

ABI-4334, a Novel Inhibitor of Hepatitis B Virus Core Protein, Disrupts DL-DNA Containing Capsids and Prevents HBV DNA Integration

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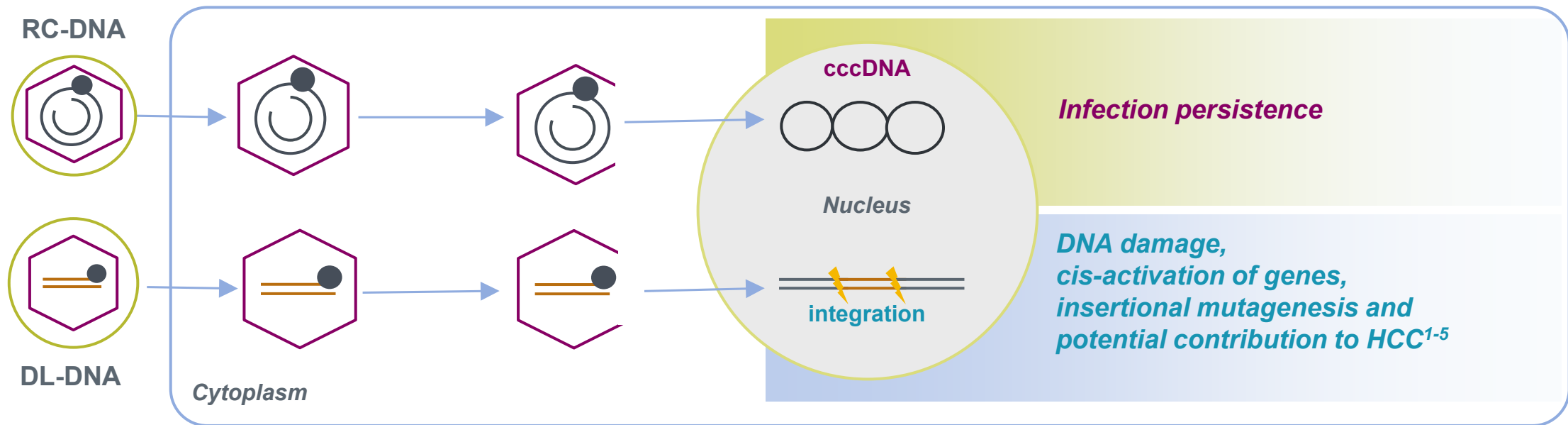


Presenter Disclosures

- Nuruddin Unchwaniwala is an employee and stockholder of Assembly Biosciences, Inc.



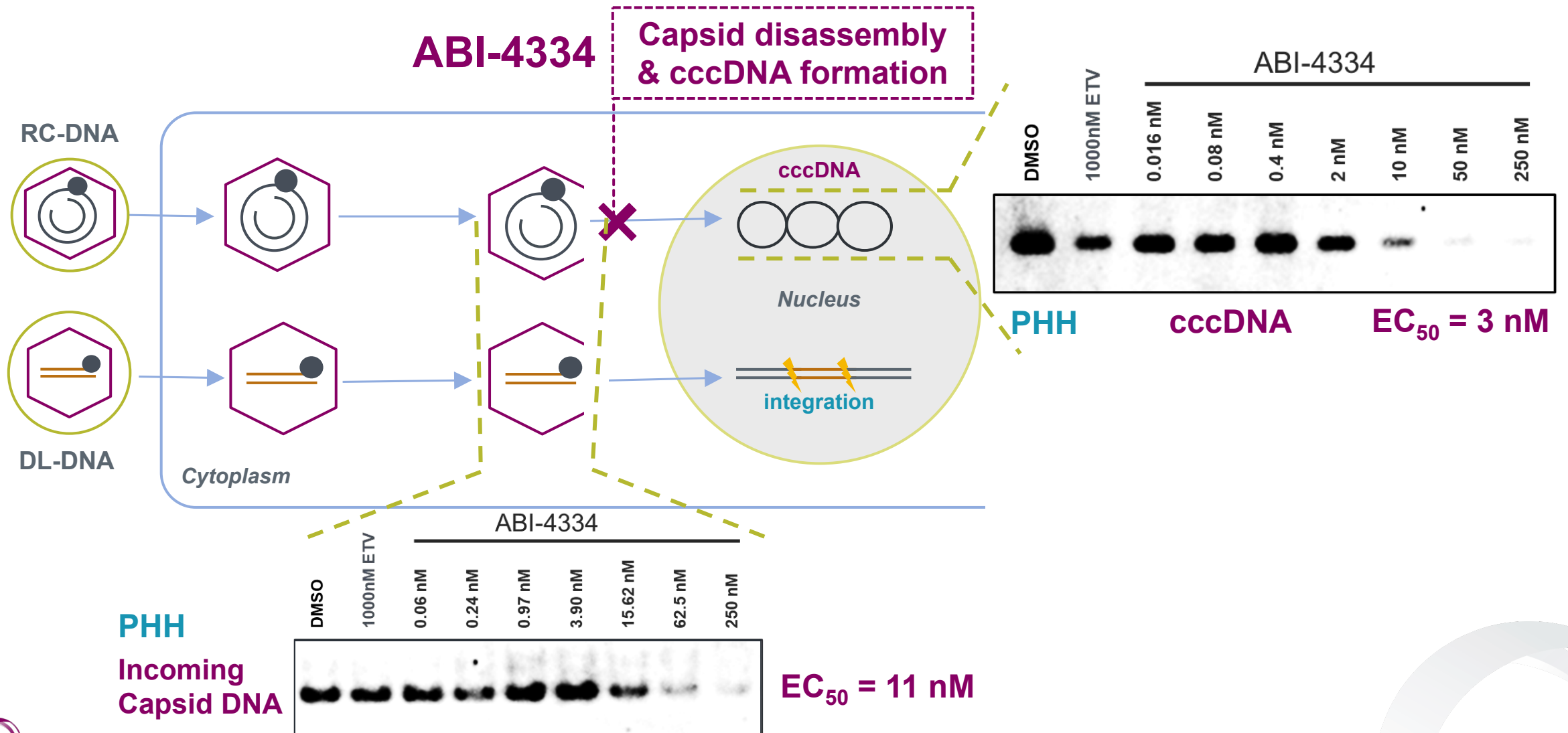
Two Forms of HBV DNA Can Enter the Nucleus Upon Infection



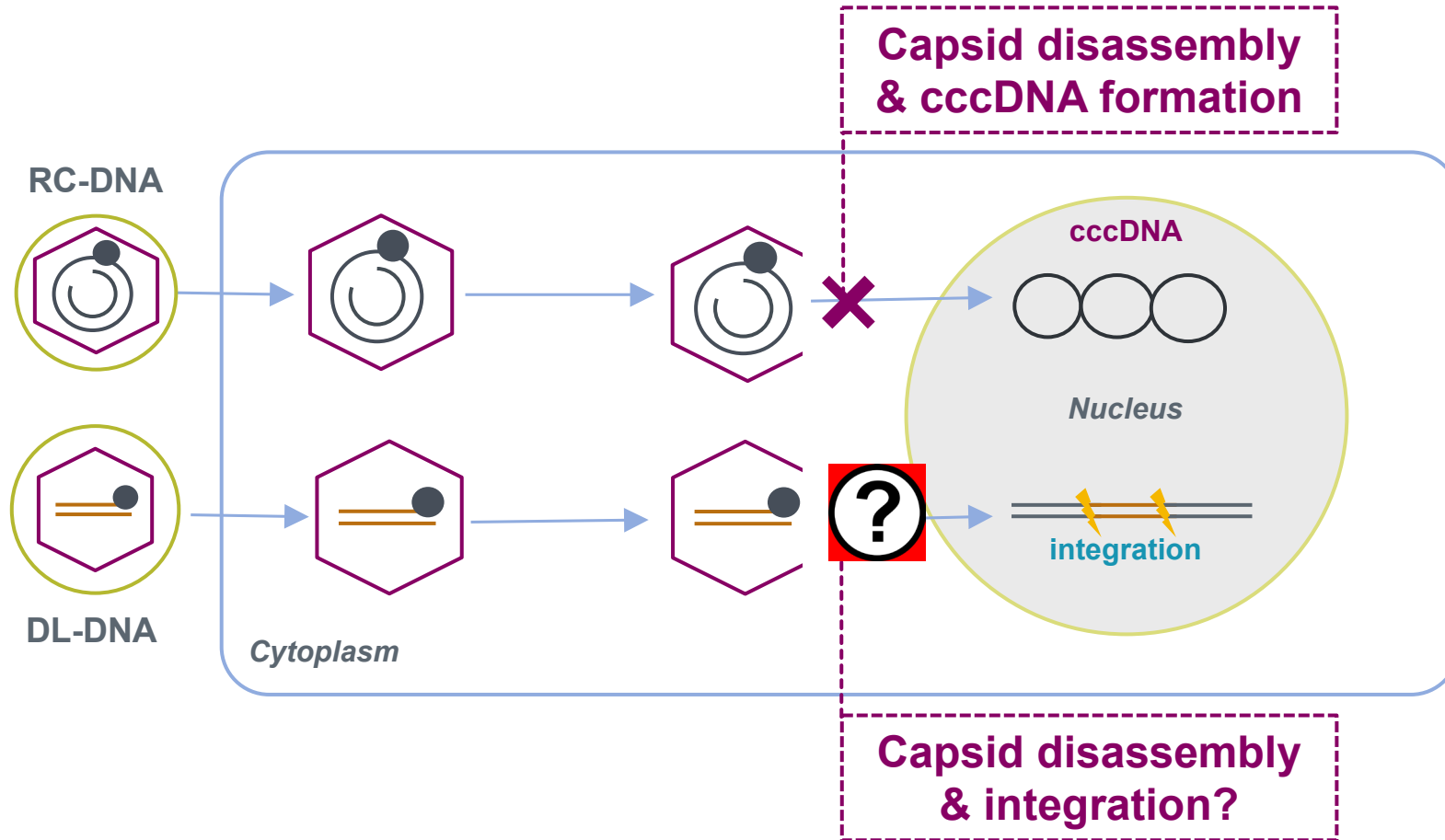
- 1) Peneau C, et al. *Gut*. 2022 Mar;71(3):616-626
- 2) van Buuren N, et al. *JHEP Rep*. 2022;4(1):100388.
- 3) Salpini R, et al. *Front. Microbiol*. 2022;13:972687.
- 4) Ramirez R, et al. *J Virol*. 2021;95(19):e00299-21.
- 5) Jiang Z, et al. *Genome Res*. 2012;22(4):593-601.



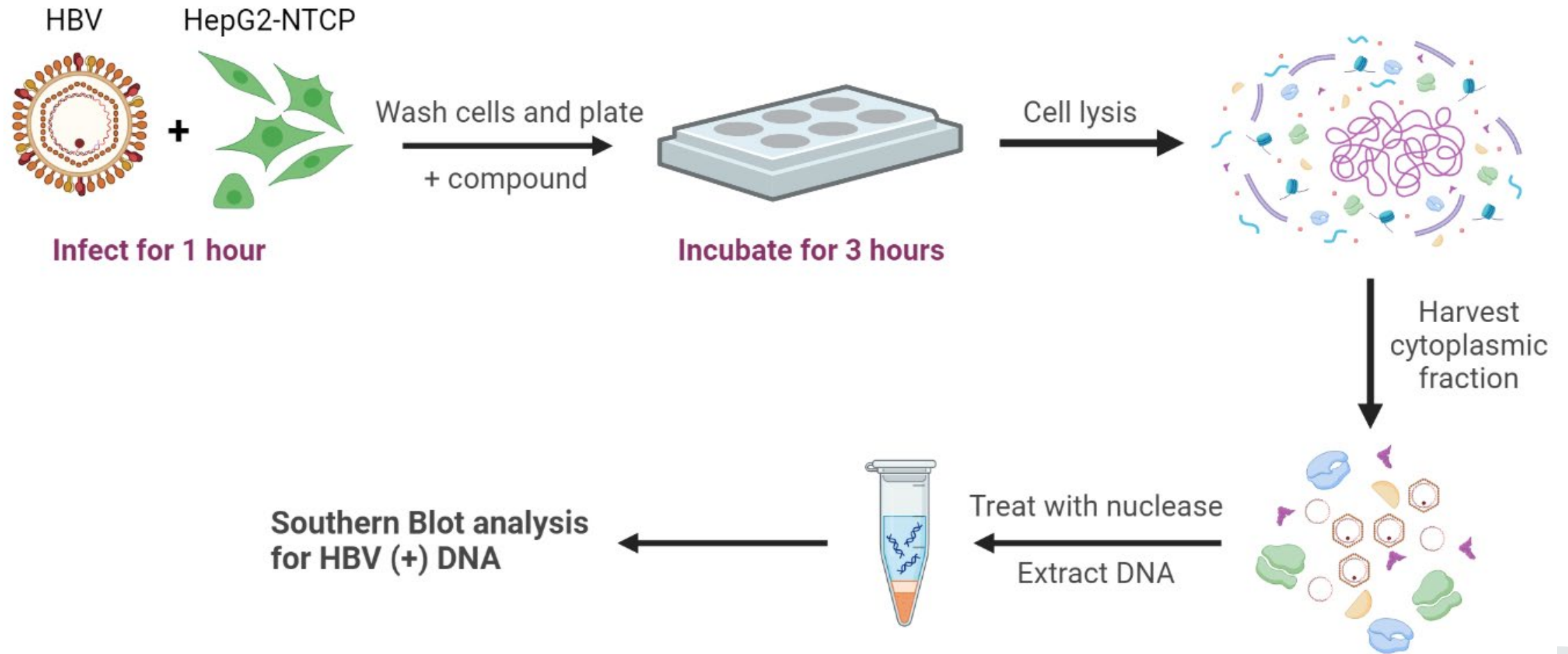
Two Forms of HBV DNA Can Enter the Nucleus Upon Infection



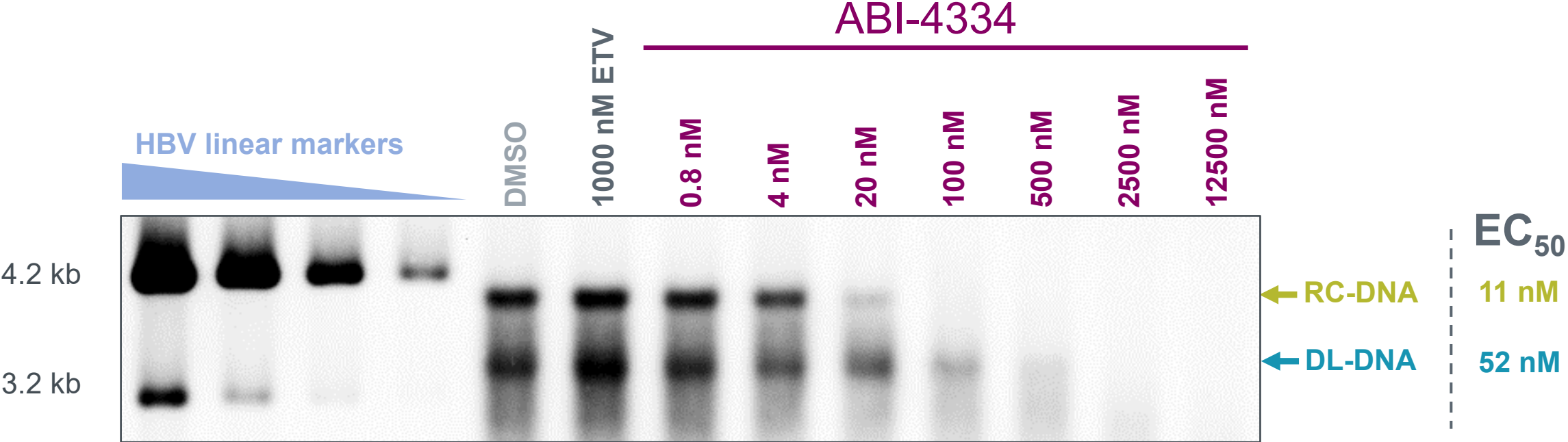
Two Forms of HBV DNA Can Enter the Nucleus Upon Infection



Experiment to Evaluate Impact of ABI-4334 on DL-DNA Capsids



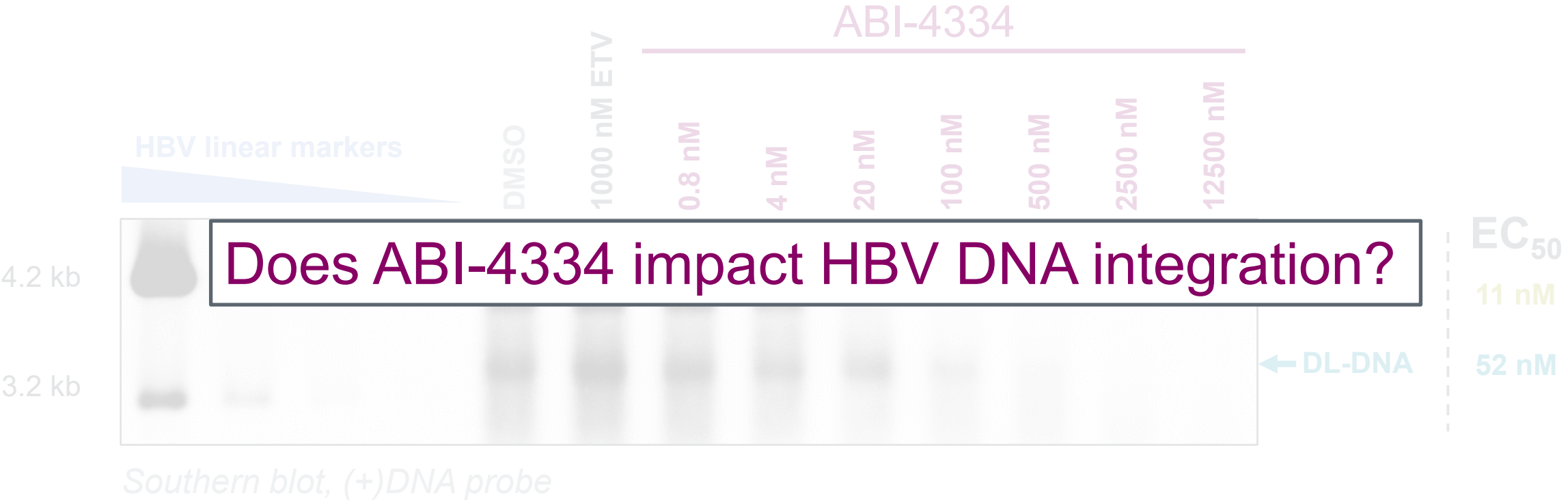
ABI-4334 Disrupts DL-DNA-Containing Capsids



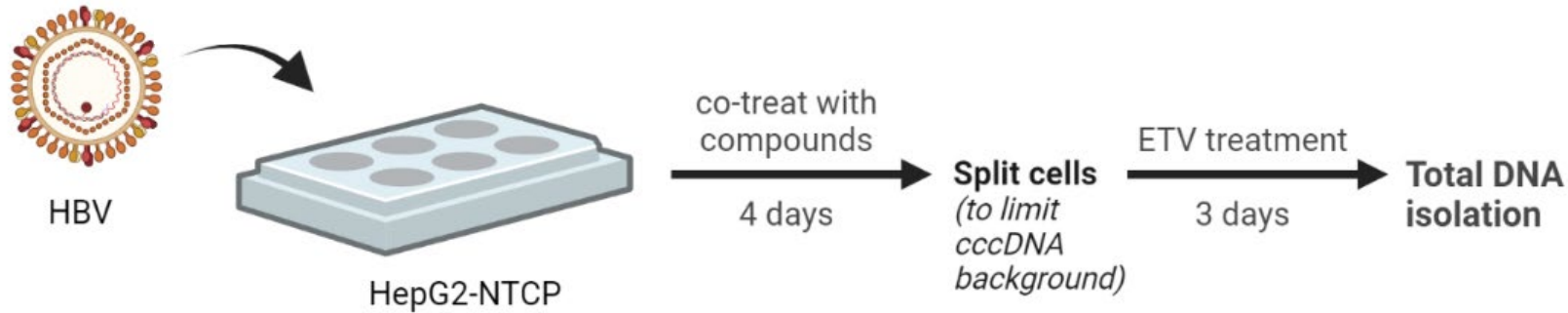
Southern blot, (+)DNA probe



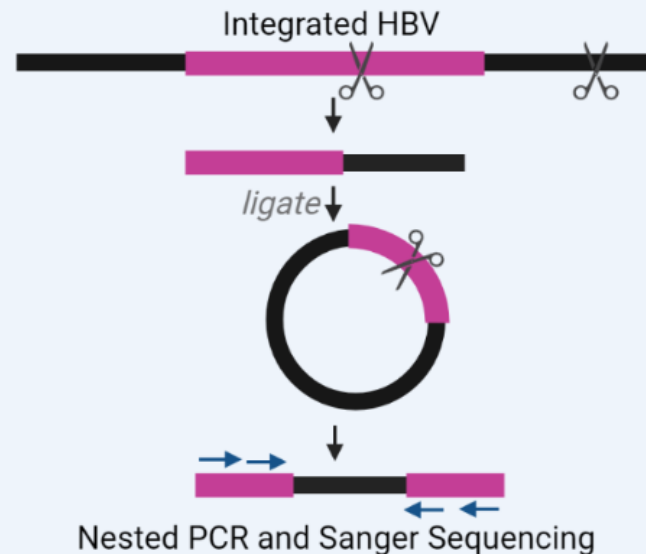
ABI-4334 Disrupts DL-DNA-Containing Capsids



Experimental Design to Evaluate Impact of ABI-4334 on Integration via Inverse PCR (invPCR)



InvPCR detection of integrated HBV DNA



Adapted from Tu T, et al.
*J Virol.*2018;92(11):e02007-17.

InvPCR Shows That ABI-4334 Can Inhibit HBV DNA Integration

Condition	# PCR bands	# Integrants	HBV breakpoint	Int. frequency ^a
Uninfected	0	0	ND	ND
Untreated	54	4 (chr 6, 8, 14, and 16)	nt1806, nt1825, nt1785, nt1624-nt1700	4×10^{-5}
200 nM Myrcludex B	2	0	ND	ND
2.4 μM ABI-4334	28	0	ND	ND

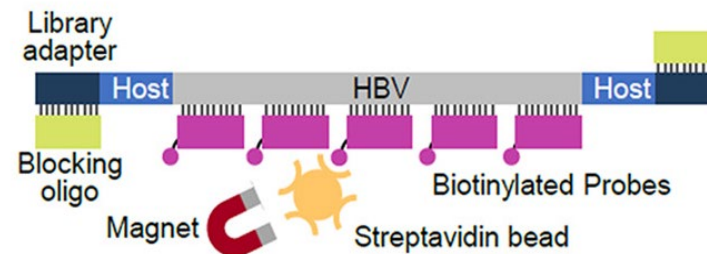
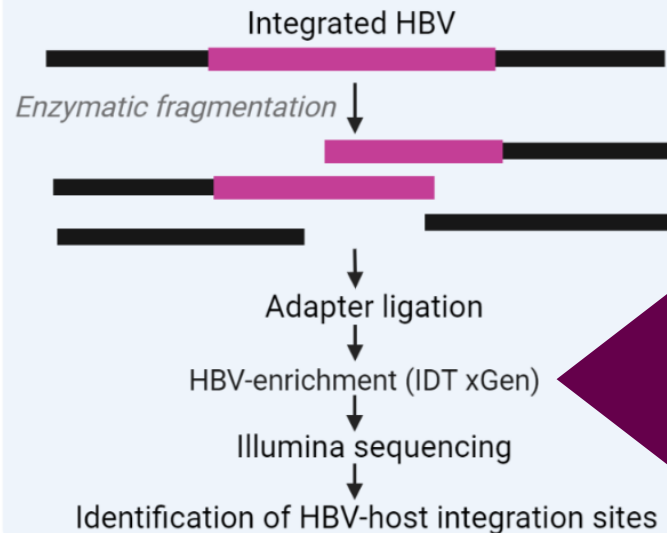
^aBased on 500 ng total DNA screened (~50,000 cells).
ND, not detected.



Experimental Design to Evaluate Impact of ABI-4334 on Integration via HBV Enrichment and NGS



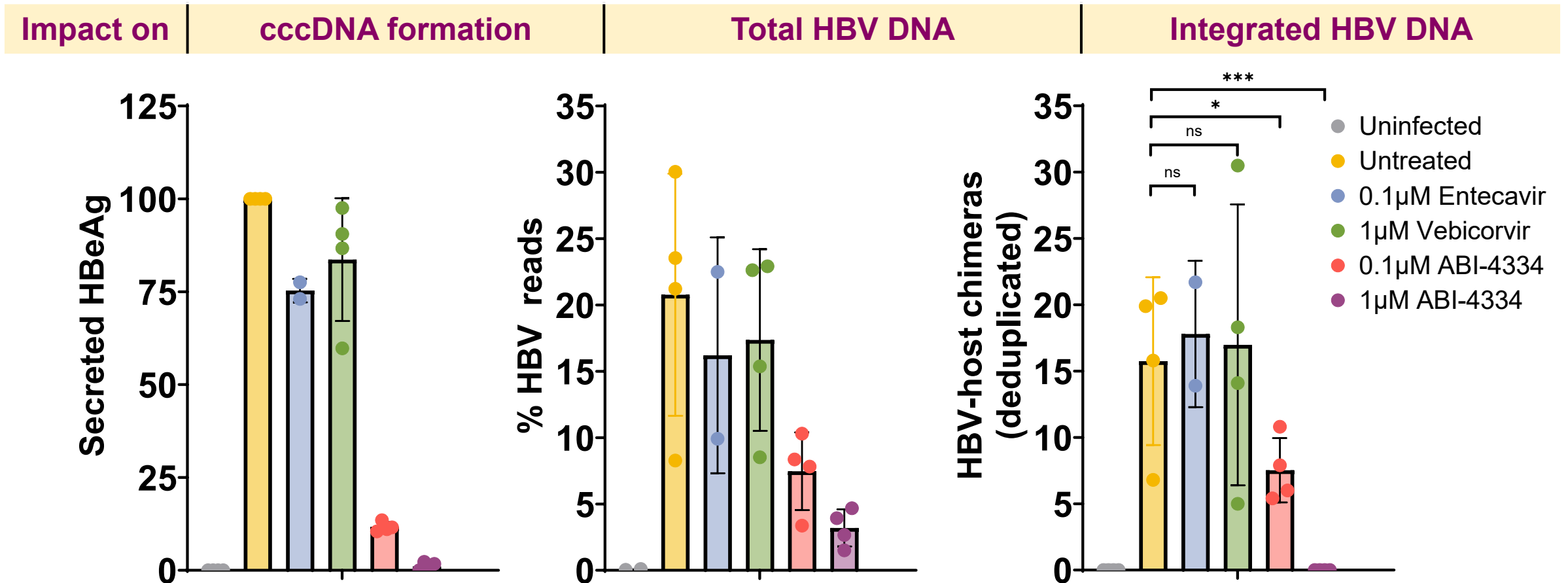
NGS sequencing on HBV-enriched DNA



Reproduced from Ramirez R, et al. *J Virol.* 2021;95(19):e0029921.



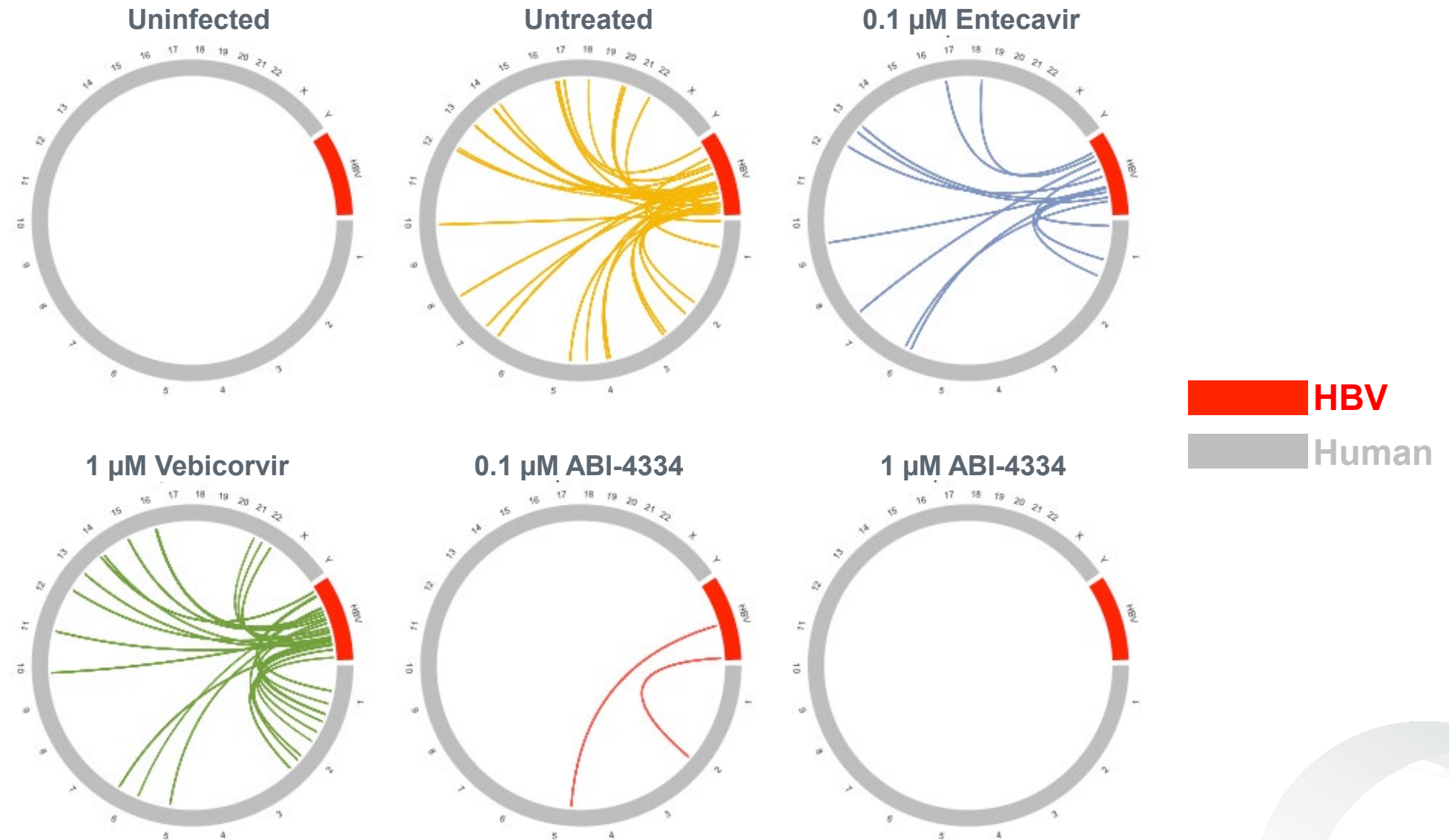
ABI-4334 Prevents HBV Integration in a Dose-Propportional Manner



Statistics: unpaired t-test. *p-value<0.05; ***p-value<0.001.
ns, not significant.



HBV Integration Breakpoints Mapped Throughout the Human Genome



Summary

- HBV integration is a driving mechanism of oncogenesis
- ABI-4334, a highly potent, next-generation capsid assembly modulator, disrupts RC- and DL-DNA-containing capsids
- ABI-4334 inhibits HBV DNA integration as shown by invPCR and NGS analyses
- Plasma levels of ABI-4334 required to inhibit integration are achievable based on Phase 1a PK data¹
- ABI-4334 has potential to lower long-term risk of developing HCC by preventing HBV integration

1) Gane EJ et al. Poster presented at EASL 2023 in Vienna, Austria. SAT-186.



Acknowledgments

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