Amyloidosis (Pre-clinical)

"… it might be better to describe CRISPR not as scissors but as a Swiss army knife, a tool with a panoply of functionalities that all stem from the action of a single molecular machine."

Jennifer Doudna, PhD

A Crack in Creation: Gene Editing and the Unthinkable Power to Control Evolution

NEW APPLICATION: AT-HOME DIAGNOSTICS KIT

MammothDiagnostics

Disclosed Funding: $120K

Select Investors: NFX Guild

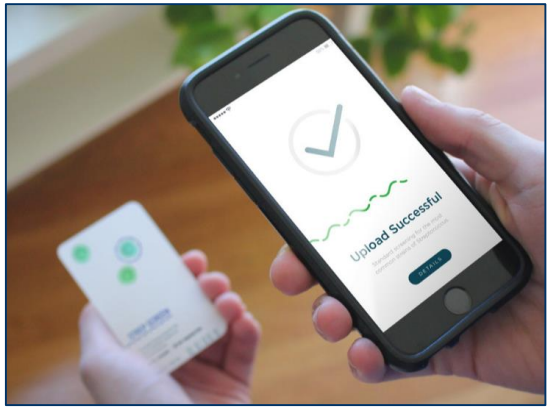
Mammoth Diagnostics provides a CRISPR-based platform for disease detection.

It uses a simple paper-based test in which a liquid sample (e.g. saliva) is applied and subsequently, a color change becomes visible. A smartphone app can be used to upload that data to the cloud, in which an analysis is delivered in 30 minutes.

Key team members:

Trevor Martin
Co-Founder, CEO

Jennifer Doudna
Co-Founder, Chair of Scientific Advisory Board



01 Test sample.

Add a fluid sample to the credit card-sized strip, and wait for the panel to change colors.

02 Upload image.

Take a picture of the strip through the Mammoth companion app for analysis.

03 Receive results.

Test results will be returned through the companion app within 30 minutes from when the sample hits the strip.

Images: *Mammoth Diagnostics*

PRECISION GENETIC MEDICINE: BASE-EDITING

Beam

Disclosed Funding:

$87M

Select Investors:

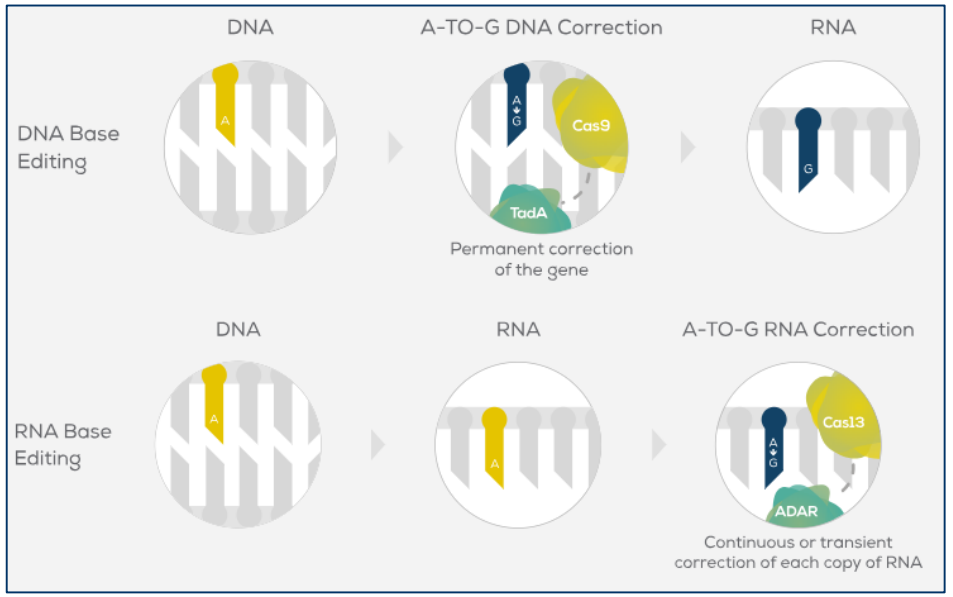
ARCH Venture Partners,
F-Prime Capital

Beam Therapeutics develops therapeutics using a more precise method of CRISPR called base-editing. By tethering a modified CRISPR enzyme and an editing enzyme together, this technology allows editing to occur without cutting into the DNA at all.

Key team members:

David Liu, PhD
Co-Founder

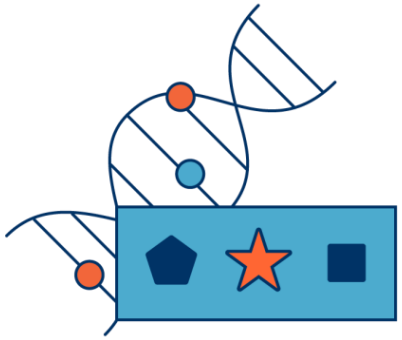
Feng Zhang, PhD
Co-Founder, Board Member



Images: *Beam Therapeutics*

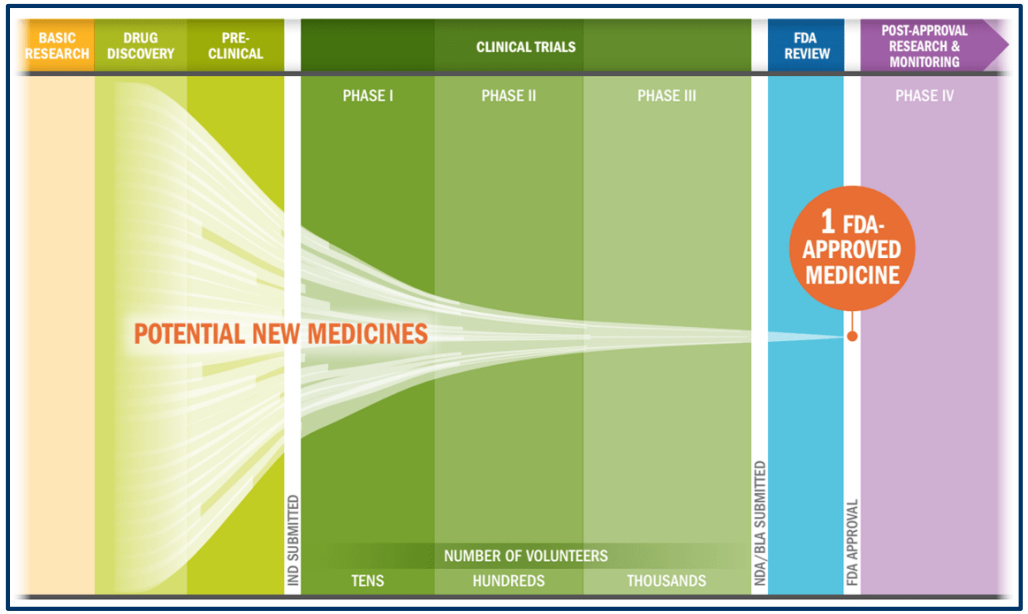
APPLICATIONS & LIMITATIONS

CRISPR will spur cross-industry innovation



Drug discovery process could be transformed

Current process



With CRISPR

- Faster
- Cheaper
- Precision medicine

CRISPR could transform food supply & quality

April 2016

1st CRISPR-edited organism to bypass USDA

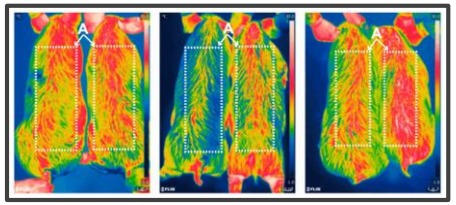
The white button mushroom, edited to not brown as quickly, bypassed USDA regulations.

Gene-edited CRISPR mushroom escapes US regulation
4/14/2016 nature

Sept 2017

Another USDA approval

Yield10 Bioscience's CRISPR plant *Camelina sativa* with enhanced omega-3 oil bypasses regulations.



October 2017

Leaner livestock

Scientists at the Chinese Academy of Sciences in Beijing used CRISPR to genetically engineer pig meat with 24% less body fat

Jan 2018

CRISPR saving chocolates

Innovative Genomics Institute at Berkeley is working with candy company Mars to genetically engineer cacao plants

MARS

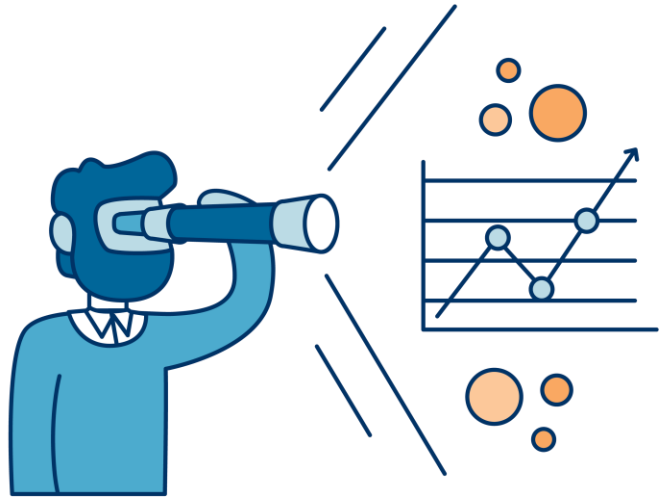
LIMITATIONS

… Yet, there are still some hurdles ahead

1	Off-target activity	Different cutting enzymes (molecular scissors)
2	Mosaic generation	Edit stem cells in egg or sperm cells
3	Immune system complications	Use a different Cas protein or ex-vivo therapies to bypass immune system

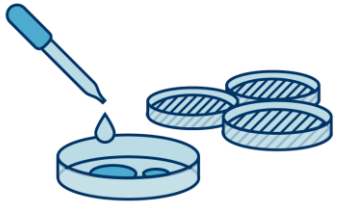
CONTROVERSIES & FUTURE OF CRISPR

What lies ahead for CRISPR

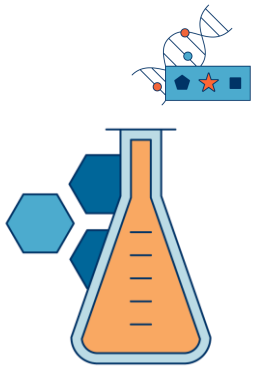


CONTROVERSIES LIE AHEAD

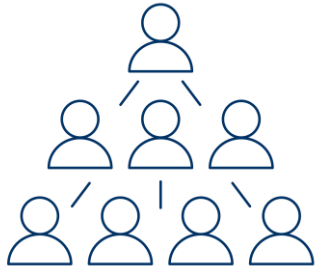
CRISPR applications present ethical concerns



Designing-your-own-baby



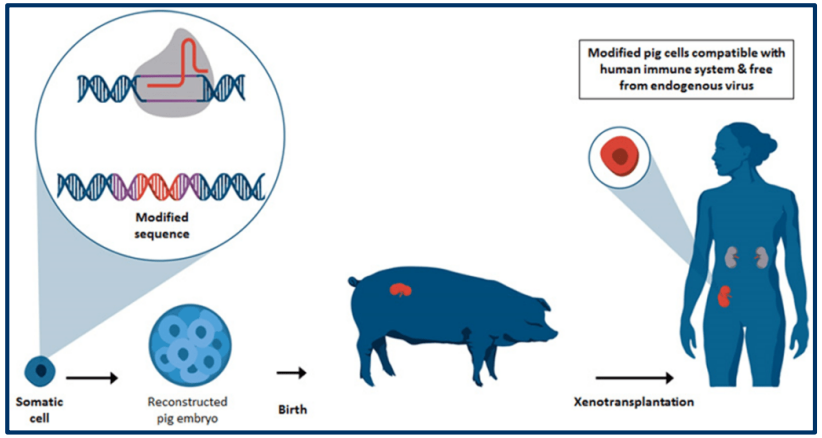
Bringing back extinct species



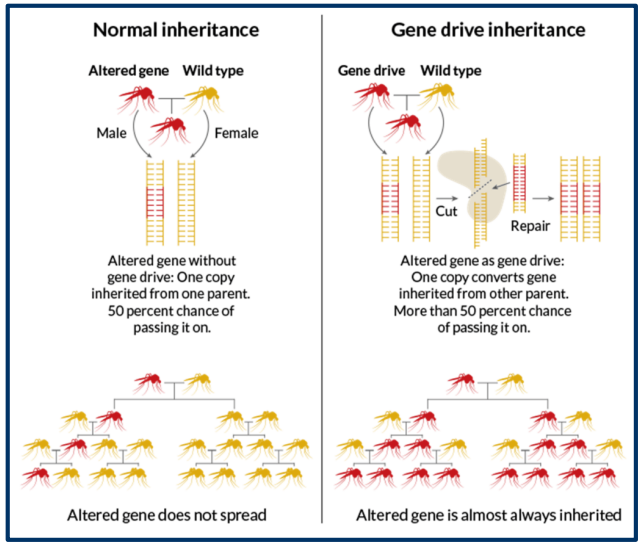
Germline modifications

Biohacking

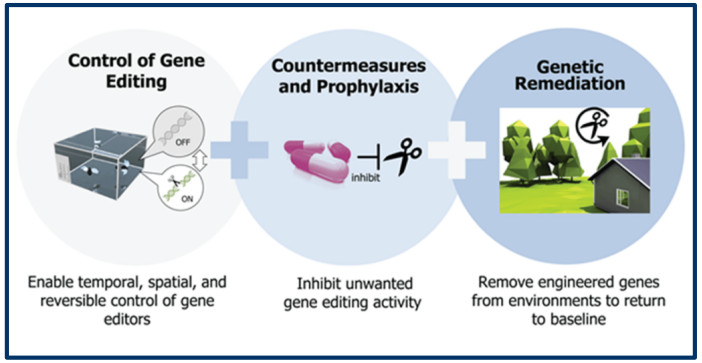
Future applications of gene-editing



Xenotransplantation



Gene drive



Genome editing as a weapon of mass destruction?

Images: *eGenesis; E. OTWELL AND M. TELFER, ScienceNews.org; DARPA*

Questions?

Twitter: @ja_lee2

jlee@cbinsights.com

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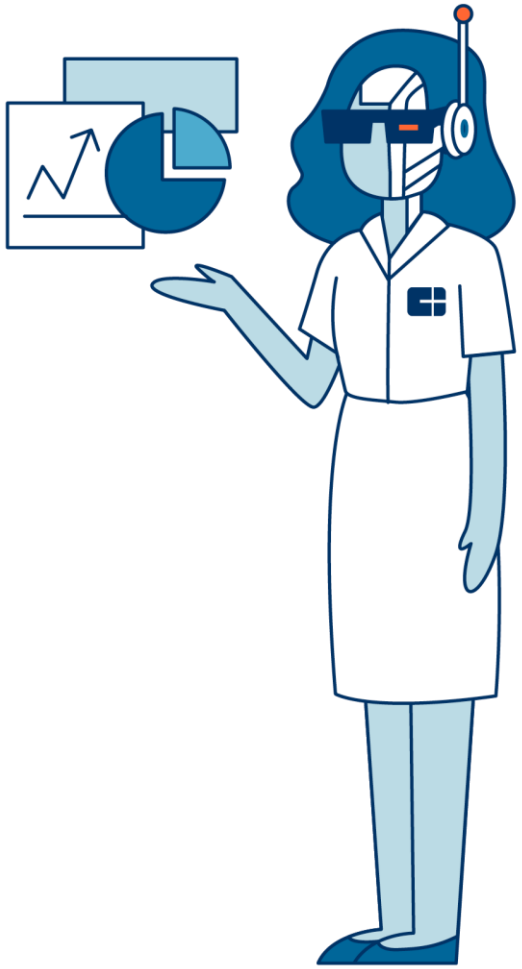
The CB Insights platform has the underlying data included in this report



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