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

Lewyn Li, Katie Kitrinos, William Delaney, Nuruddin Unchwaniwala

Assembly Biosciences, Inc., South San Francisco, CA, USA

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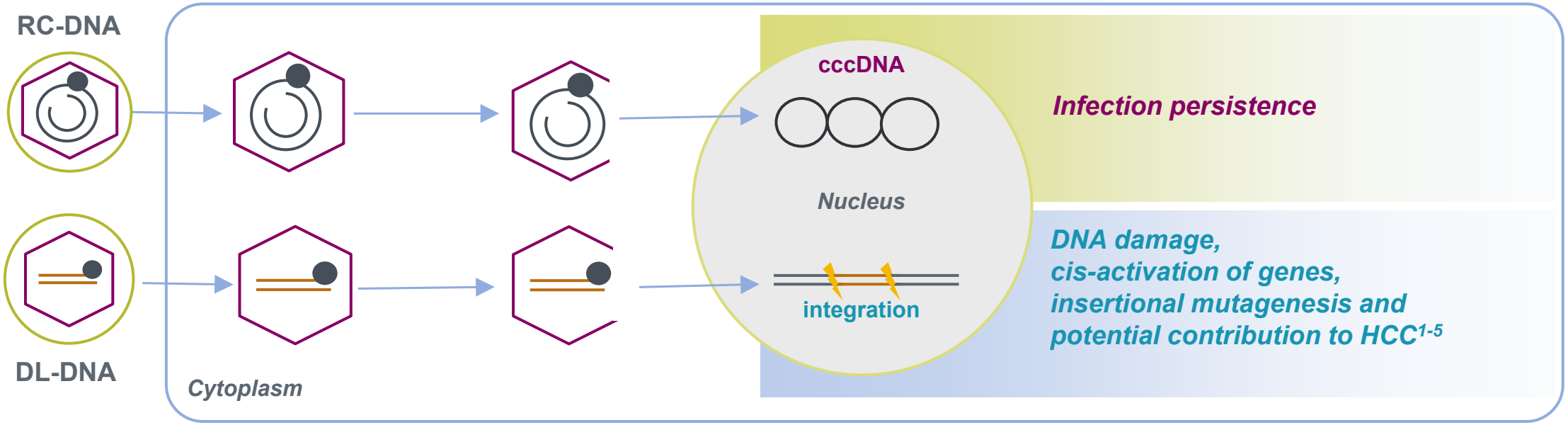
Presenter Disclosures

- 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.

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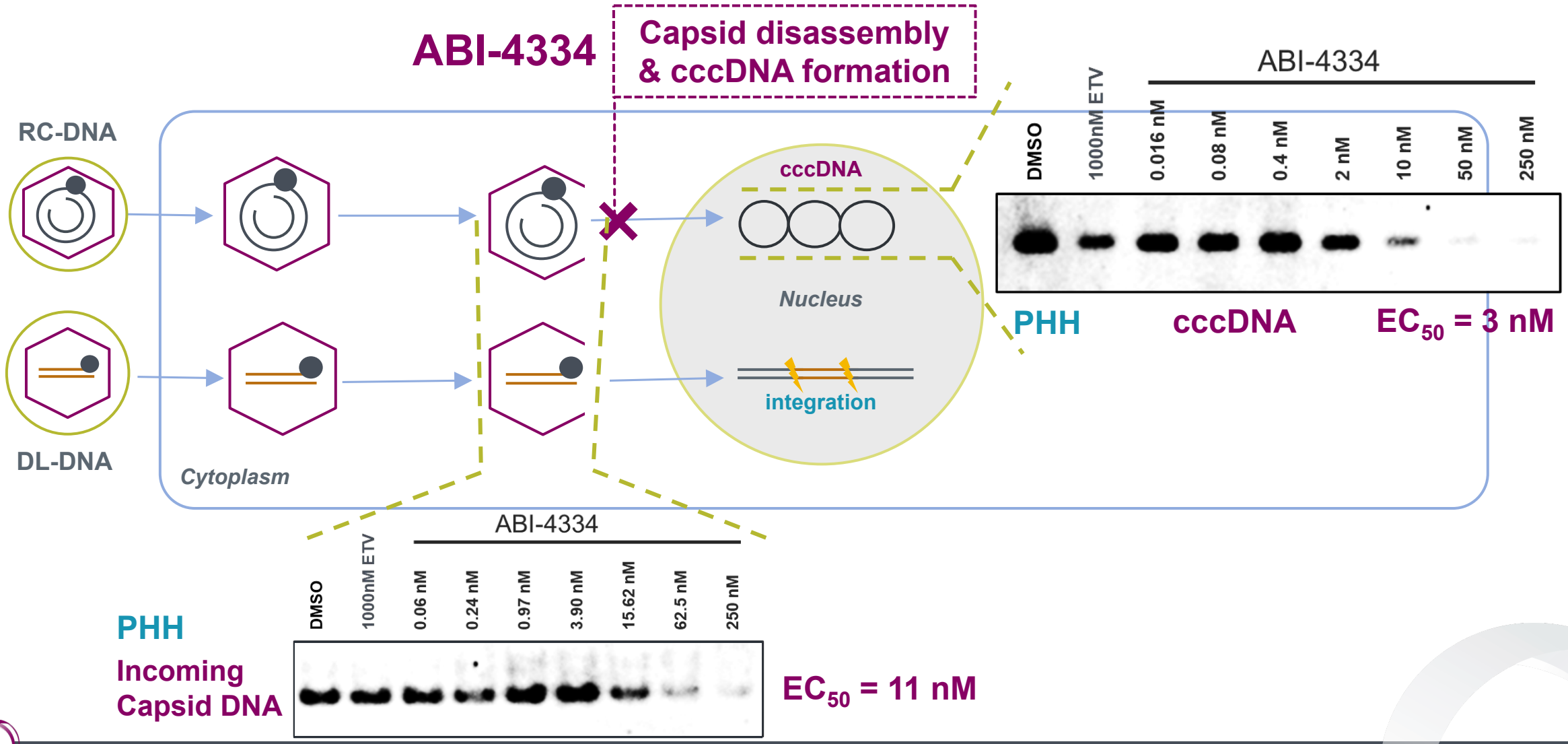
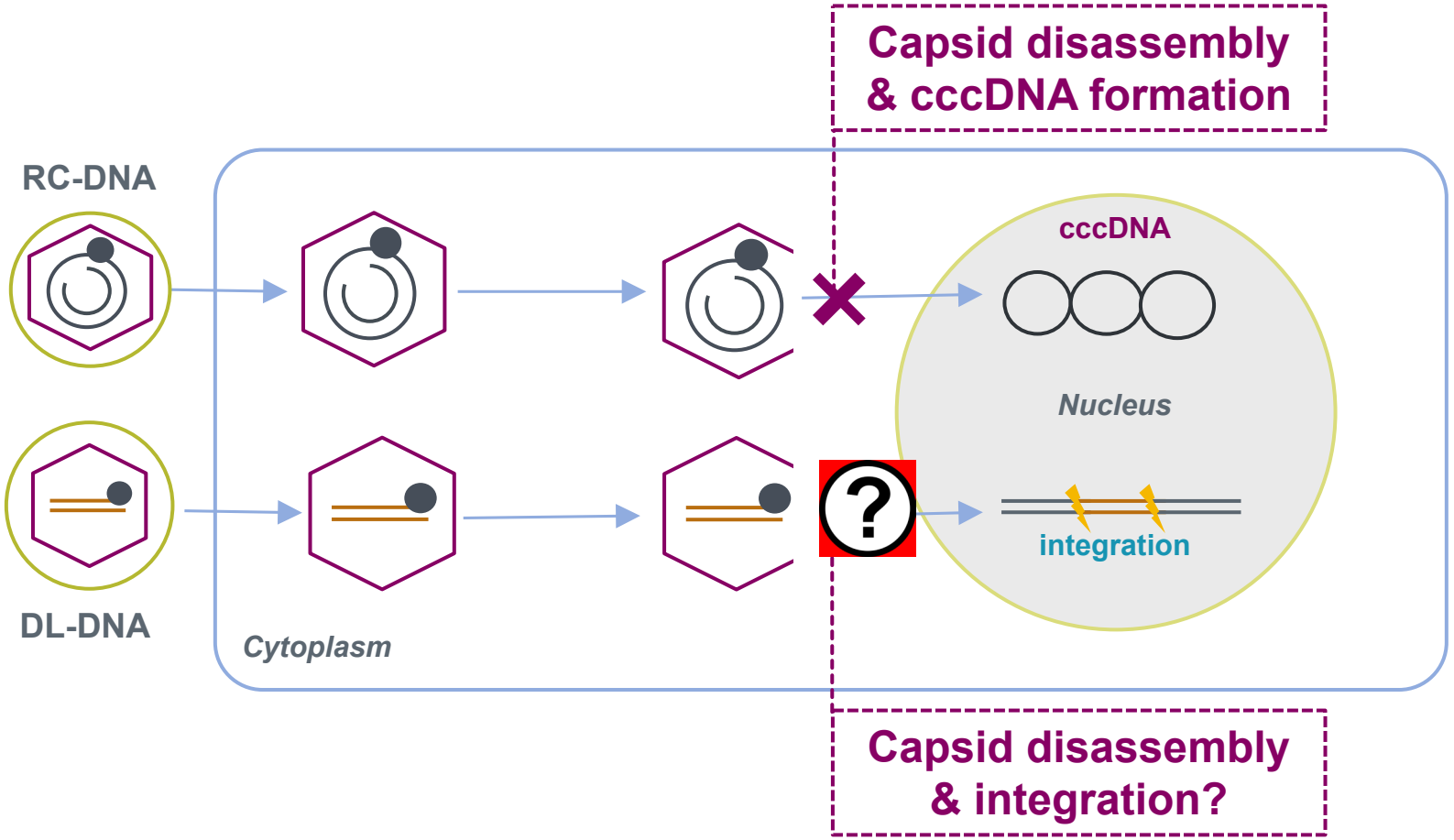
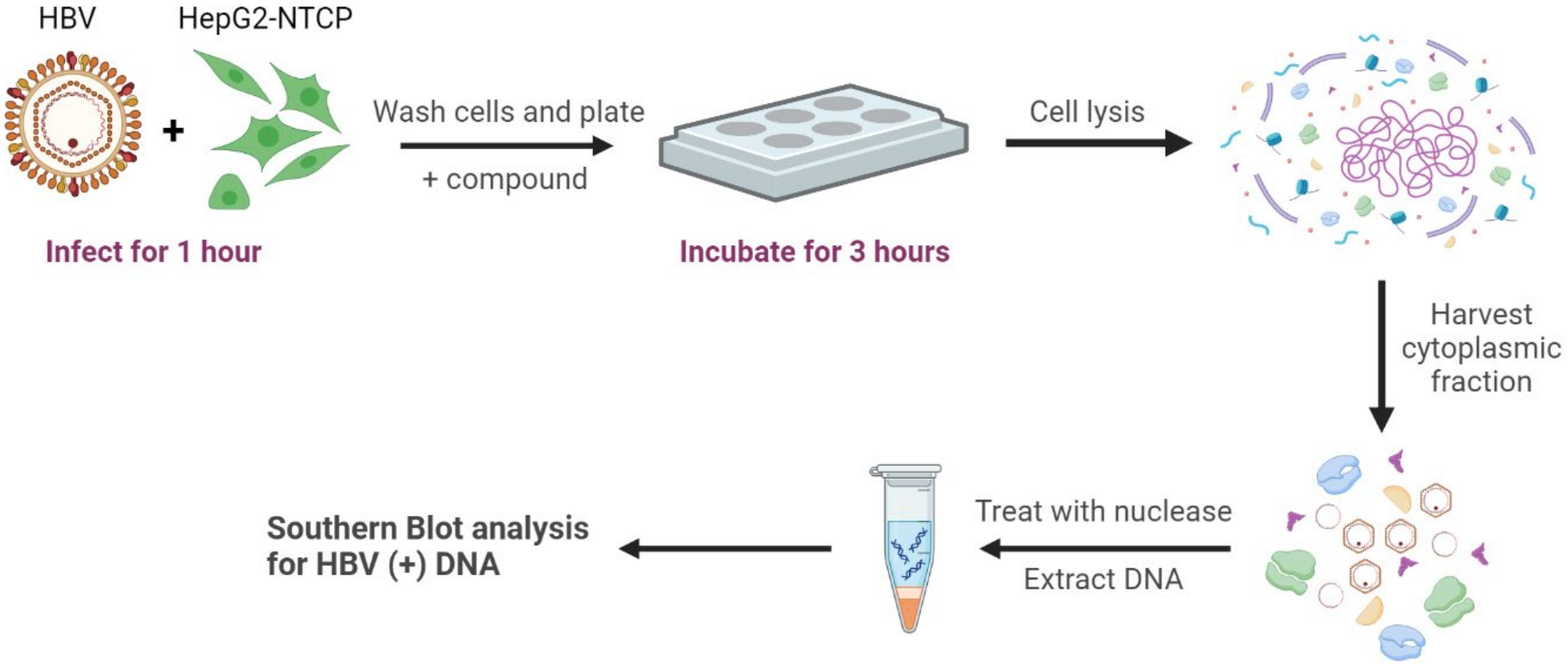


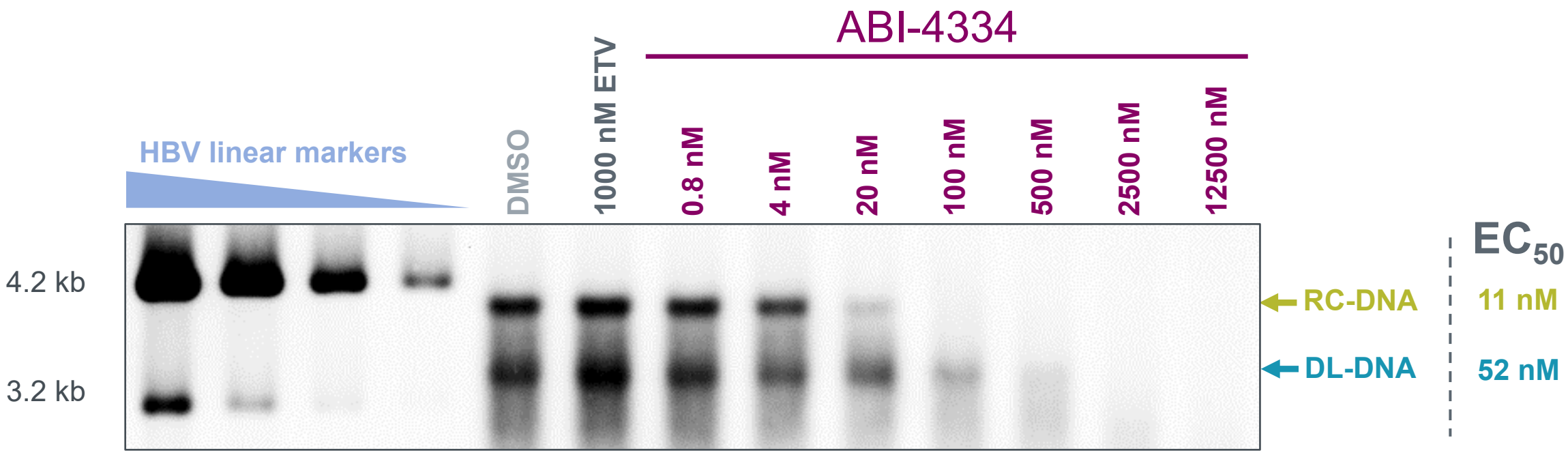
Two Forms of HBV DNA Can Enter the Nucleus Upon Infection



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

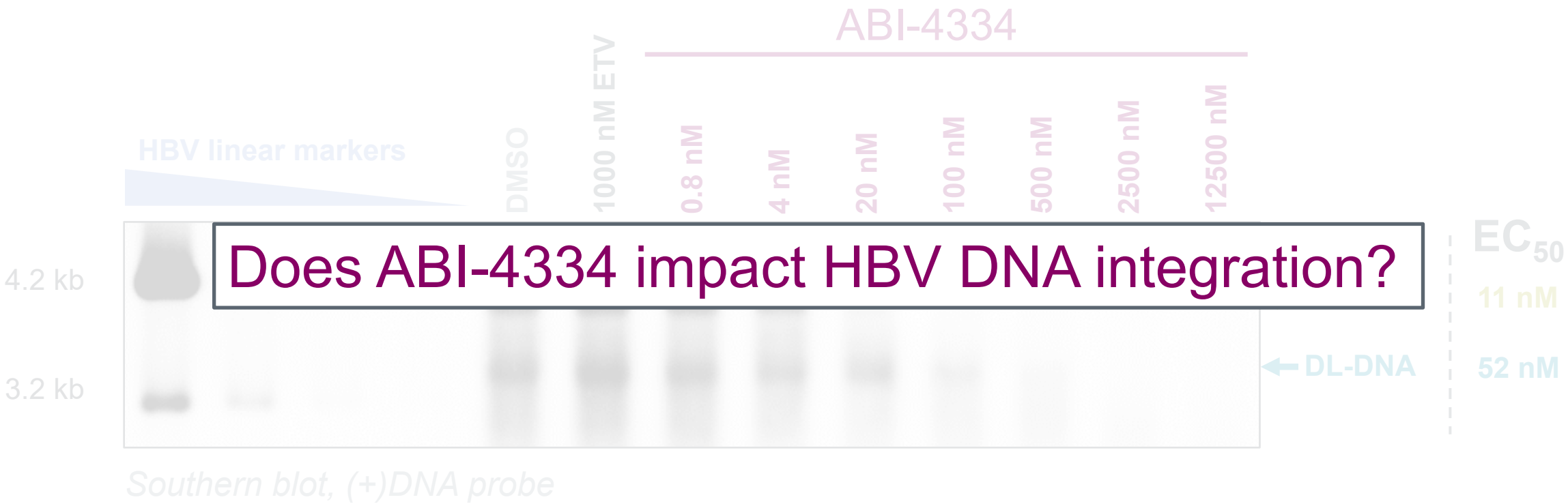


ABI-4334 Disrupts DL-DNA–Containing Capsids



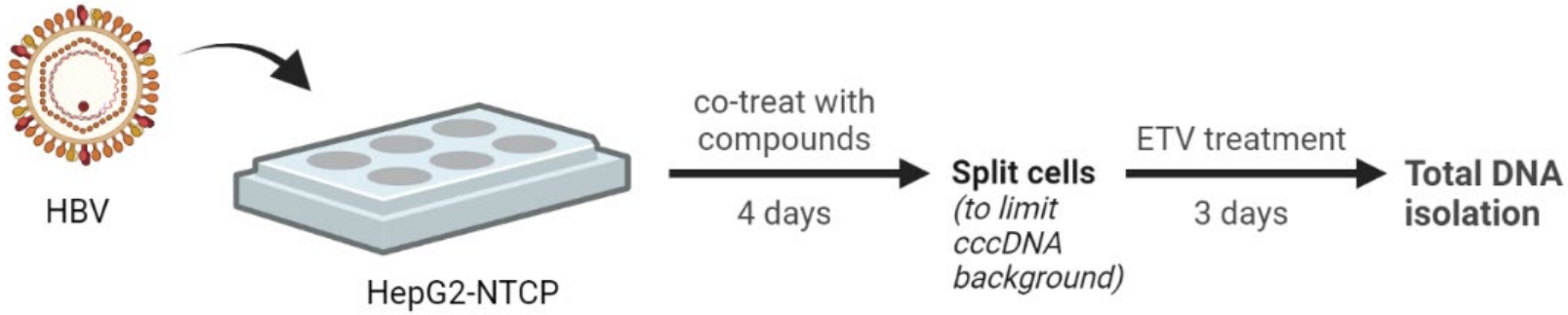
Southern blot, (+)DNA probe

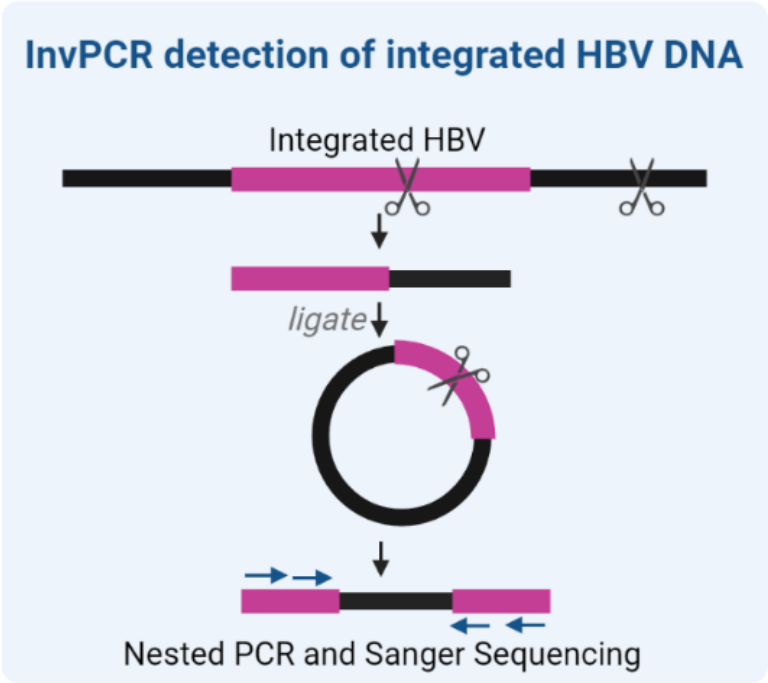
ABI-4334 Disrupts DL-DNA–Containing Capsids



Does ABI-4334 impact HBV DNA integration?

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





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

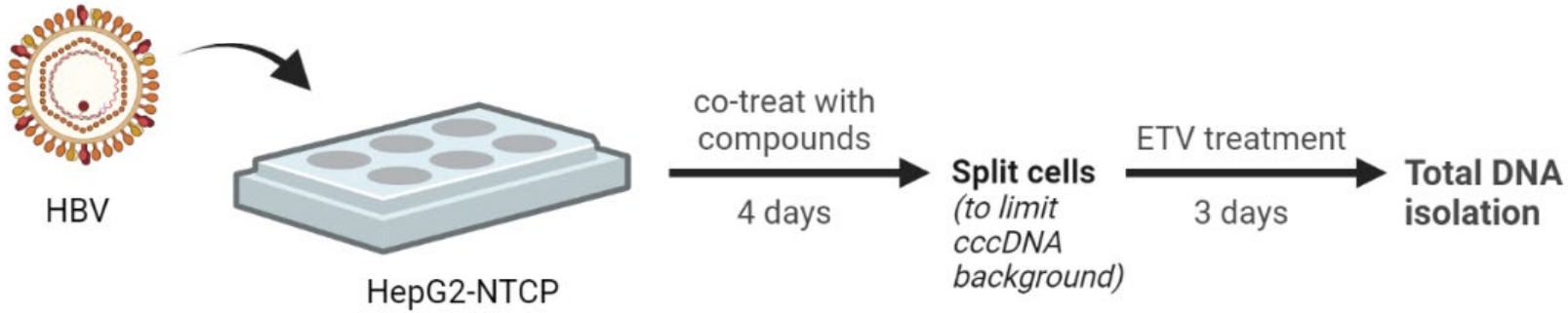
Tu T, Jilbert AR. *Methods Mol Biol*. 2017;1540:97-118.

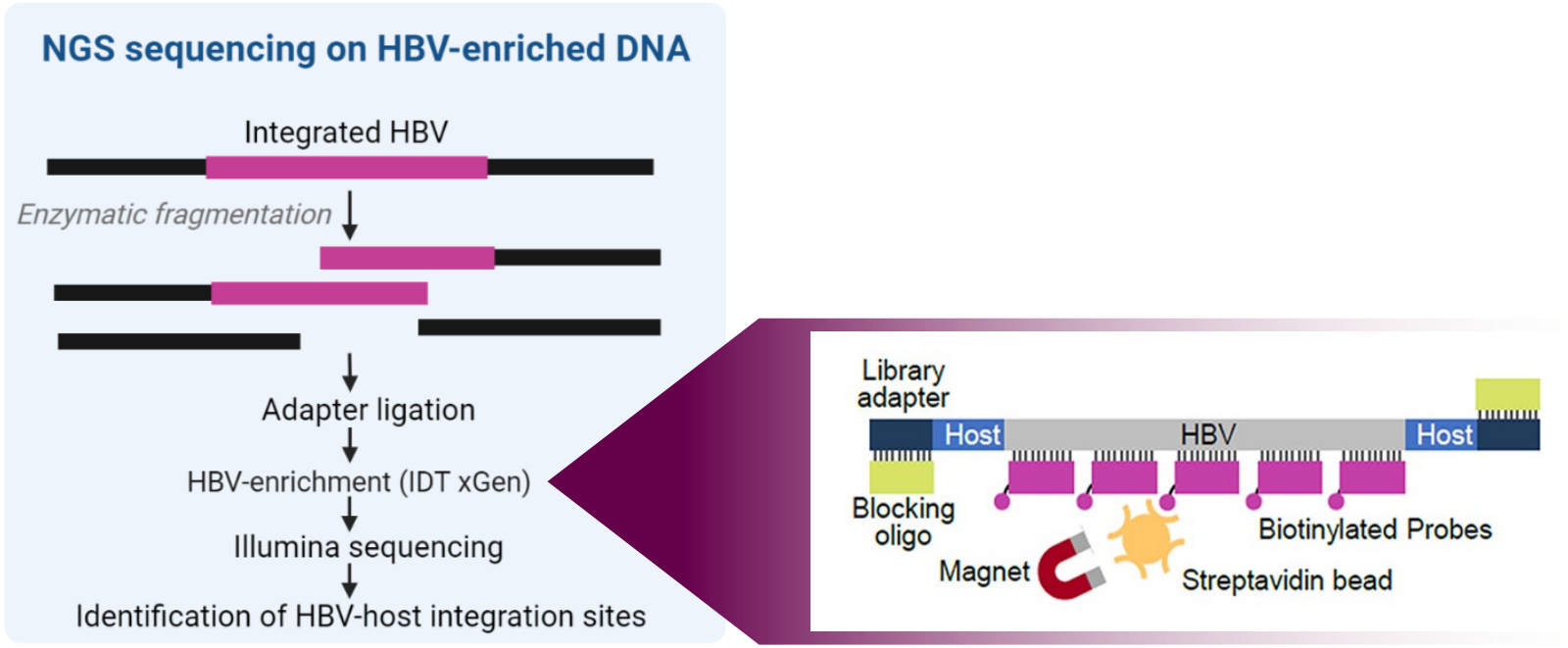
InvPCR Shows That ABI-4334 Can Inhibit HBV DNA Integration

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	$4x10^{-5}$
200 nM Myrcludex B	2	0	ND	ND
2.4 µM ABI-4334	28	0	ND	ND

[a]Based 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

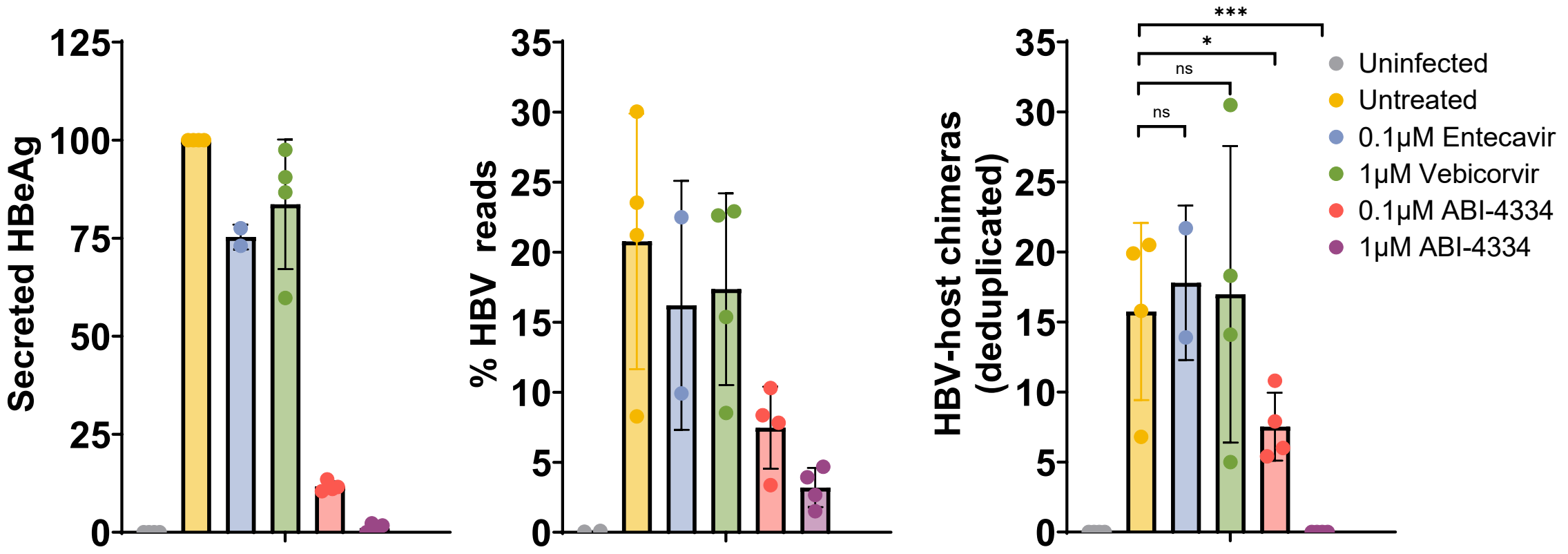




Reproduced from Ramirez R, et al. *J Virol*. 2021;95(19):e0029921.

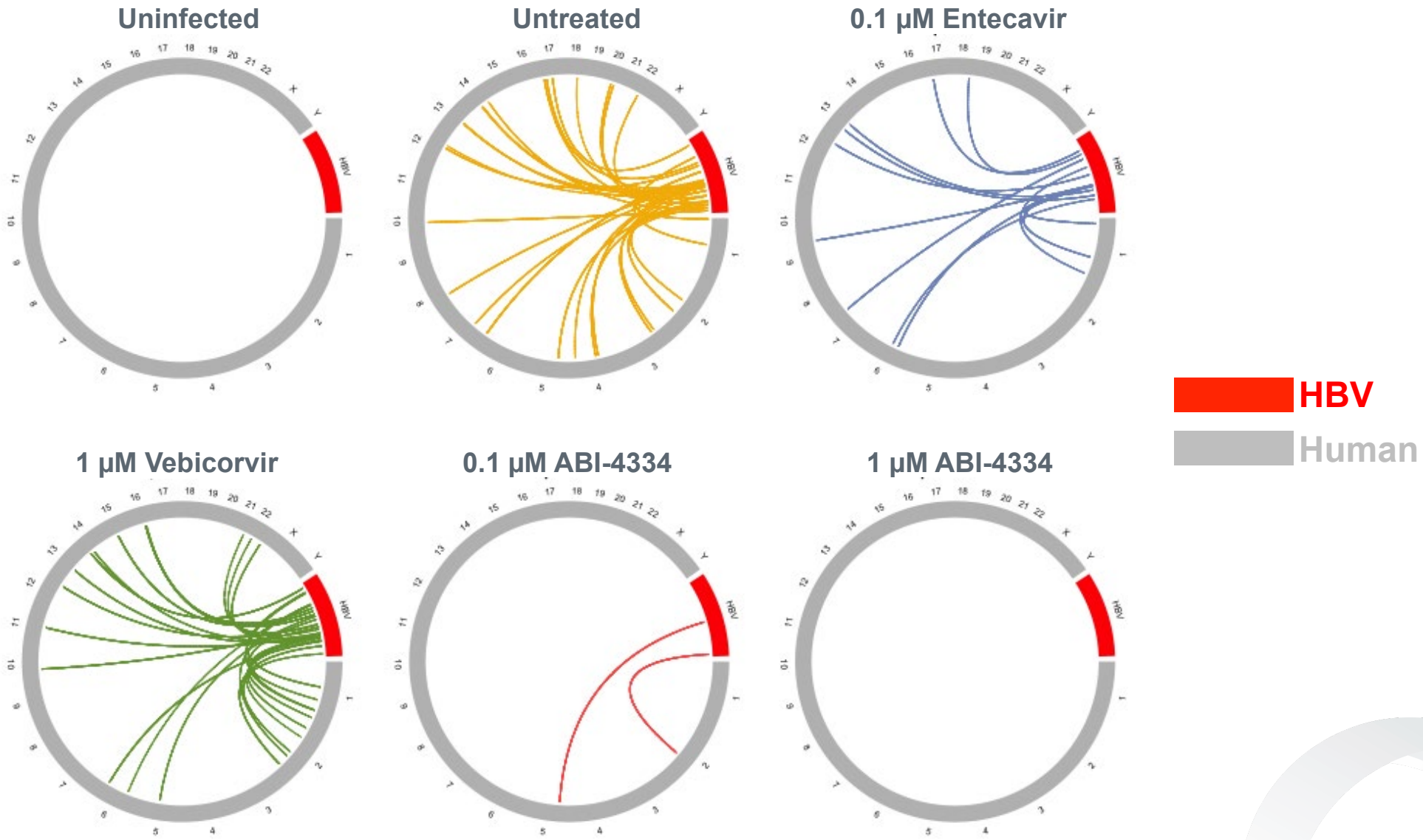
ABI-4334 Prevents HBV Integration in a Dose-Proportional Manner

Impact on	cccDNA formation	Total HBV DNA	Integrated HBV DNA



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 data[1]
- 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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- This study was sponsored by Assembly Biosciences, Inc.