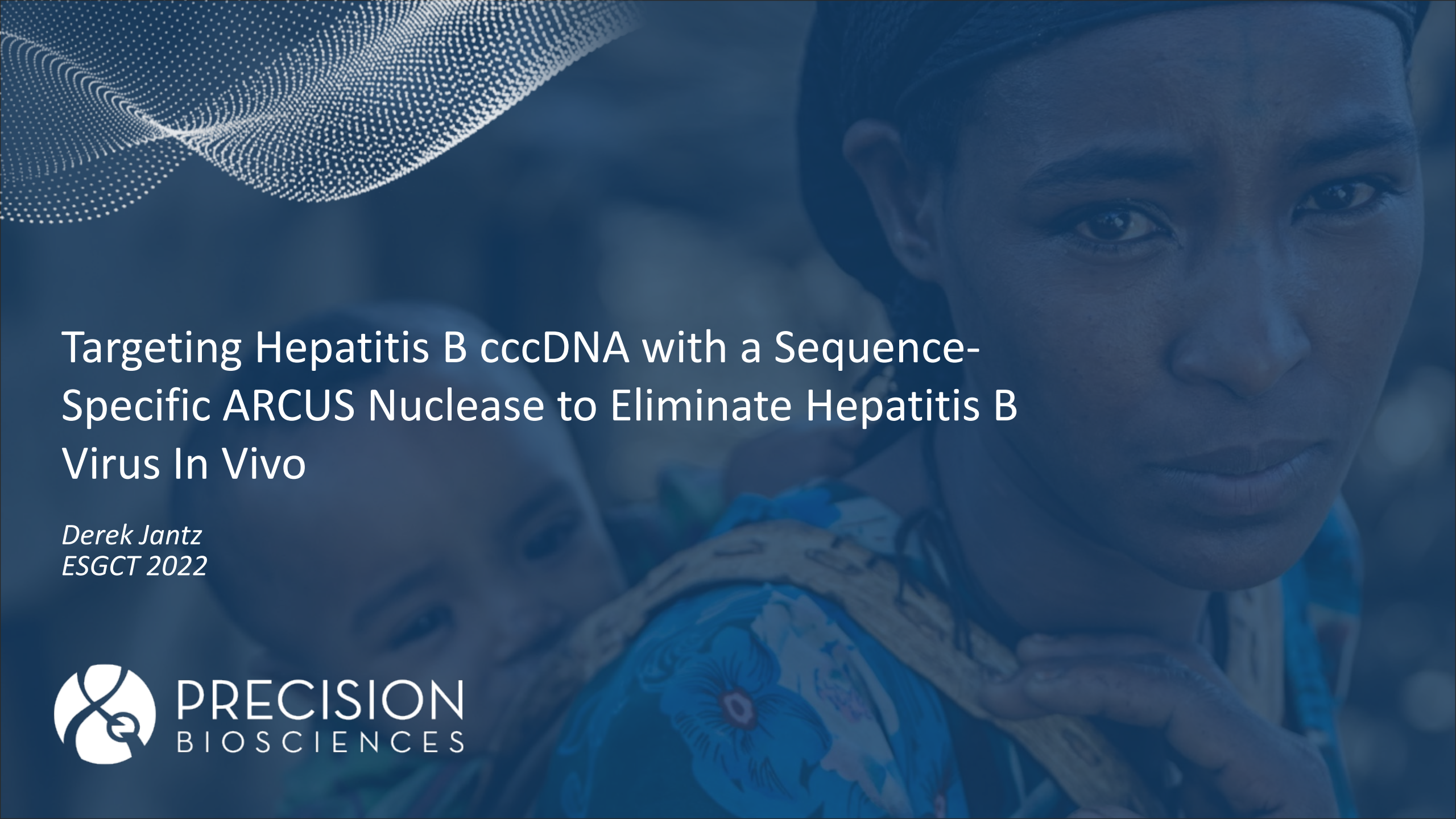


Targeting Hepatitis B cccDNA with a Sequence-Specific ARCUS Nuclease to Eliminate Hepatitis B Virus In Vivo

Derek Jantz
ESGCT 2022

PRECISION BIOSCIENCES

Forward-Looking Statements

This presentation contains forward-looking statements, as may any related presentations, within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this herein and in any related presentation that do not relate to matters of historical fact should be considered forward-looking statements, including, without limitation, statements regarding the goal of durable antigen loss and functional cure for chronic hepatitis B, clinical and regulatory development and expected efficacy and therapeutic benefit of our platform and product candidates, benefits of ARCUS and potential expansion and development using ARCUS, expectations about our operational initiatives and business strategy, achieving key milestones and additional collaborations, and expectations regarding our liquidity and ability to fund operating expenses and capital expenditures requirements. In some cases, you can identify forward-looking statements by terms such as “aim,” “anticipate,” “approach,” “believe,” “contemplate,” “could,” “estimate,” “expect,” “goal,” “intend,” “look,” “may,” “mission,” “plan,” “possible,” “potential,” “predict,” “project,” “promise,” “should,” “target,” “will,” “would,” or the negative thereof and similar words and expressions.

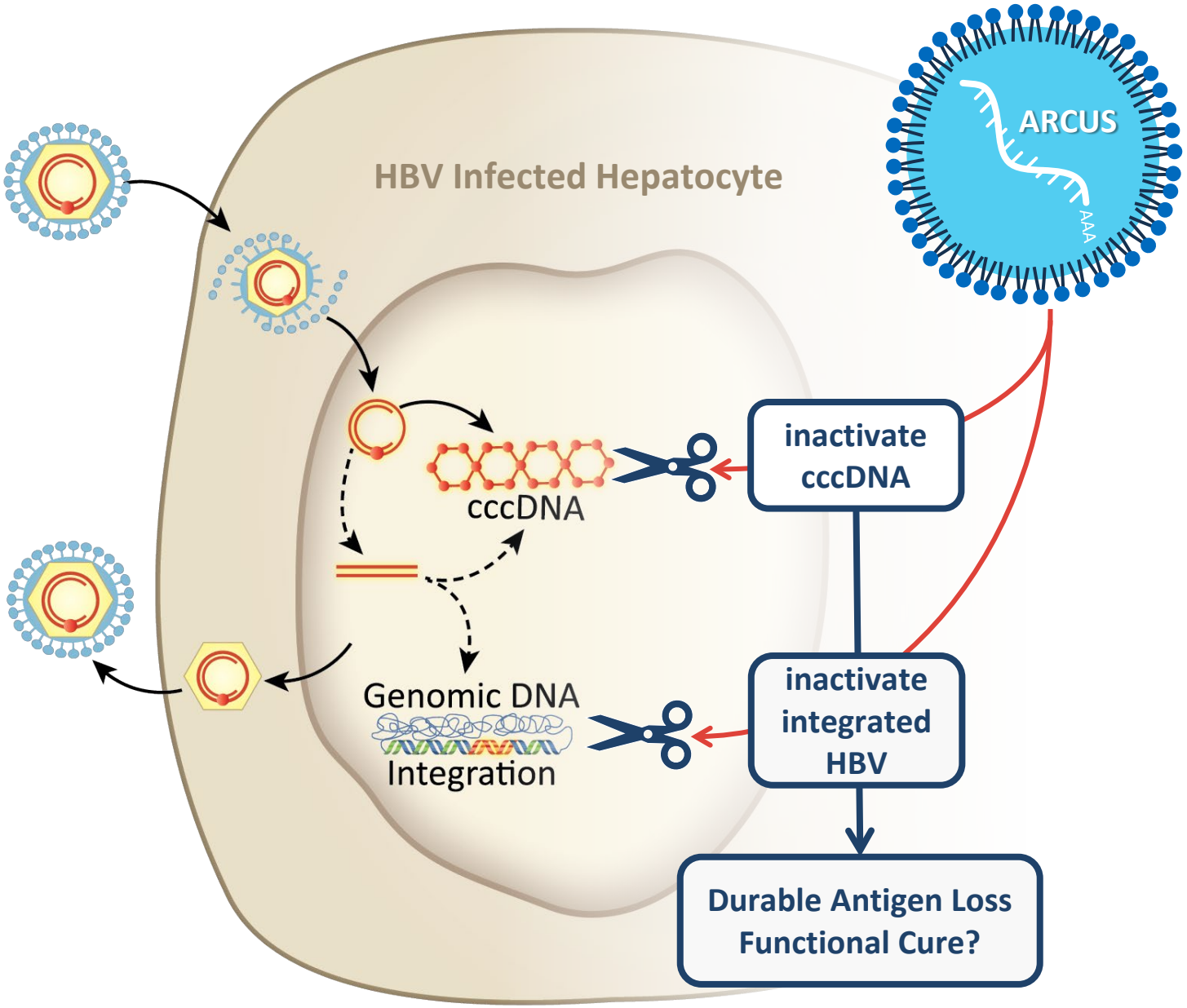
Forward-looking statements are based on management’s current expectations, beliefs and assumptions and on information currently available to us. Such statements are subject to a number of known and unknown risks, uncertainties and assumptions, and actual results may differ materially from those expressed or implied in the forward-looking statements due to various important factors, including, but not limited to: our ability to become profitable; our ability to procure sufficient funding and requirements under our current debt instruments and effects of restrictions thereunder; risks associated with raising additional capital; our operating expenses and our ability to predict what those expenses will be; our limited operating history; the success of our programs and product candidates in which we expend our resources; our limited ability or inability to assess the safety and efficacy of our product candidates; our dependence on our ARCUS technology; the initiation, cost, timing, progress, achievement of milestones and results of research and development activities, preclinical studies and clinical trials; public perception about genome editing technology and its applications; competition in the genome editing, biopharmaceutical, and biotechnology fields; our or our collaborators’ ability to identify, develop and commercialize product candidates; pending and potential liability lawsuits and penalties against us or our collaborators related to our technology and our product candidates; the U.S. and foreign regulatory landscape applicable to our and our collaborators’ development of product candidates; our or our collaborators’ ability to obtain and maintain regulatory approval of our product candidates, and any related restrictions, limitations and/or warnings in the label of an approved product candidate; our or our collaborators’ ability to advance product candidates into, and successfully design, implement and complete, clinical or field trials; potential manufacturing problems associated with the development or commercialization of any of our product candidates; our ability to obtain an adequate supply of T cells from qualified donors; our ability to achieve our anticipated operating efficiencies at our manufacturing facility; delays or difficulties in our and our collaborators’ ability to enroll patients; changes in interim “top-line” and initial data that we announce or publish; if our product candidates do not work as intended or cause undesirable side effects; risks associated with applicable healthcare, data protection, privacy and security regulations and our compliance therewith; the rate and degree of market acceptance of any of our product candidates; the success of our existing collaboration agreements, and our ability to enter into new collaboration arrangements; our current and future relationships with and reliance on third parties including suppliers and manufacturers; our ability to obtain and maintain intellectual property protection for our technology and any of our product candidates; potential litigation relating to infringement or misappropriation of intellectual property rights; our ability to effectively manage the growth of our operations; our ability to attract, retain, and motivate key executives and personnel; market and economic conditions; effects of system failures and security breaches; effects of natural and manmade disasters, public health emergencies and other natural catastrophic events; effects of COVID-19 pandemic and variants thereof, or any pandemic, epidemic or outbreak of an infectious disease; insurance expenses and exposure to uninsured liabilities; effects of tax rules; risks related to ownership of our common stock and other important factors discussed under the caption “Risk Factors” in our Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2022, as any such factors may be updated from time to time in our other filings with the SEC, which are accessible on the SEC’s website at www.sec.gov and the Investors page of our website under SEC Filings at investor.precisionbiosciences.com.

Disclosures

- I am an employee of Precision BioSciences

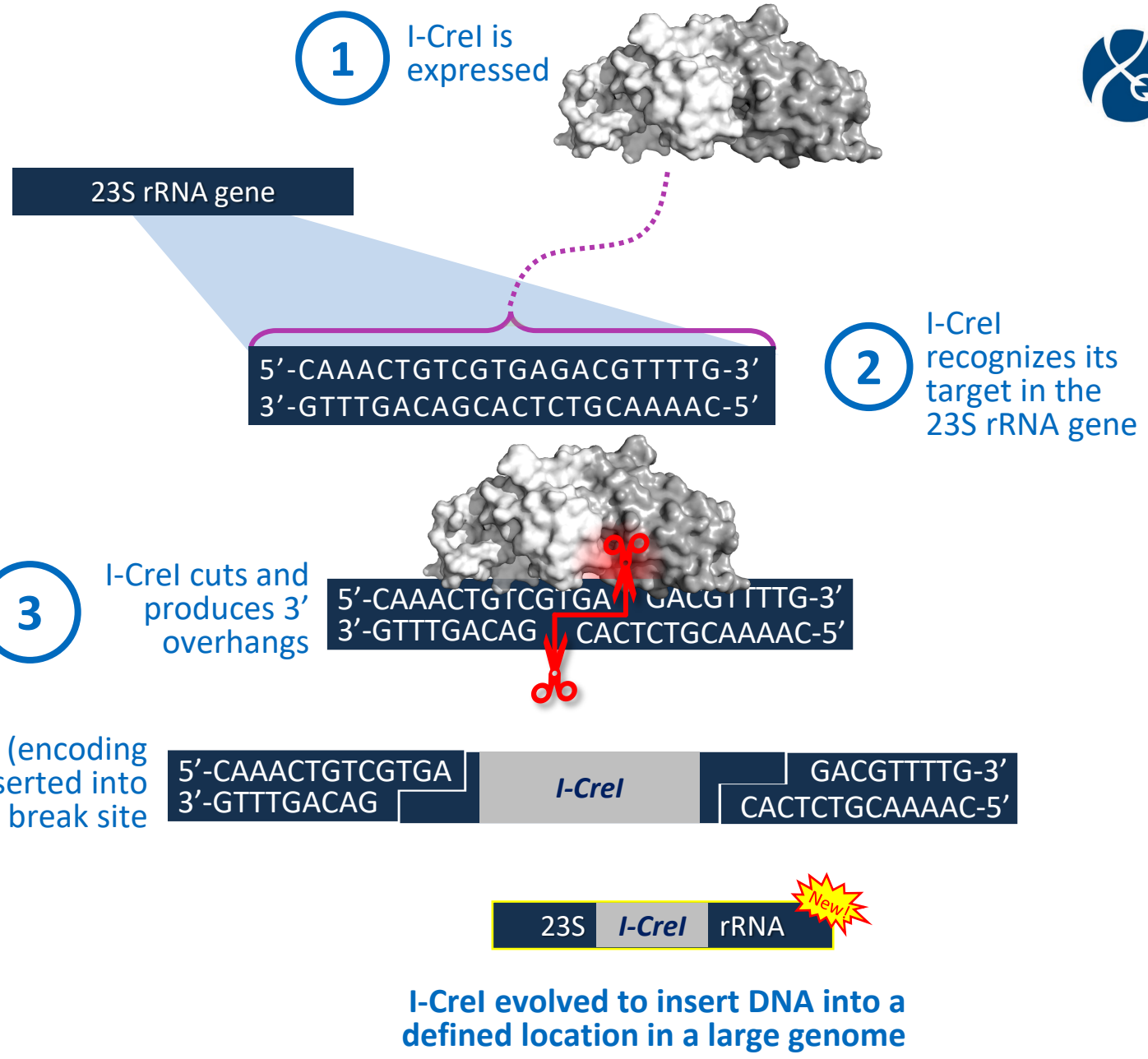
Chronic Hepatitis B affects ~250 million people

cccDNA and integrated HBV have complicated efforts to cure the disease



ARCUS is derived from **I-CreI**, a homing endonuclease from algae.

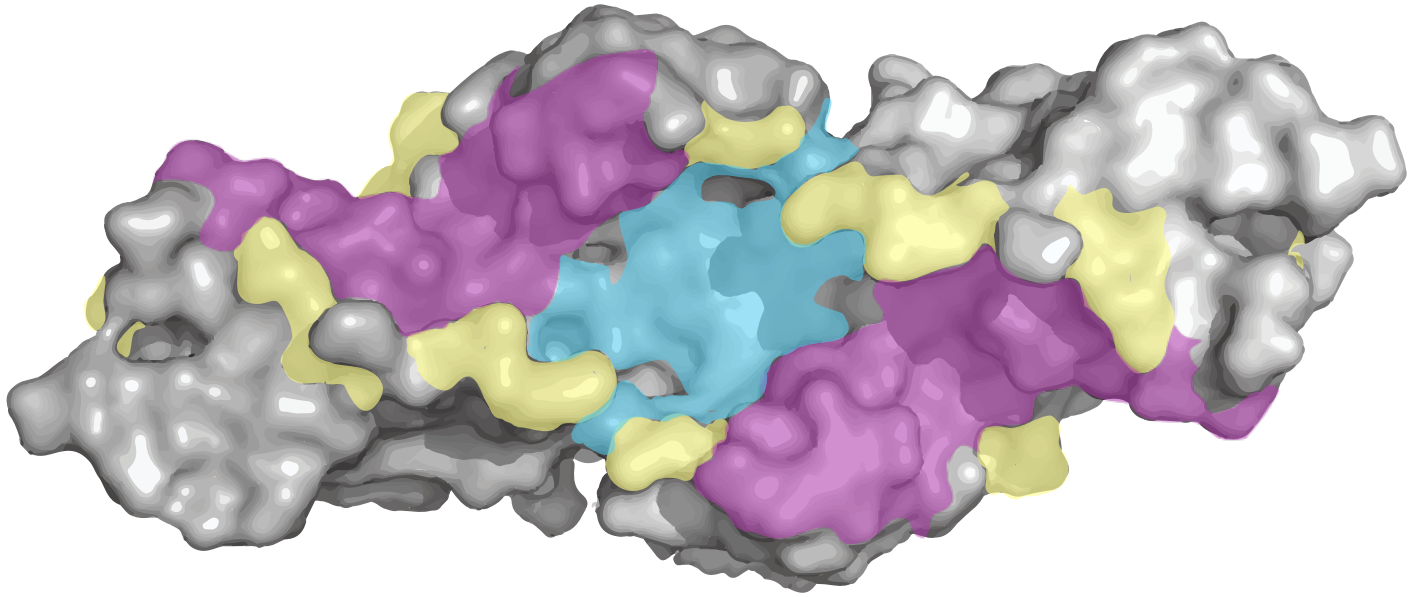
- High Specificity
- Small Size
- High Rate of HDR



I-CreI evolved to insert DNA into a defined location in a large genome

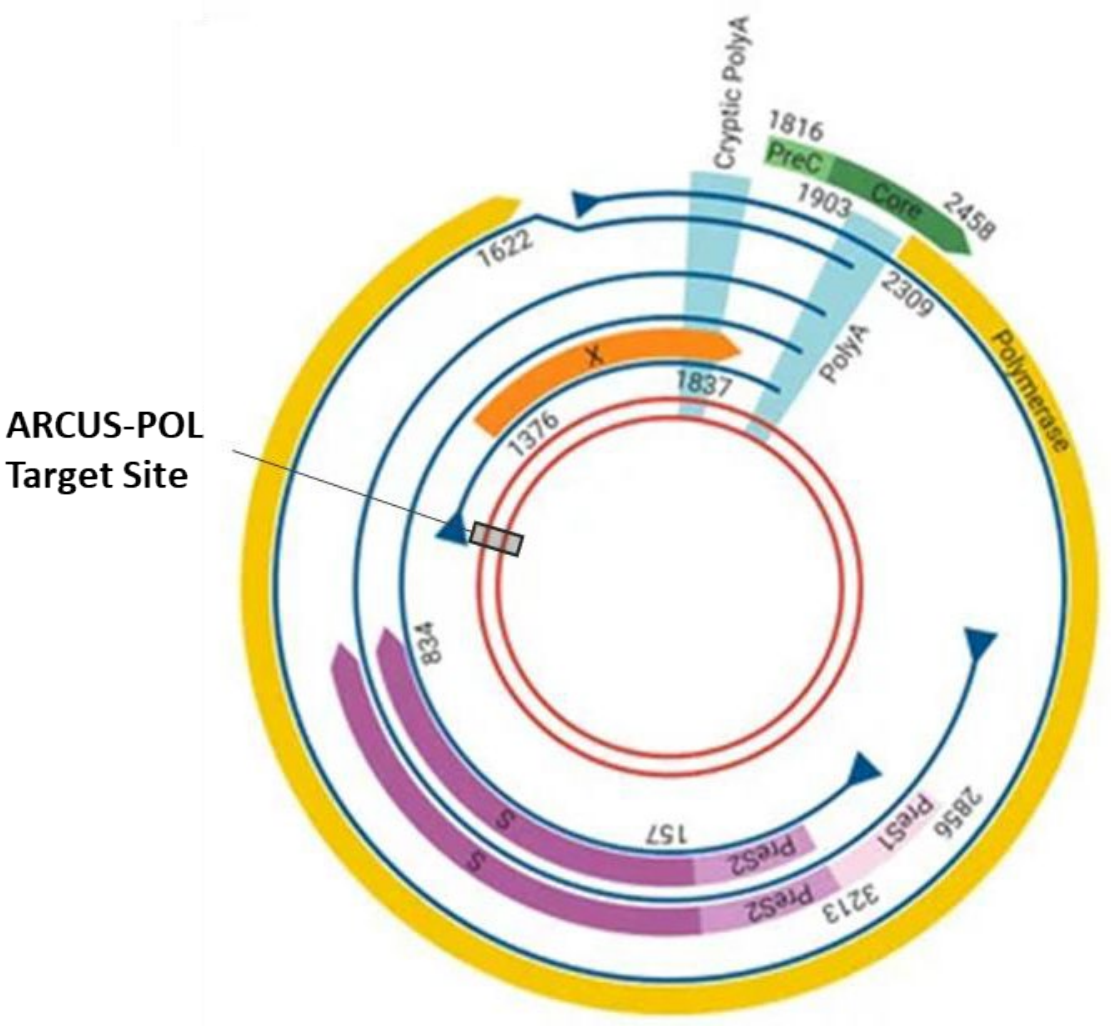
Creating and Optimizing ARCUS Nucleases

The DNA-binding surface of I-CreI must be extensively re-engineered to produce each new ARCUS nuclease

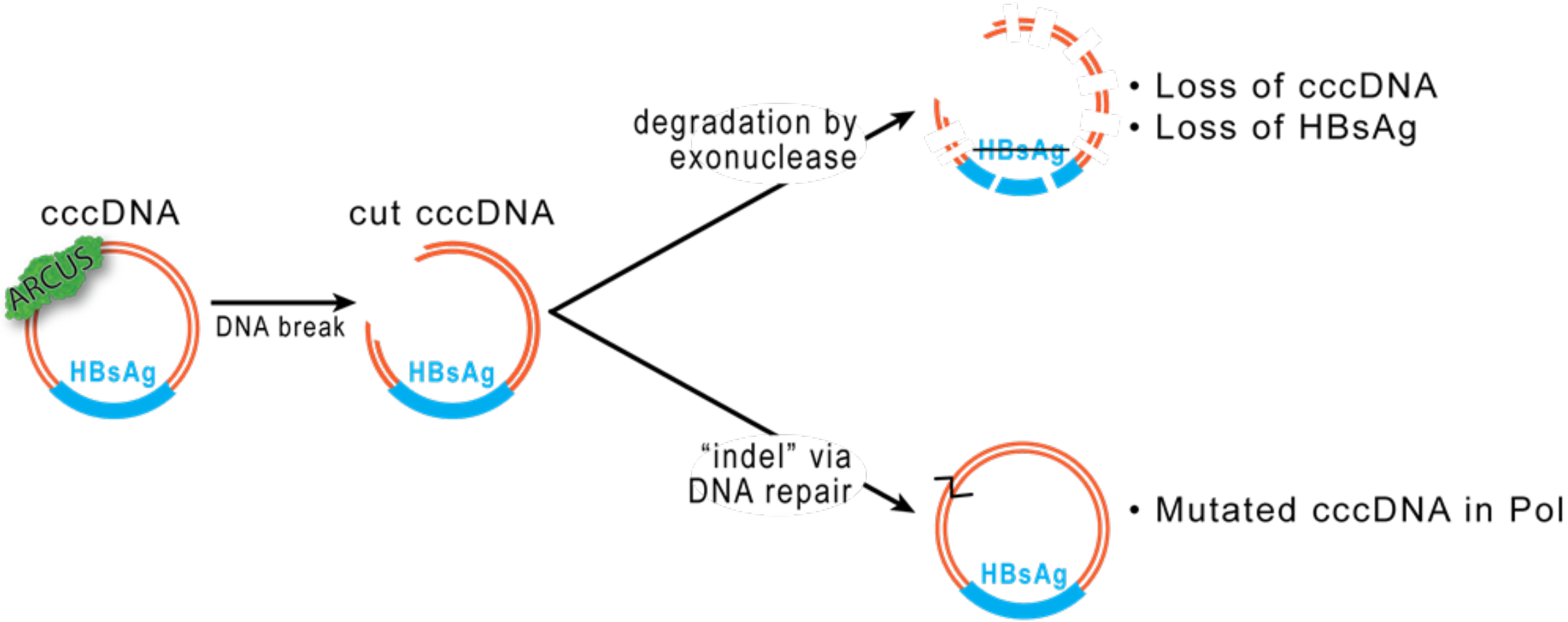


Engineering ARCUS to Recognize HBV

An ARCUS enzyme was designed to cut a conserved sequence in the HBV polymerase (POL) gene



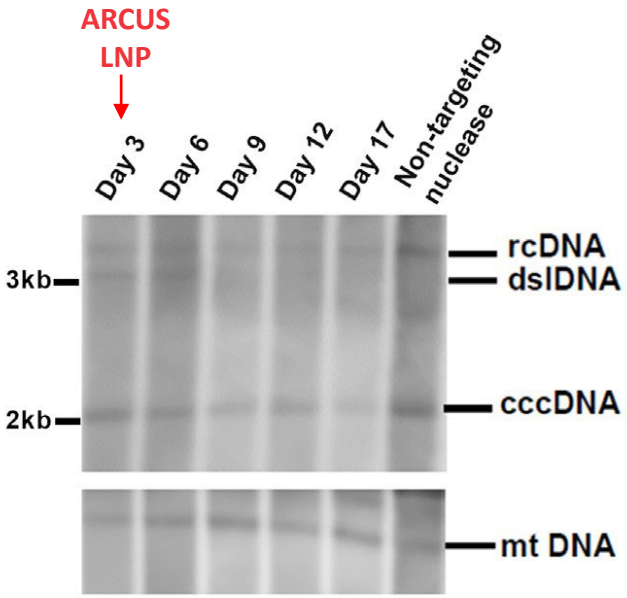
cccDNA Fate after ARCUS Cleavage

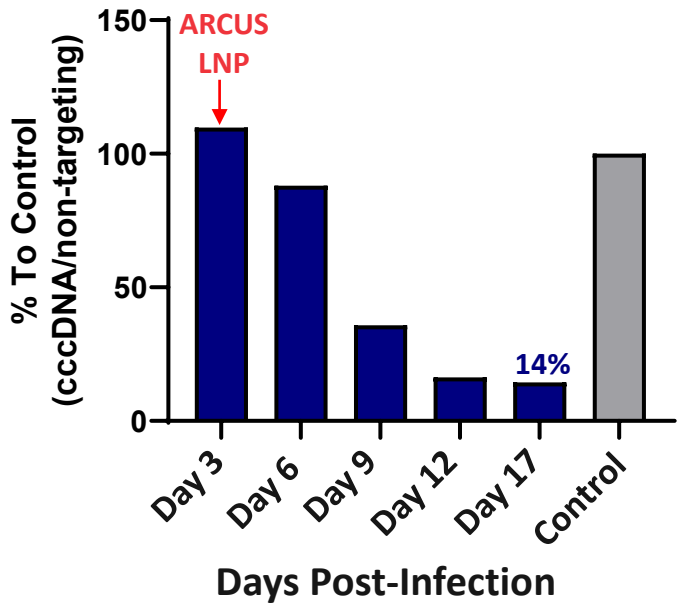


ARCUS Activity in HBV-Infected Primary Human Hepatocytes

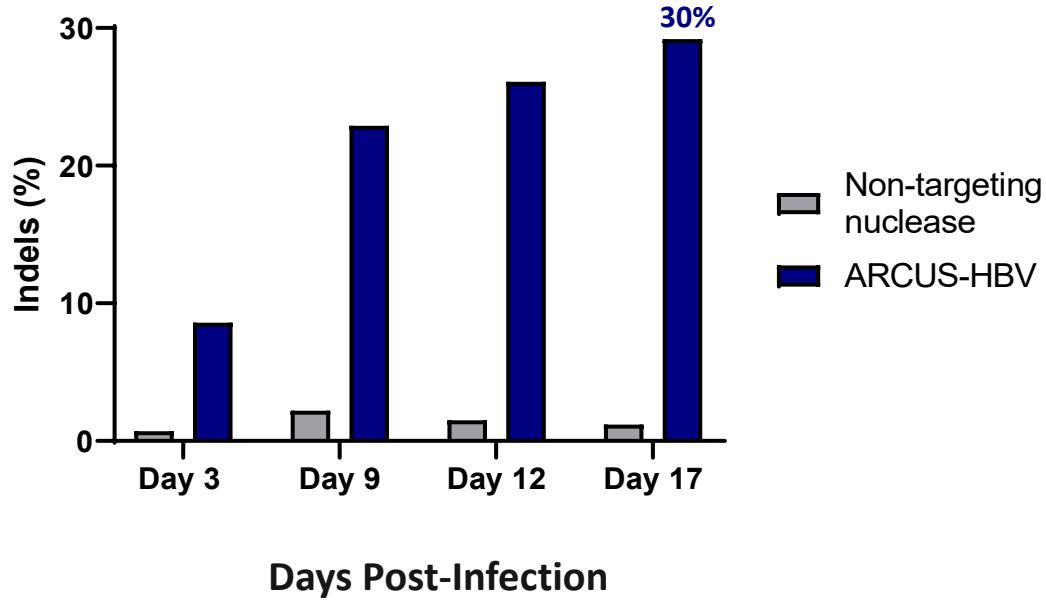
- In HBV-infected primary human hepatocytes (PHH), ARCUS delivered via LNP reduced cccDNA by 86% and created indel mutations in 30% of the remaining cccDNA.

cccDNA Degradation





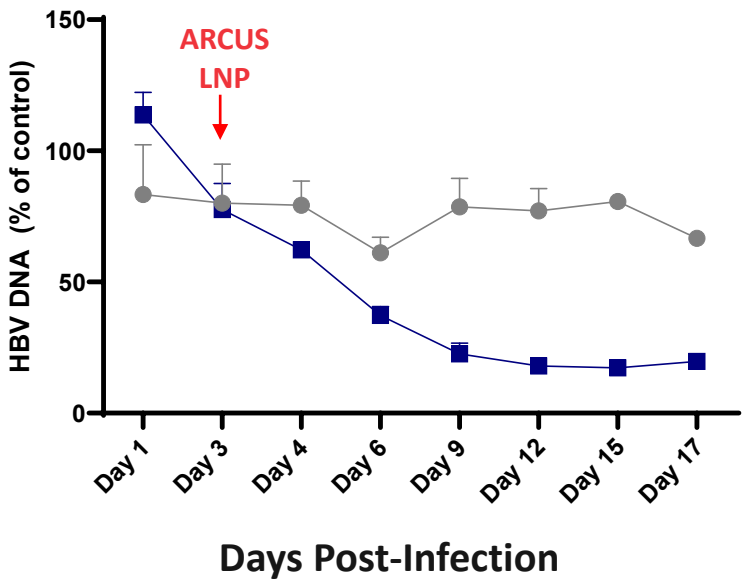
cccDNA Indels



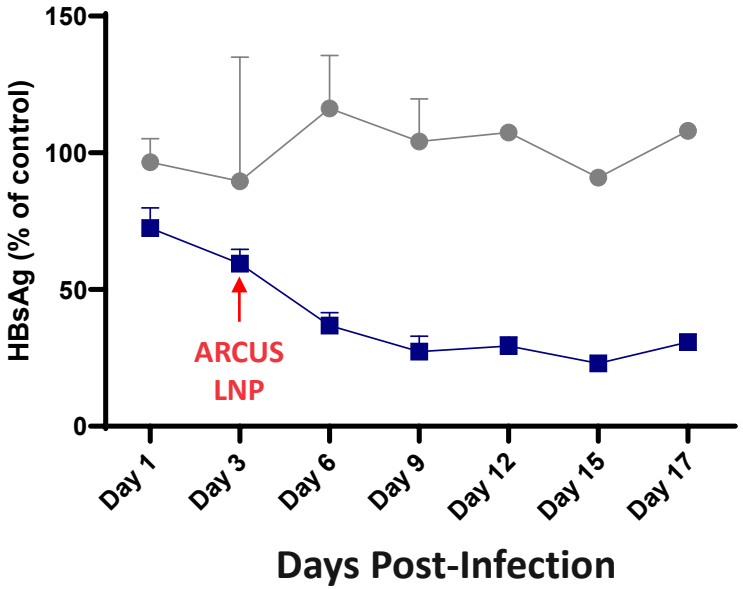
ARCUS Activity in HBV-Infected Primary Human Hepatocytes

- ARCUS treated cells demonstrated an 80% reduction in extracellular HBV DNA and a 77% reduction in secreted sAg with no change in albumin.

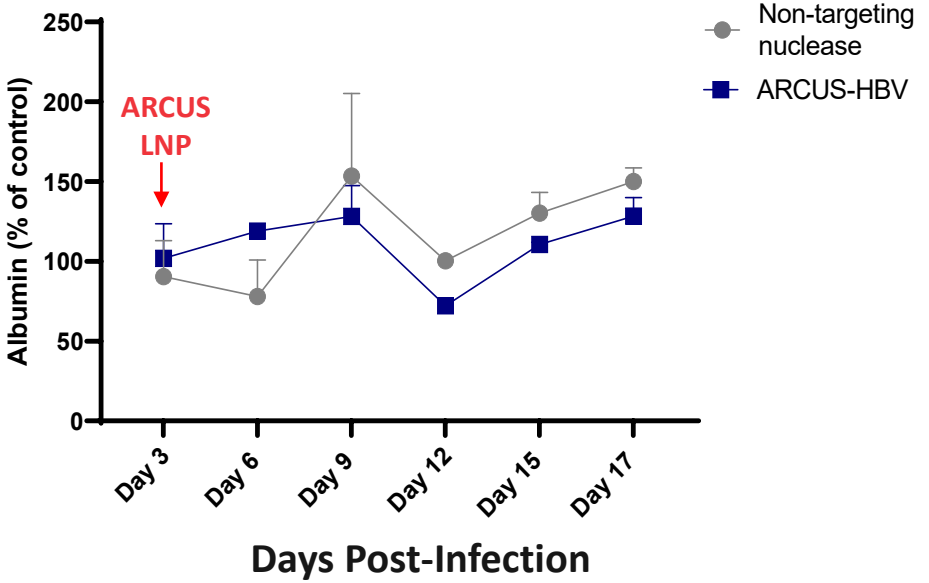
Extracellular HBV DNA



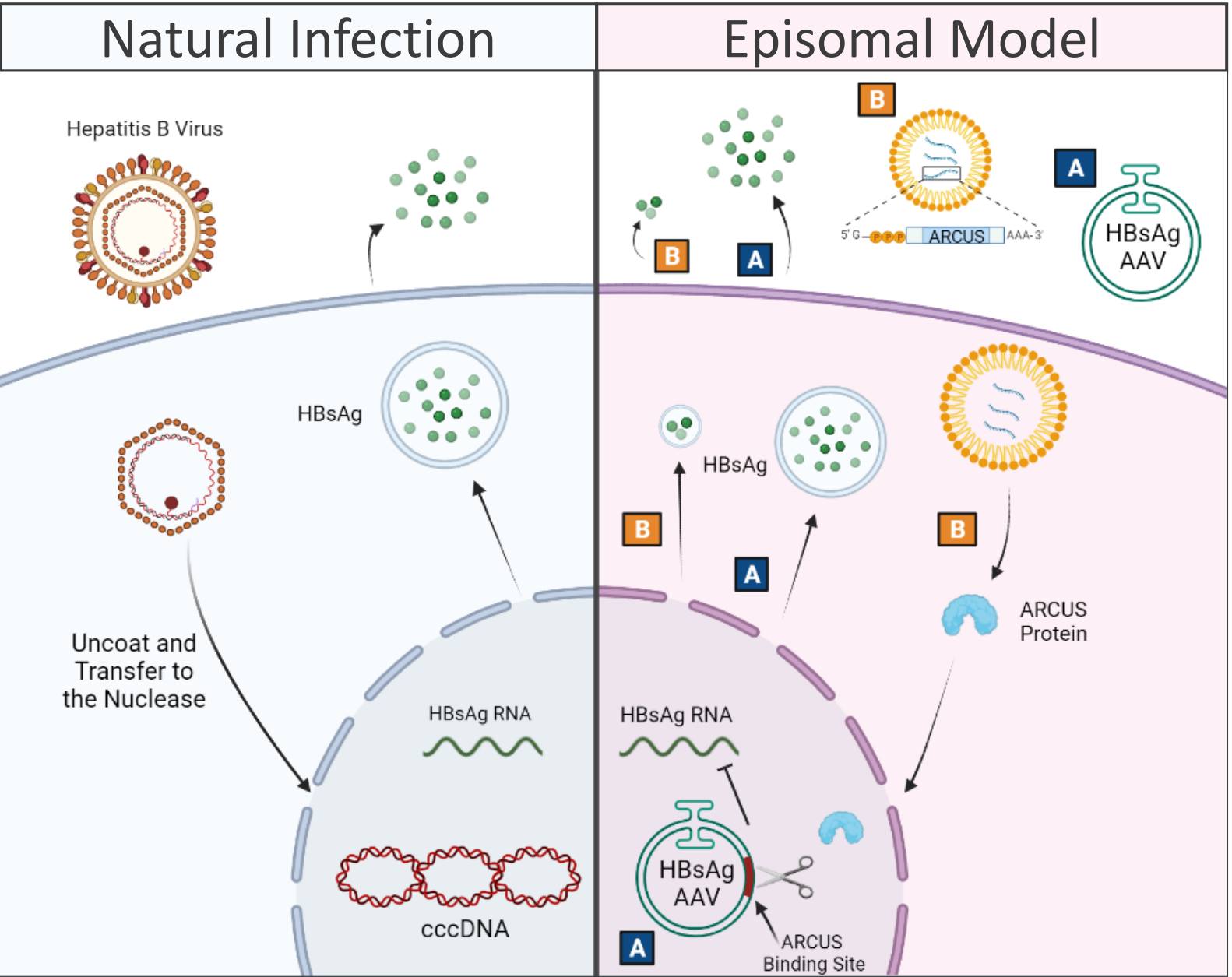
Extracellular HBsAg



Extracellular Albumin



HBV Episomal In Vivo Model



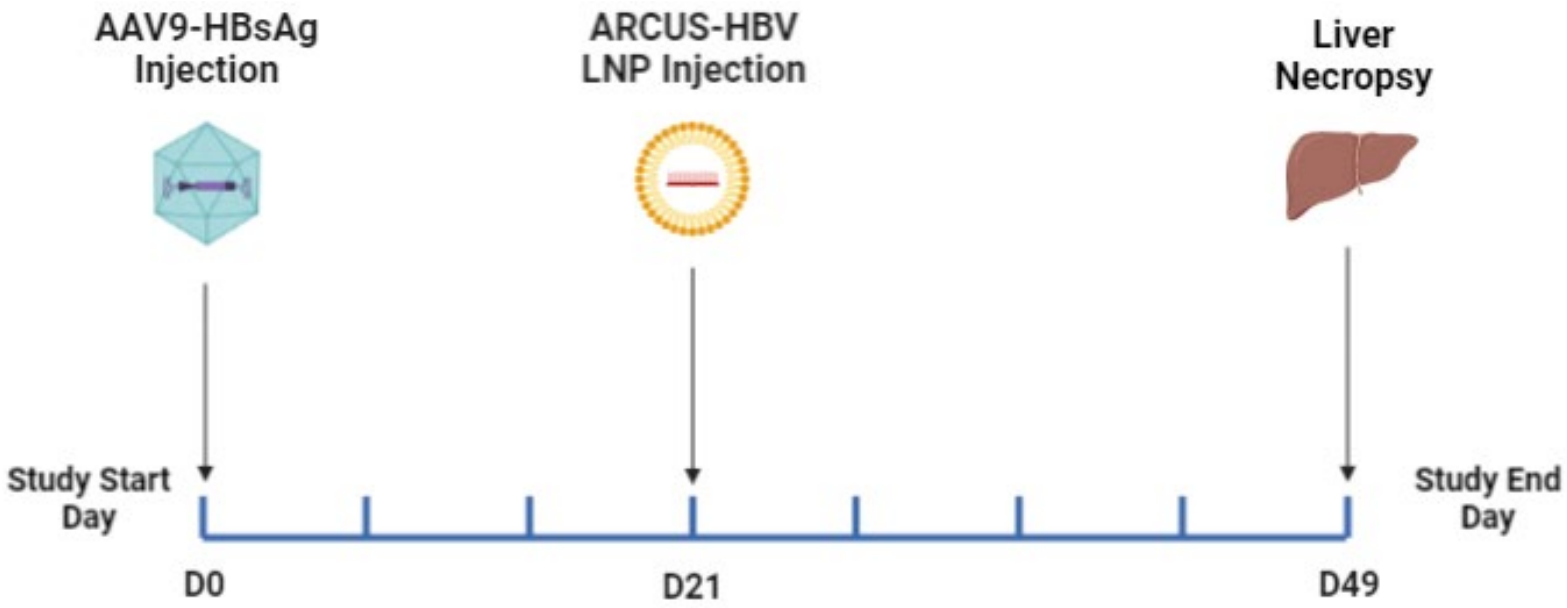
A

- AAV with a partial HBV sequence expressing HBsAg is administered and is present as the cccDNA surrogate.

B

- An HBV nuclease is subsequently delivered via a lipid nanoparticle (LNP) which can then cut the cccDNA surrogate, AAV-HBsAg.

Episomal Mouse Model Study Design

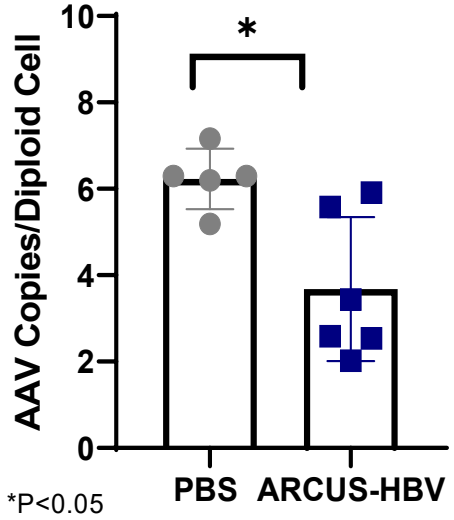


- **AAV8 HBsAg Dose:** 5e11vg
- **ARCUS LNP Dose:** 2 mg/kg
- Weekly blood draws for HBsAg

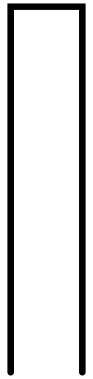
Episomal Mouse Model—Molecular Analyses

- The ARCUS-HBV nuclease significantly reduced AAV copies in the liver compared to the PBS control group.
- The remaining AAV had an average of 86% indels in the ARCUS-HBV treated group.
- The AAV degradation and indel formation resulting from ARCUS-HBV cutting resulted in a 96% sustained reduction in HBsAg from one week post ARCUS-HBV administration until necropsy at week 7.

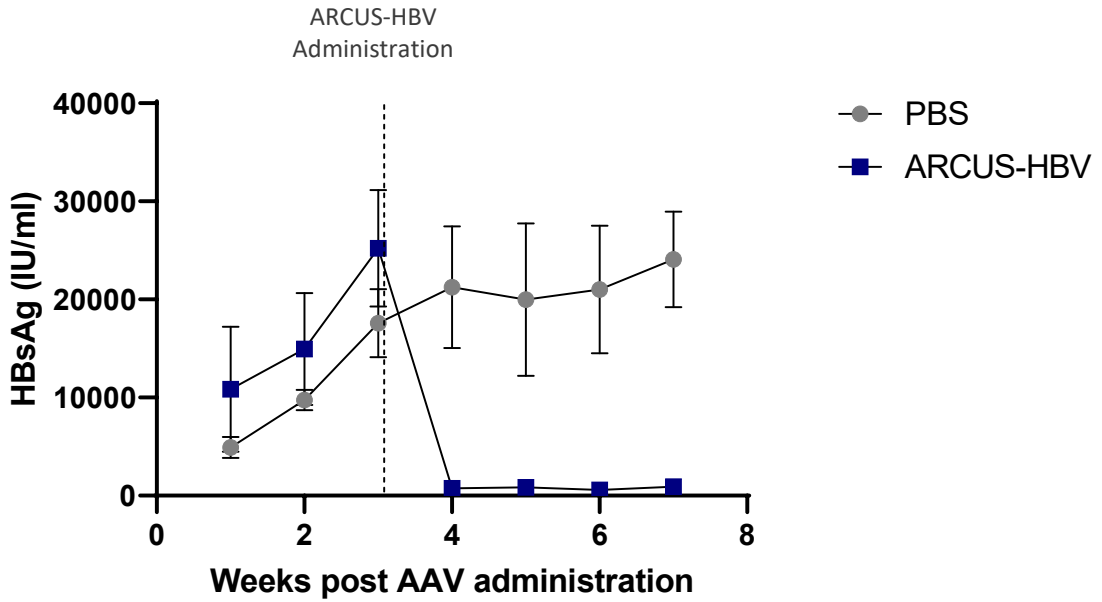
AAV Copy Number



AAV Indels



Secreted HBsAg

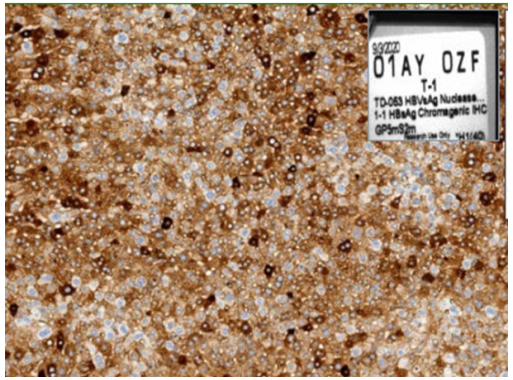
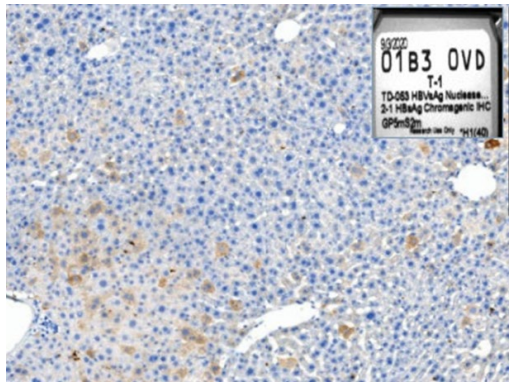
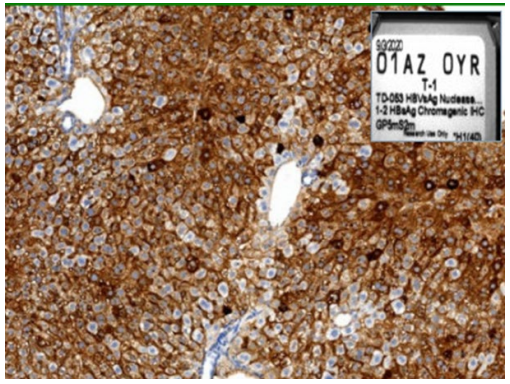
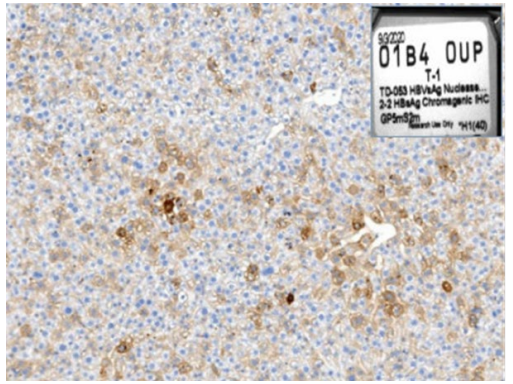


Episomal Mouse Study—Liver HBsAg Immunohistochemistry

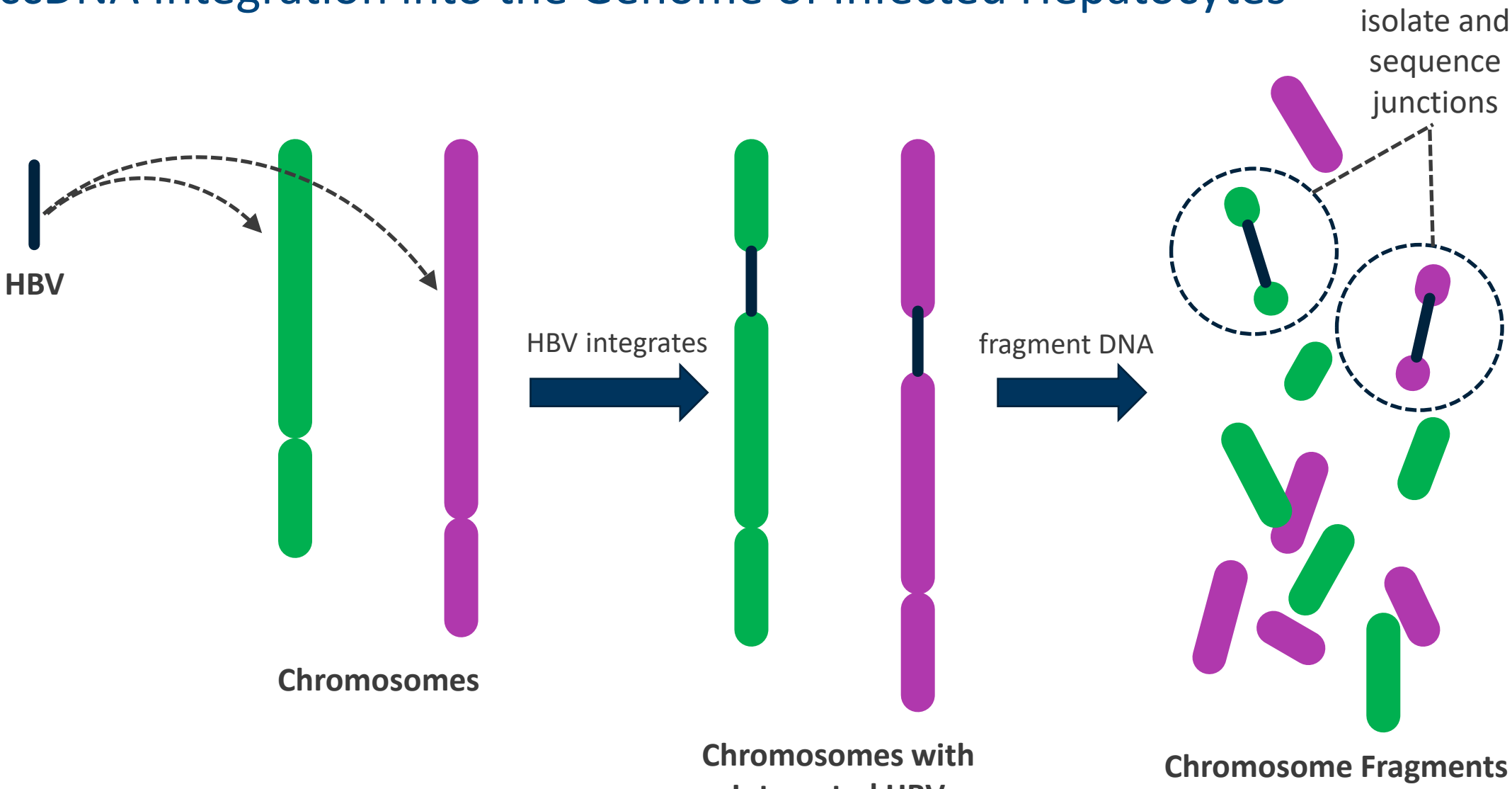
- Mice treated with ARCUS show a significant loss in HBsAg in the liver compared to untreated mice.

Blue = Nucleus

Brown = HBsAg

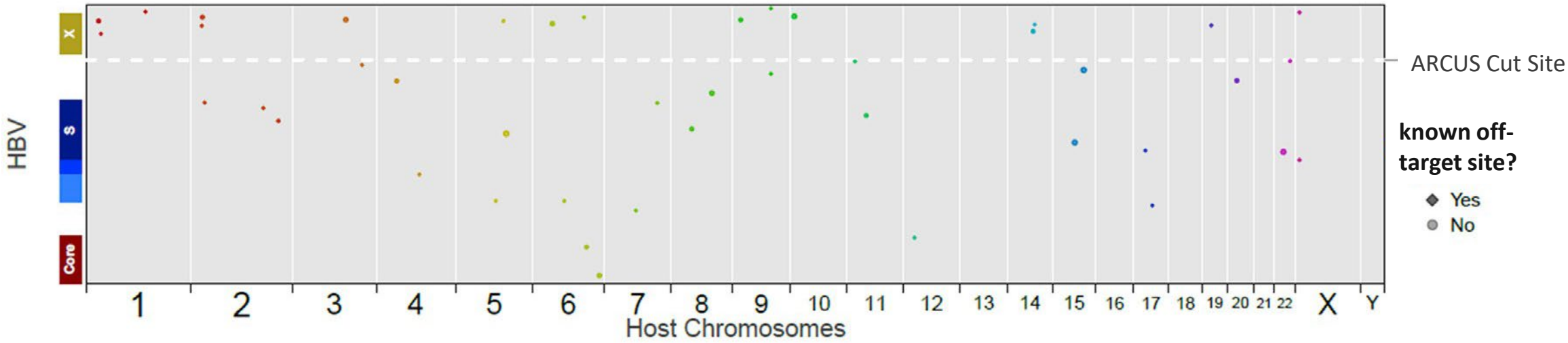
Group 1—No Nuclease	Group 2—ARCUS-HBV
	
	

cccDNA Integration into the Genome of Infected Hepatocytes

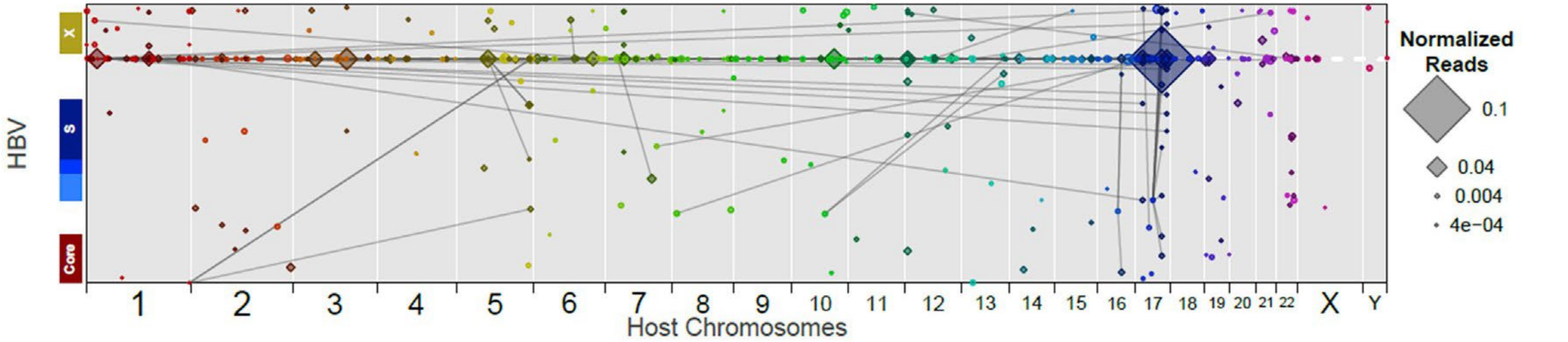


cccDNA Integration into the Genome of Infected Hepatocytes

Mock (HBV only)

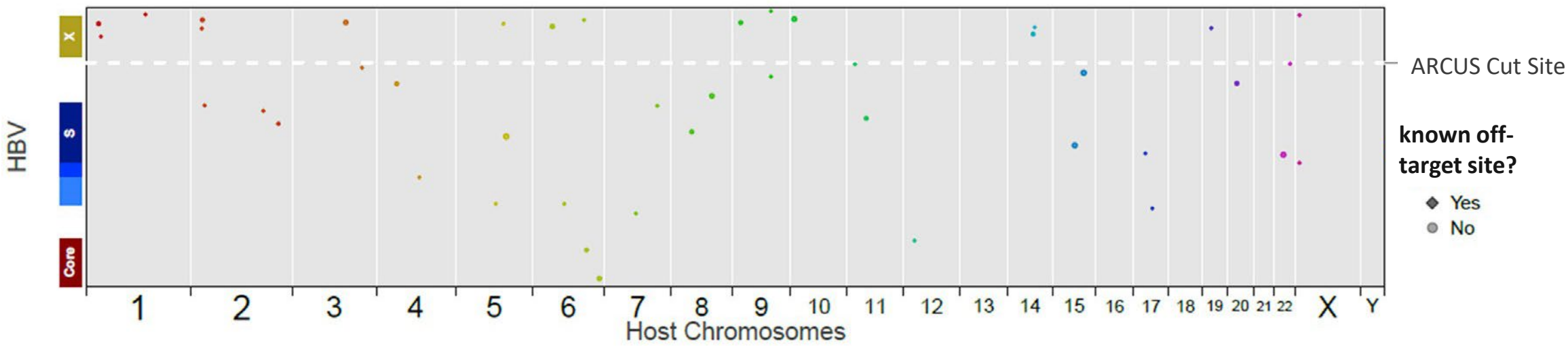


Early Generation ARCUS Treated

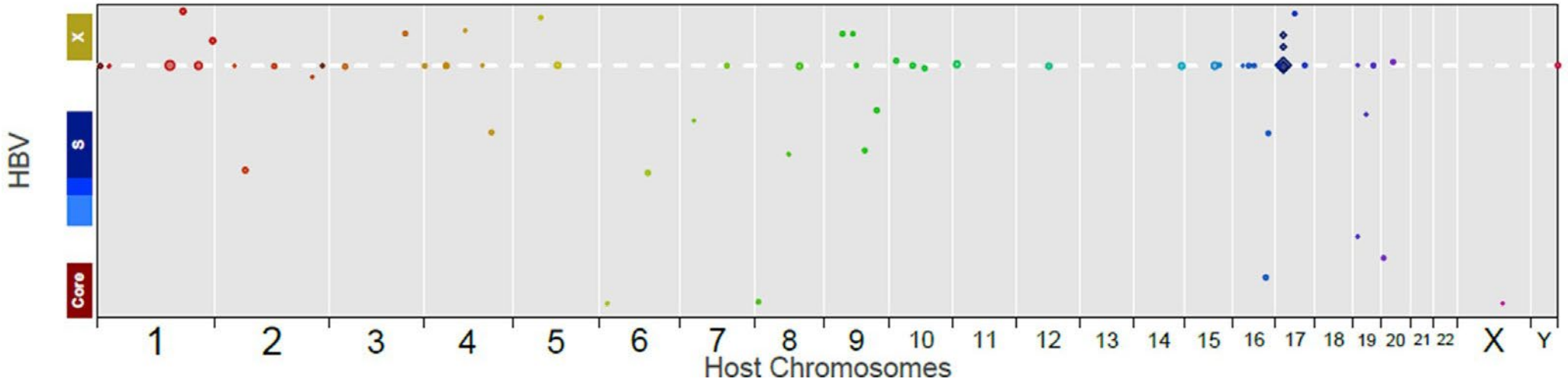


cccDNA Integration into the Genome of Infected Hepatocytes

Mock (HBV only)



Optimized ARCUS Treated



Conclusions

- ARCUS demonstrates high levels of editing against cccDNA with subsequent reduction of HBsAg levels in PHHs.
- We have developed a novel HBV model suitable for mice and NHPs which demonstrated high levels of editing and HBsAg reductions.
- Our gene editing approach demonstrates high on-target activity and specificity against the HBV polymerase gene and could be a promising therapeutic approach for an HBV cure.

Acknowledgements

Precision BioSciences

- Cassie Gorsuch
- Paige Nemec
- Amy Rhoden Smith
- Jeff Smith
- Janel Lape
- Greg Falls
- Jason Holt
- Wendy Shoop
- Emma Sevigny
- Forrest Karriker
- Amod Joshi
- Tyler Goodwin
- Neil Leatherbury
- Rob Brown

Gilead Sciences

- Mei Yu
- Simin Xu
- Robert Muench
- Meghan Holdorf
- Dong Han
- Bill Delaney
- Ricardo Ramirez
- Nick van Buuren
- Becket Feierbach

Acuitas Therapeutics

- Ying Tam
- Paulo Lin
- Sean Semple