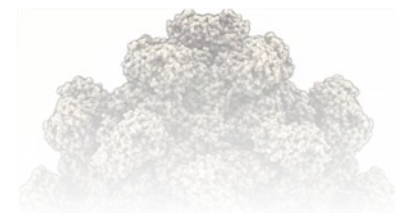
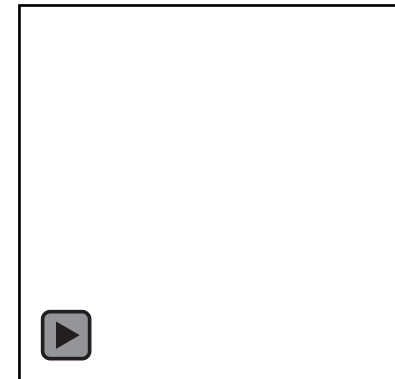


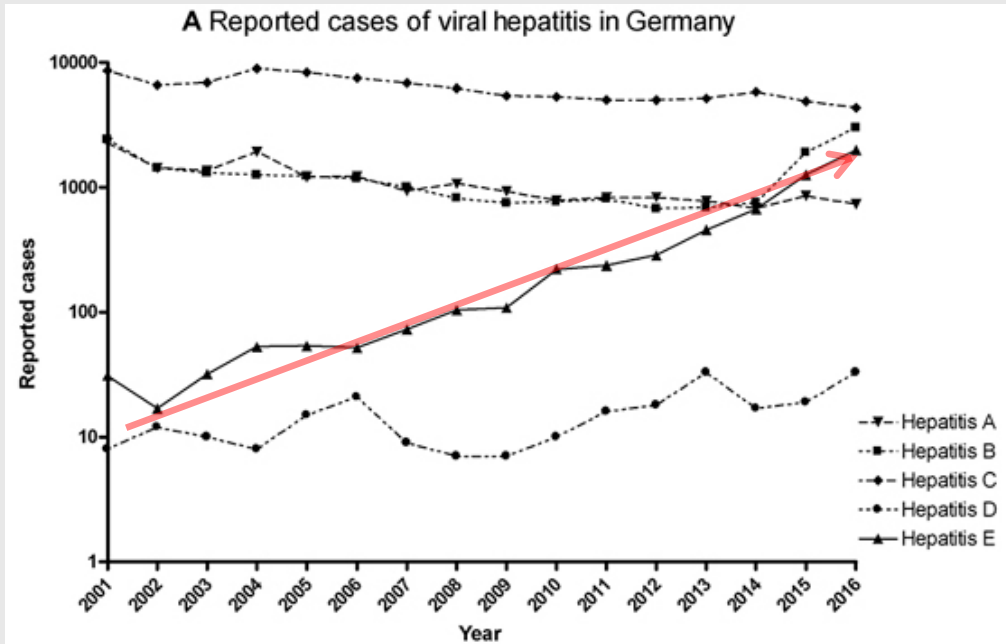
In vivo evidence for ribavirin-induced mutagenesis of the hepatitis E virus genome


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Faculty of Medicine - Institute of Hygiene and Microbiology



Increasing prevalence of Hepatitis E virus



 most common cause of acute viral hepatitis

- > 3 million symptomatic cases p.a.
- about 70,000 deaths p.a.



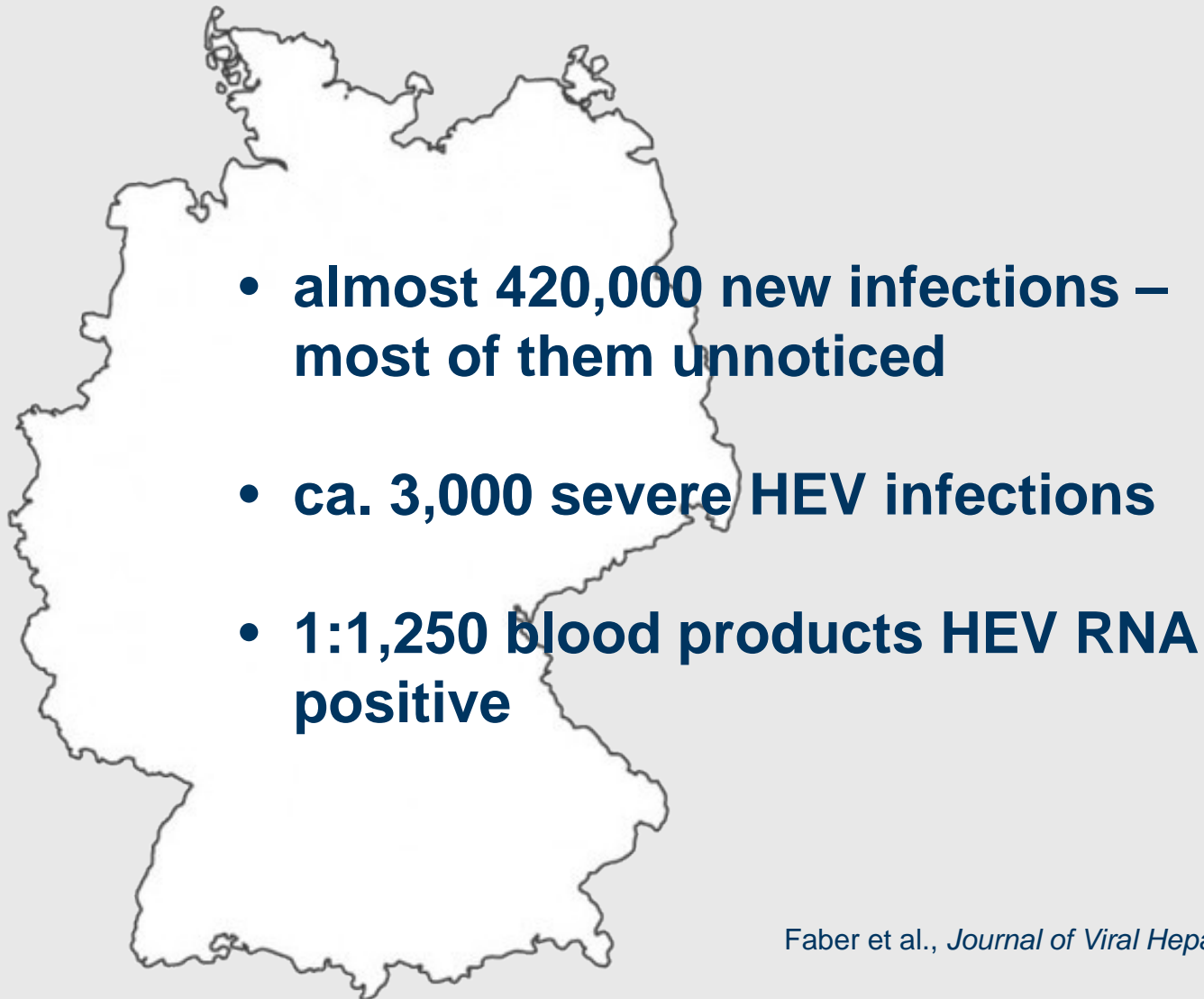
EUROPE'S NEW HEPATITIS PROBLEM

Many get infected with hepatitis E, and a few get very sick. How can the virus be stopped?

By Kai Kupferschmidt *Science*, 2016

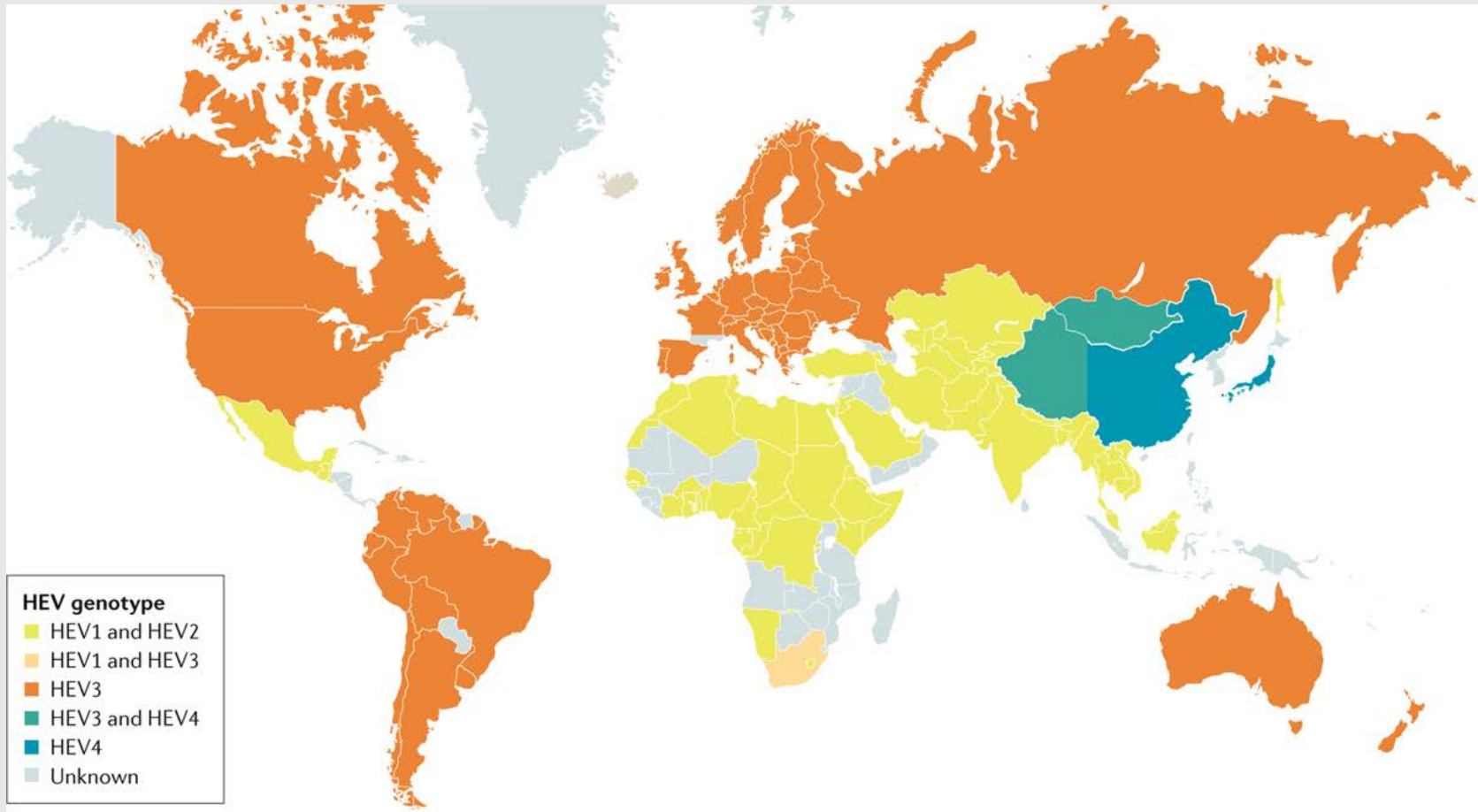
Wehmeyer et al., *Z Gastroenterol.* 2018

Increasing prevalence of Hepatitis E virus



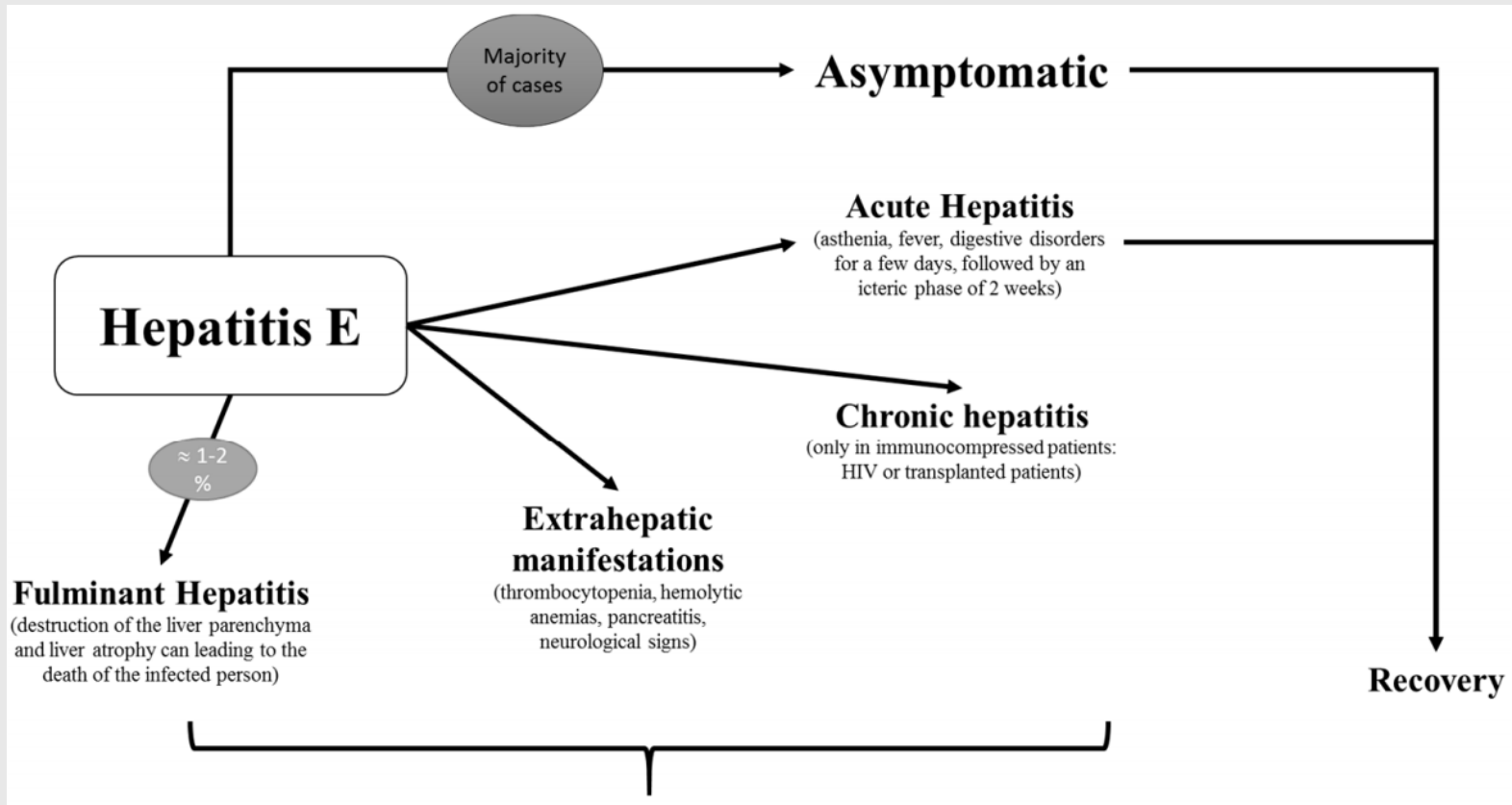
Faber et al., *Journal of Viral Hepatitis* . 2017

Worldwide distribution of hepatitis E virus



Nimgaonkar et al., *Nat Rev Gastroenterol Hepatol.* 2018

Course of infection of Hepatitis E



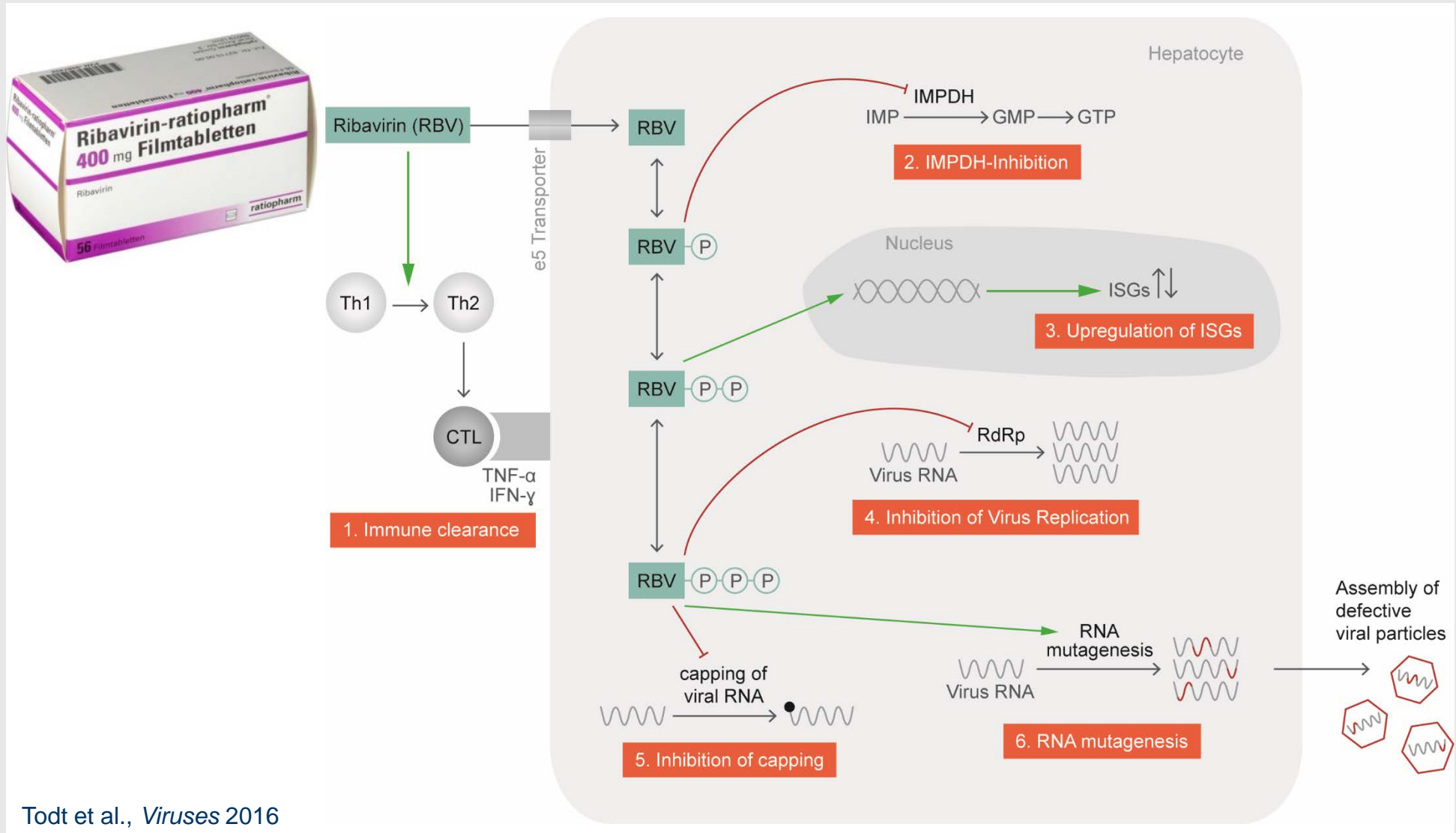
Capai et al., *Viruses* 2018

SVR



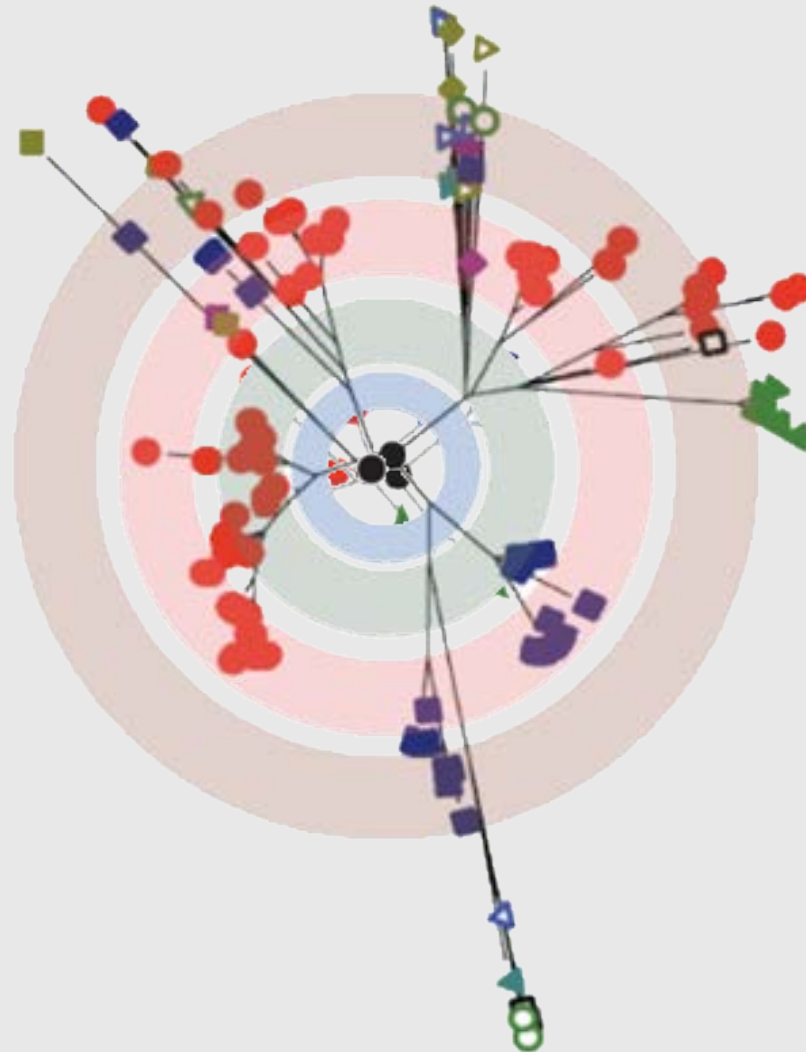
treatment failure

Ribavirin – Modes of action



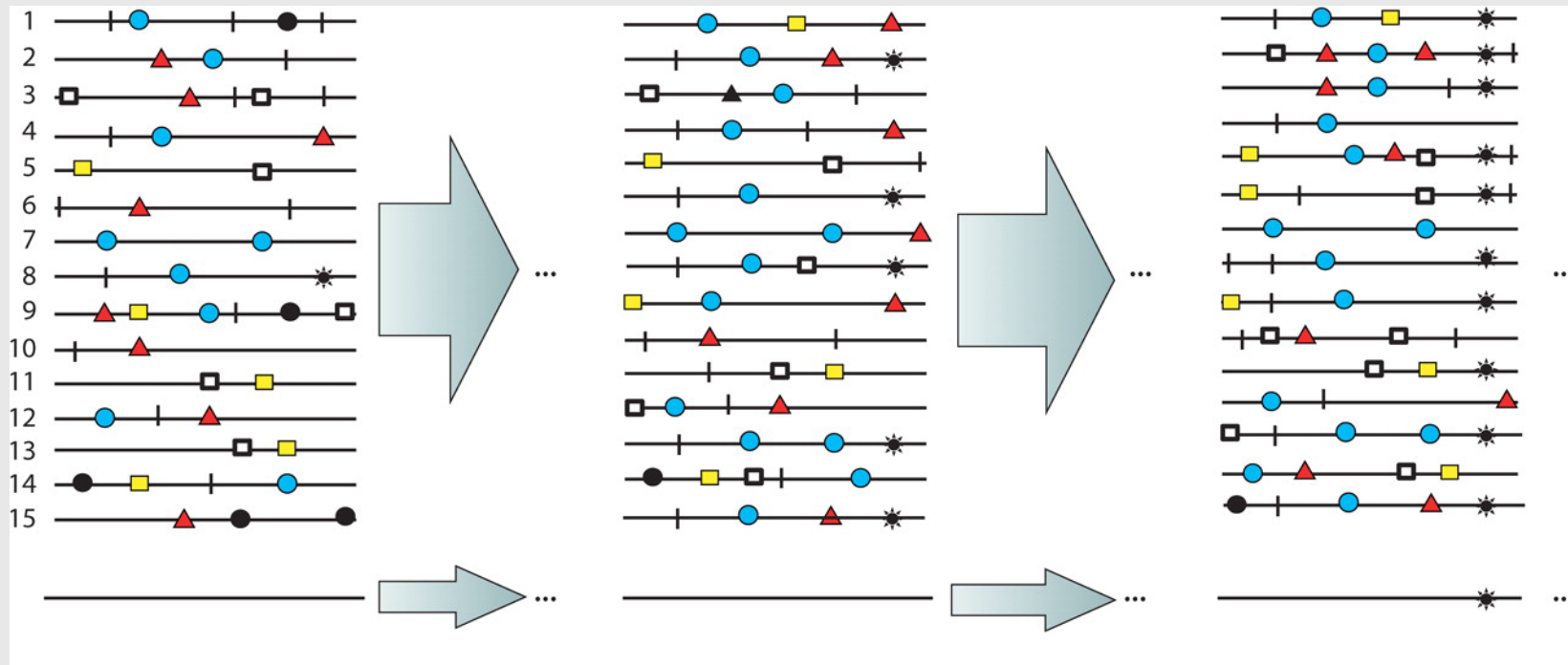
Todt et al., *Viruses* 2016

Sequencing of viral populations



adopted from Lauring et al. *PloS Pathogens* 2010

Sequencing of viral populations



Domingo et al., *Microbiol and Mol. Biol Reviews* 2012

Selected patients for our study



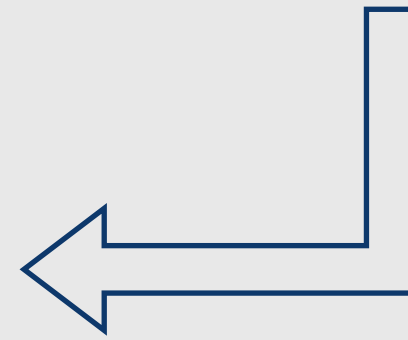
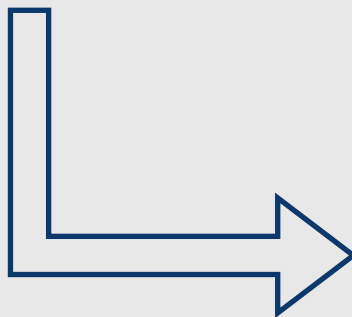
acute resolver



chronic - SVR

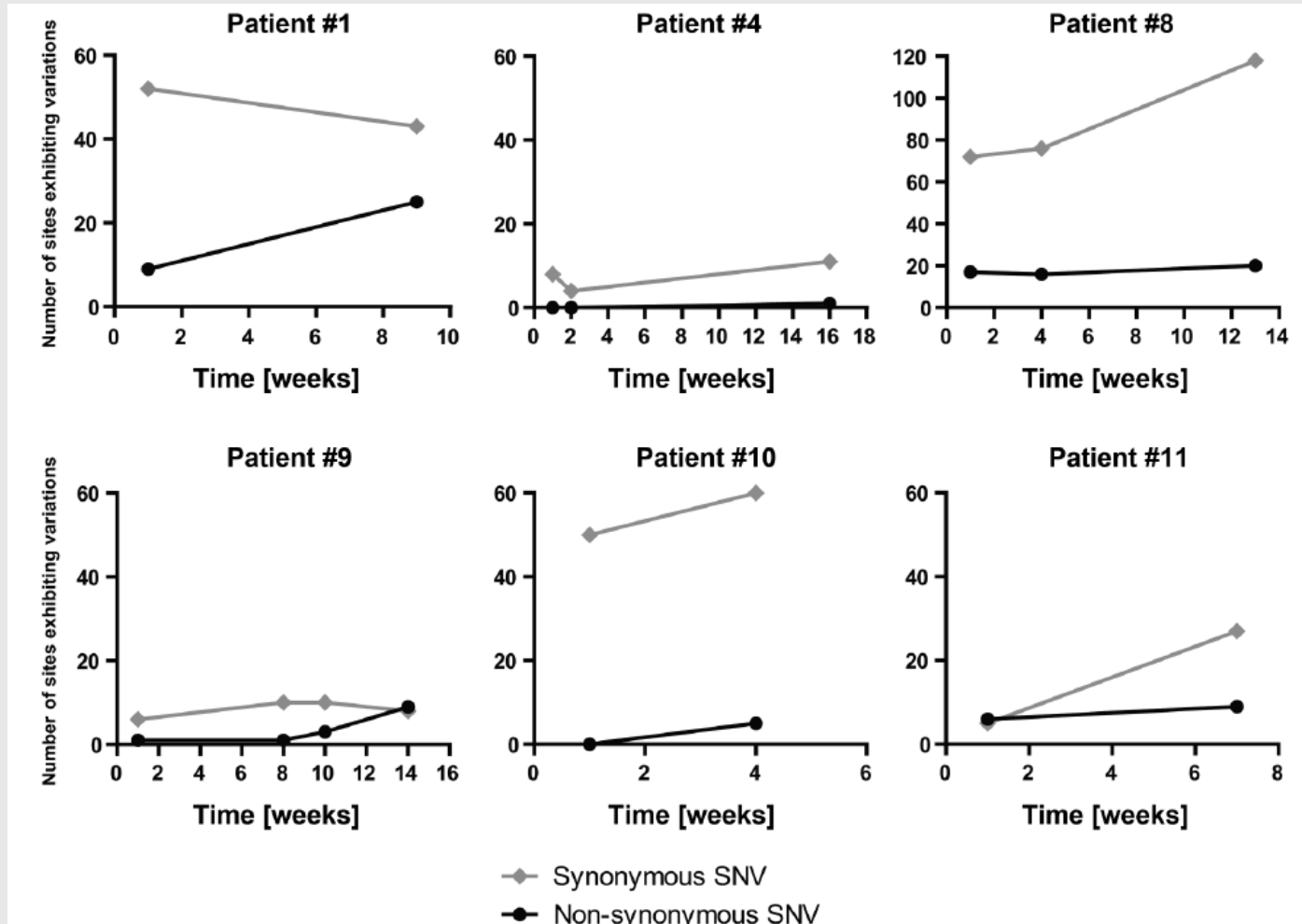


chronic non-responder



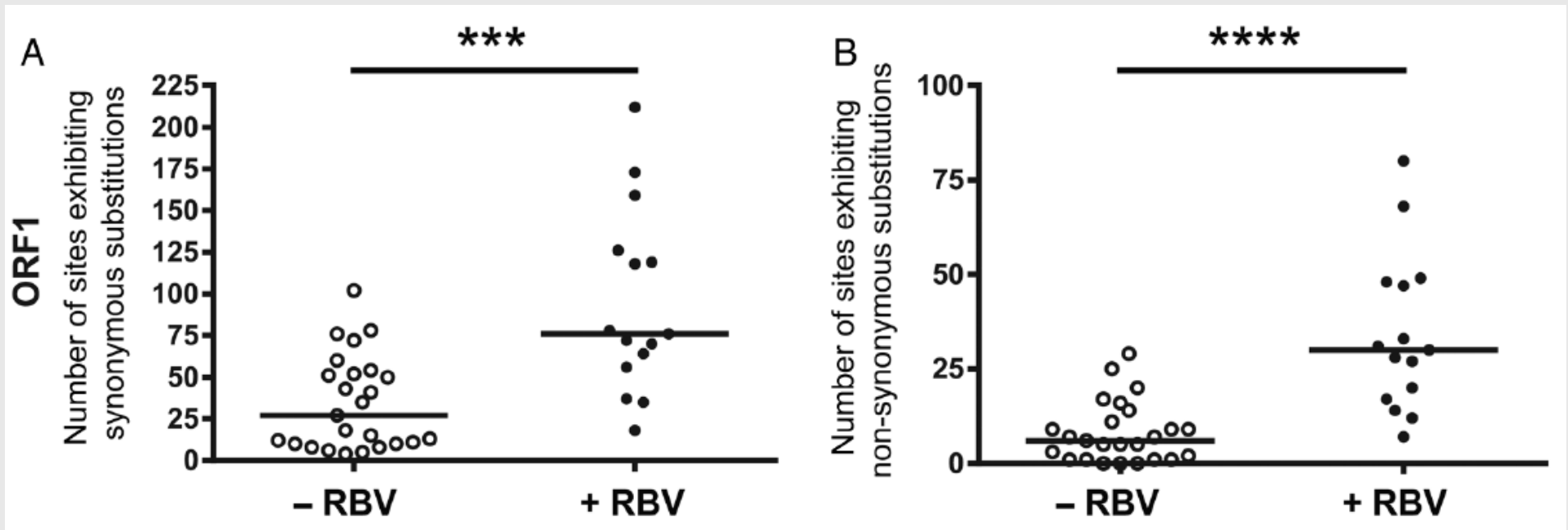
Todt & Gisa et al., Gut 2016

Number of sites exhibiting variations in the HEV ORF1 region without the influence of RBV



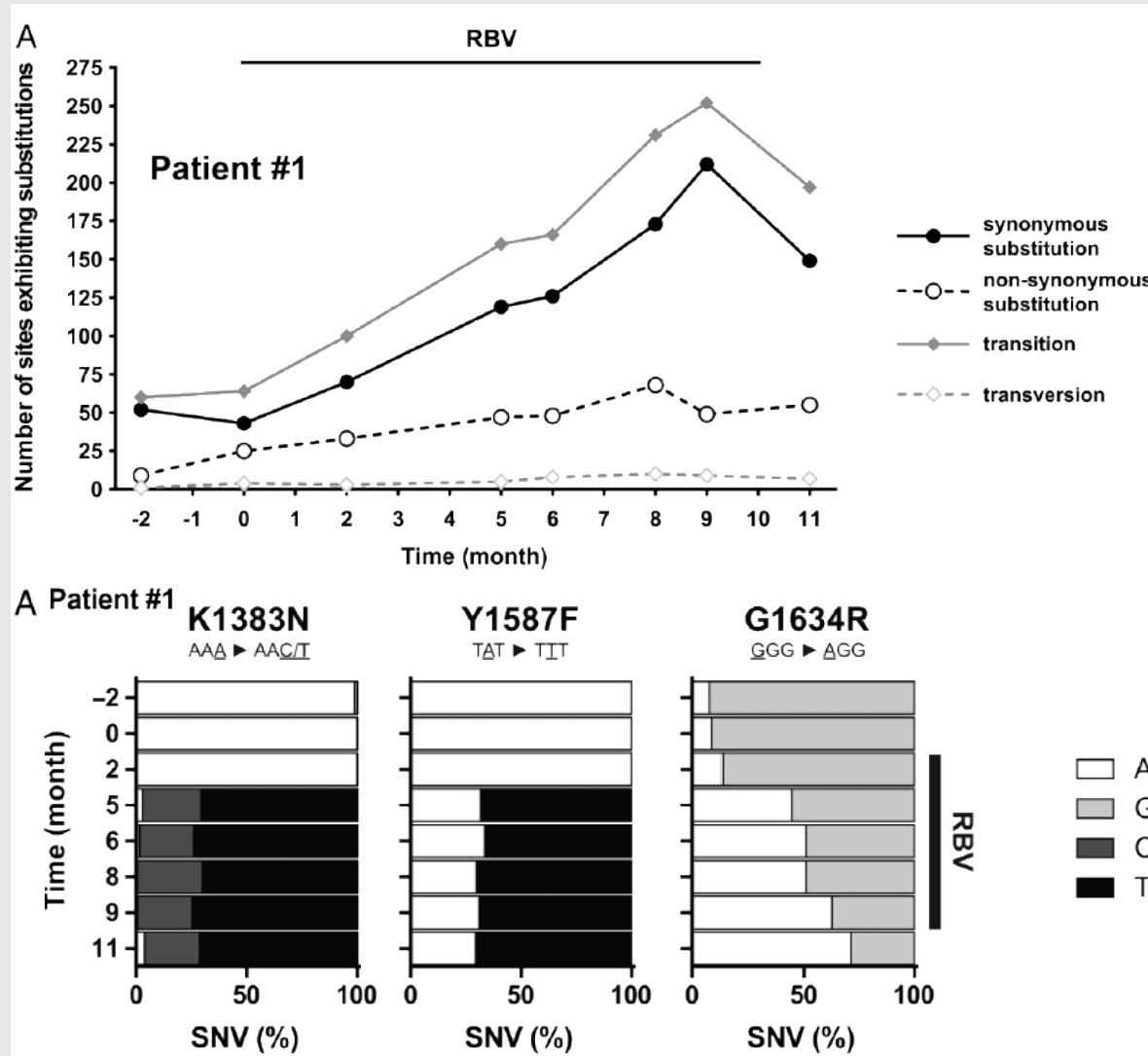
Todt & Gisa et al., *Gut* 2016

RBV increases the heterogeneity of the viral intra-host population



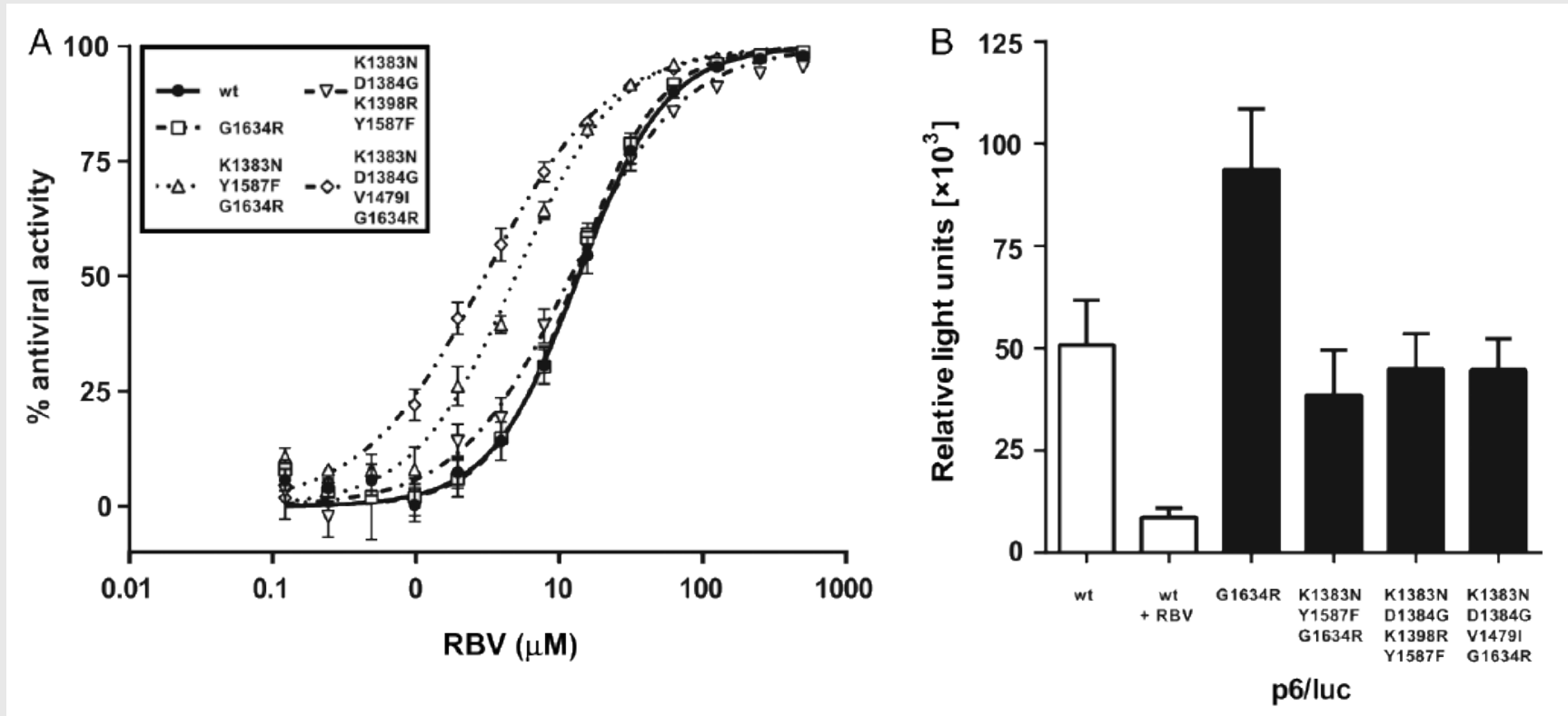
Todt & Gisa et al., *Gut* 2016

A *in vivo* identified SNV confers increase in fitness



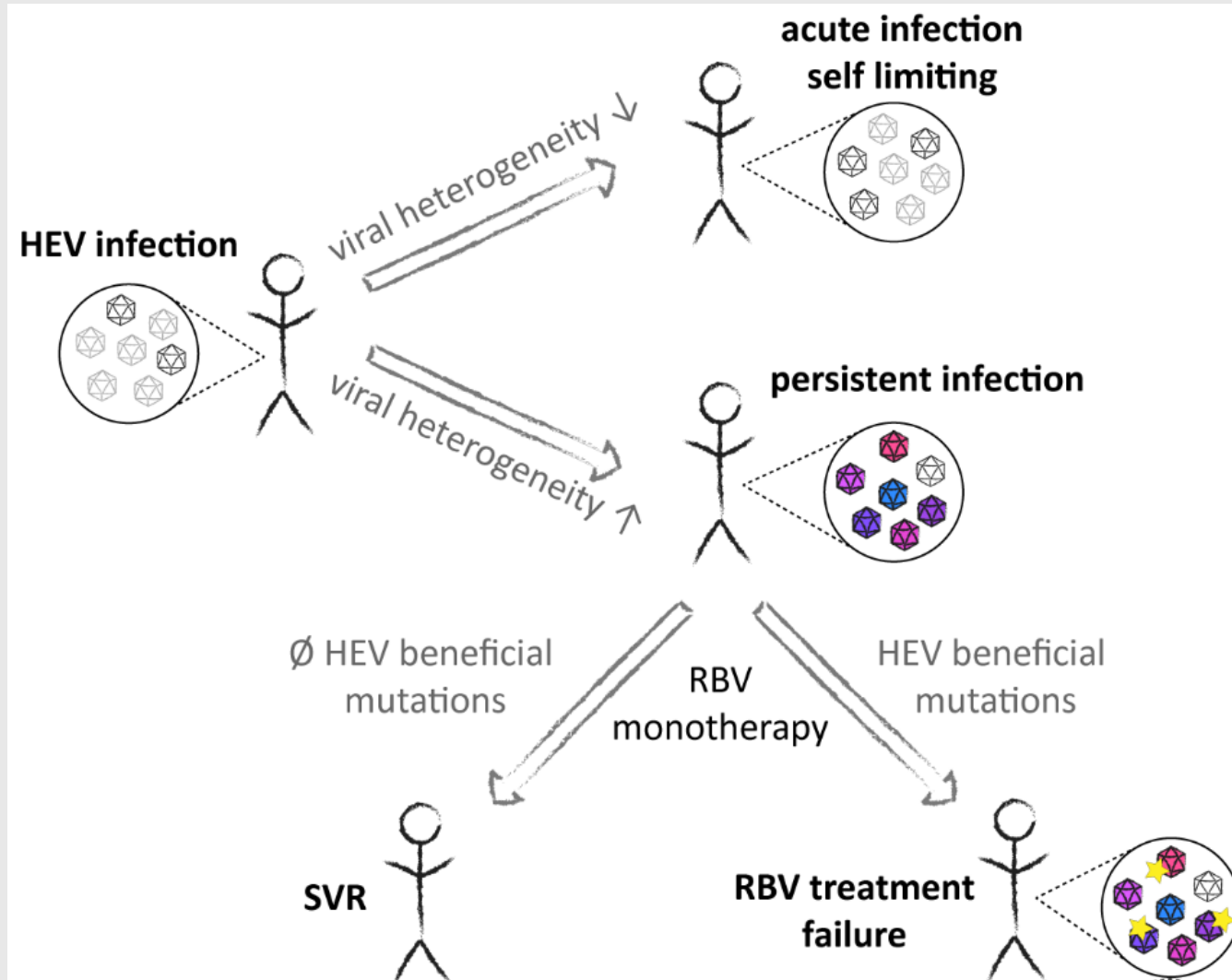
Todt & Gisa et al., *Gut* 2016

A *in vivo* identified SNV confers increase in fitness



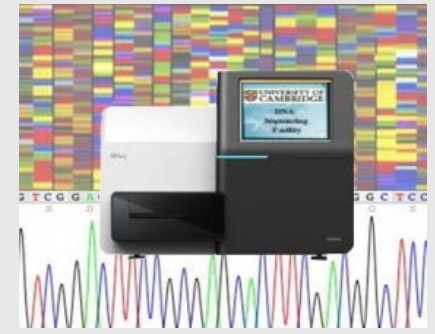
Todt & Gisa et al., *Gut* 2016

Summary



Todt et al., *Curr Opin Virol* 2018

Outlook





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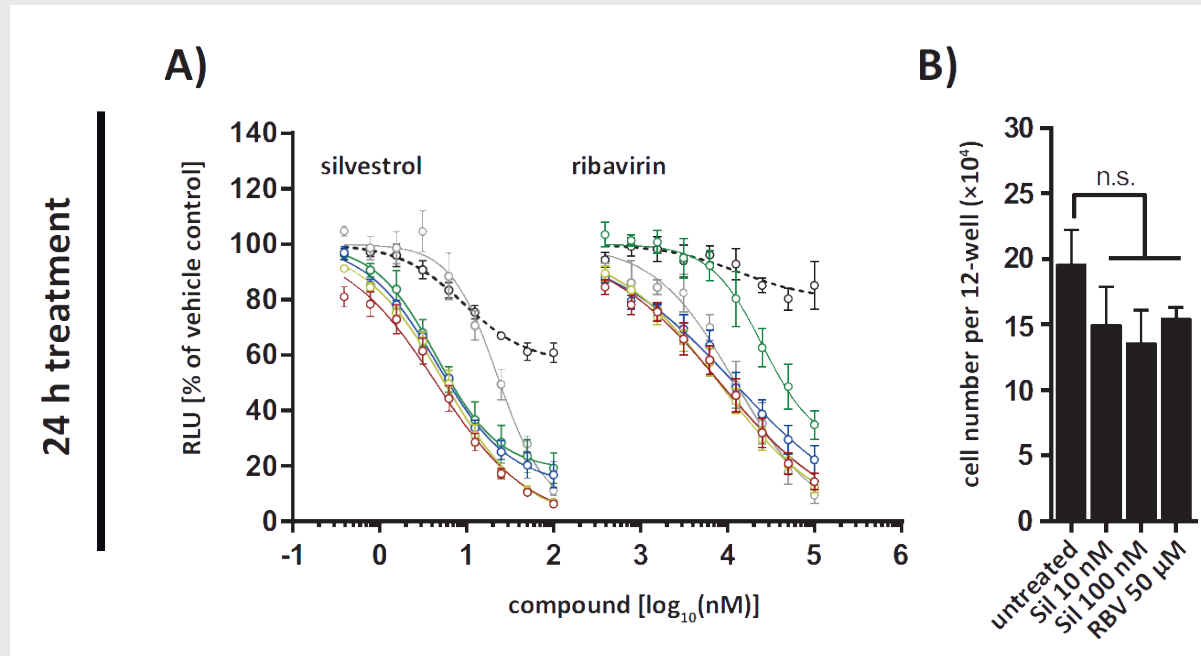
journal homepage: www.elsevier.com/locate/antiviral



The natural compound silvestrol inhibits hepatitis E virus (HEV) replication *in vitro* and *in vivo*



Daniel Todt^{a,b,1}, Nora Moeller^{b,1}, Dimas Praditya^b, Volker Kinast^b, Martina Friesland^b, Michael Engelmann^b, Lieven Verhoye^c, Ibrahim M. Sayed^{c,d}, Patrick Behrendt^{b,e}, Viet Loan Dao Thi^{f,g}, Philip Meuleman^c, Eike Steinmann^{a,b,*}





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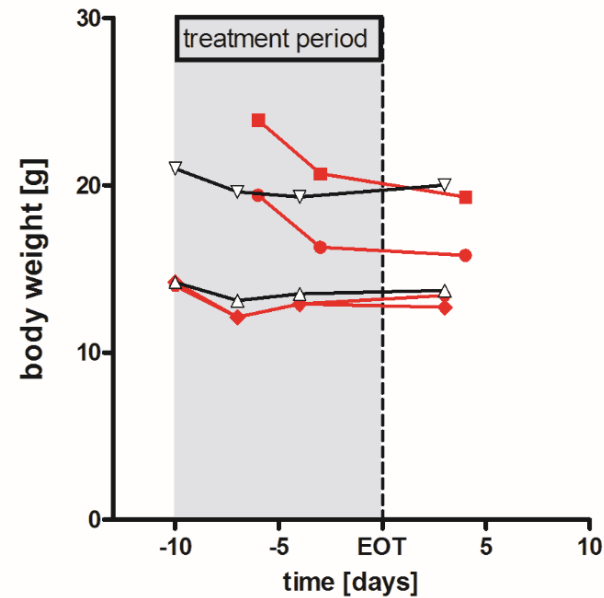
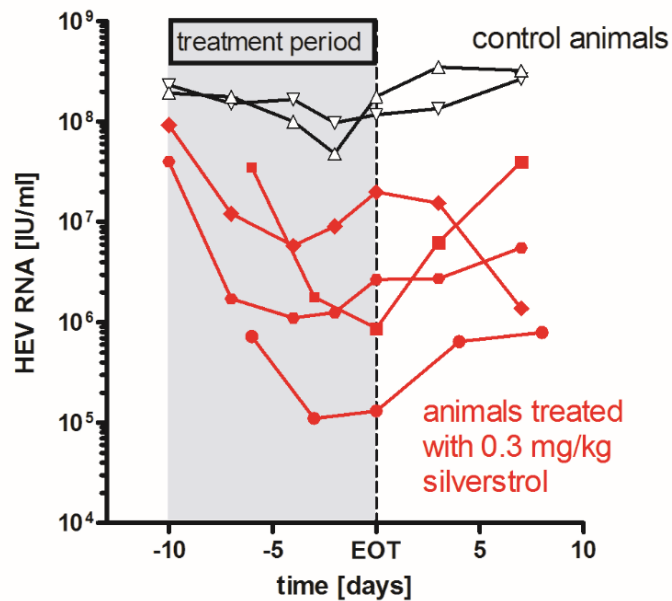
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