

**GUERIR DE L'HEPATITE B ?**

**YES WE CAN !**

**Professeur Christian TREPO**

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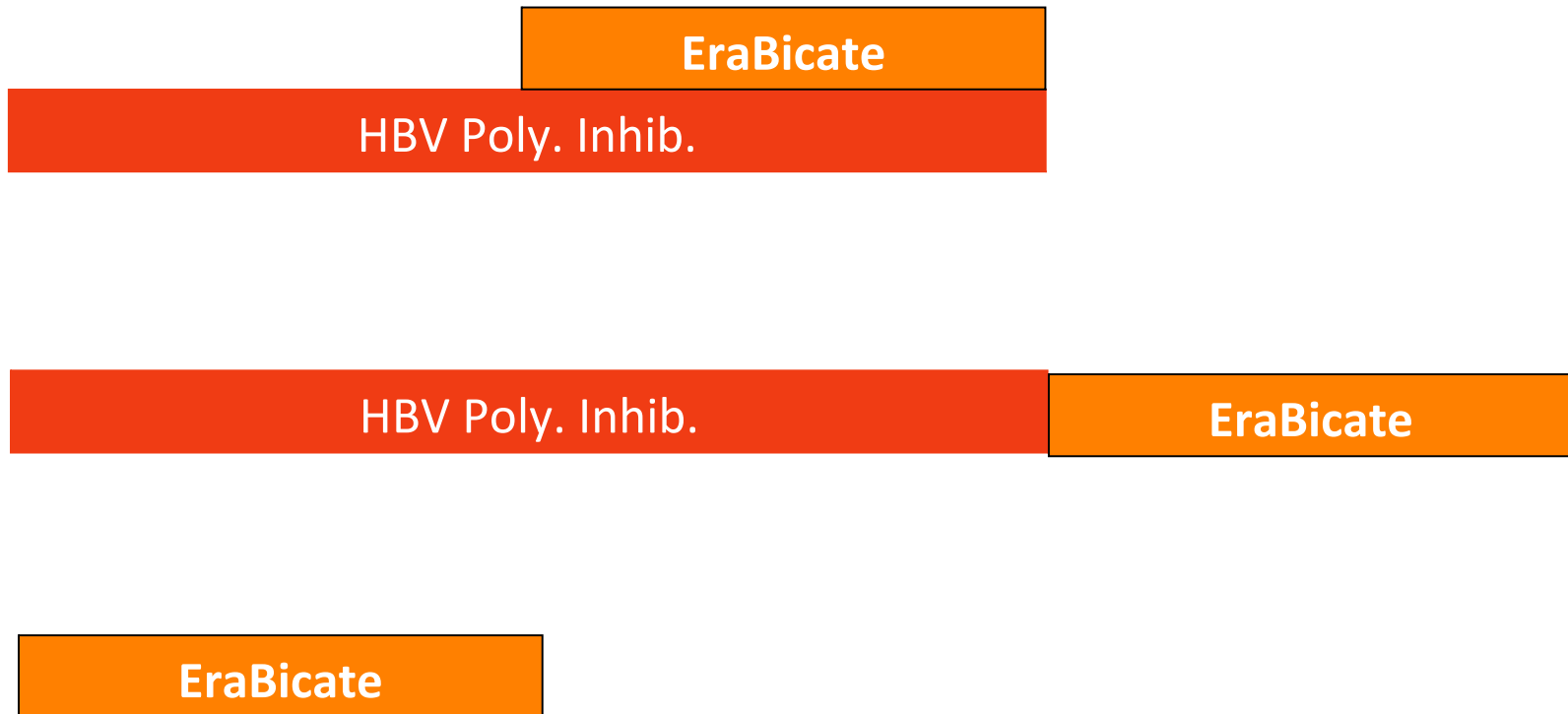
# **Pr. Christian TREPO, MD, PhD**

## **Liens d'intérêt :**

Grants, Boards, Workshops et Invitations à des congrès : Gilead, BMS, MDS, Janssen, AbbVie, ABIVAX,

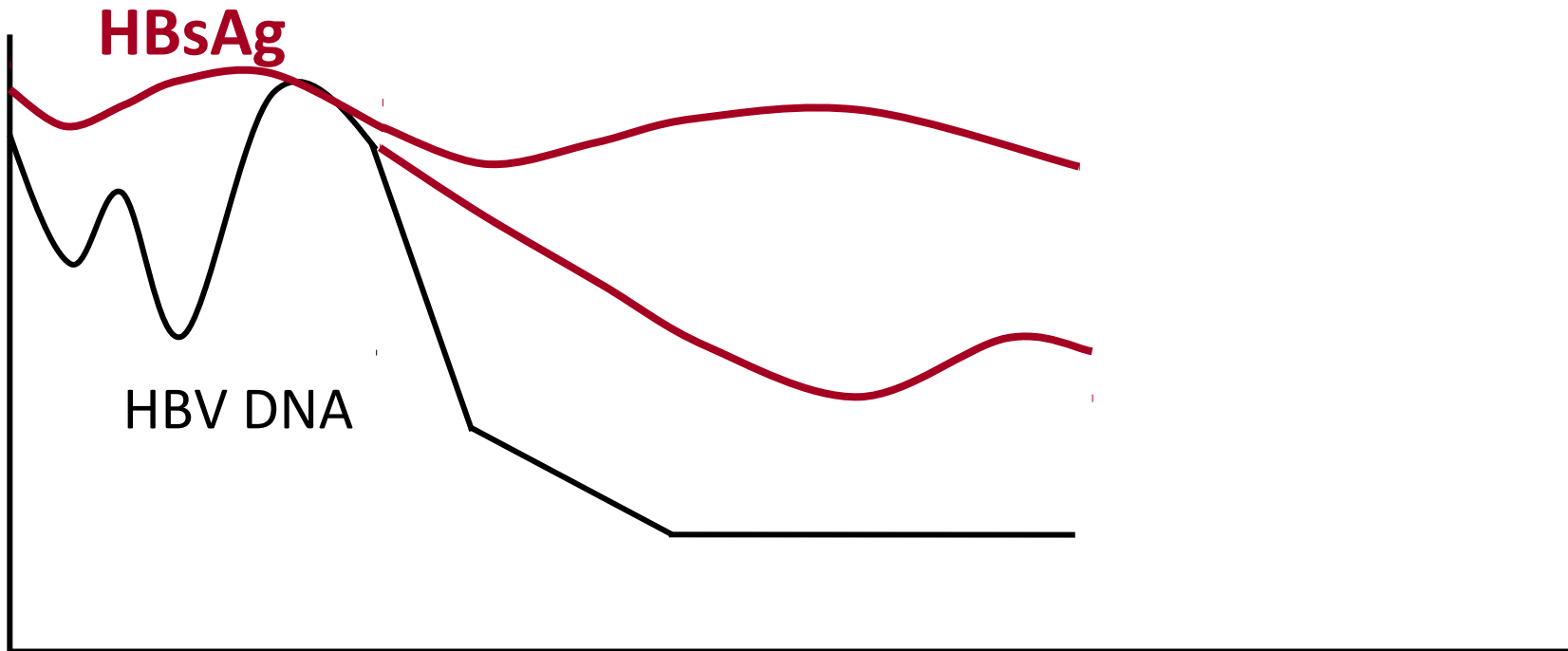
„Cure“ in Hepatitis B  
=  
HBsAg loss +  
Anti-HBs seroconversion

# The Magic Drug X

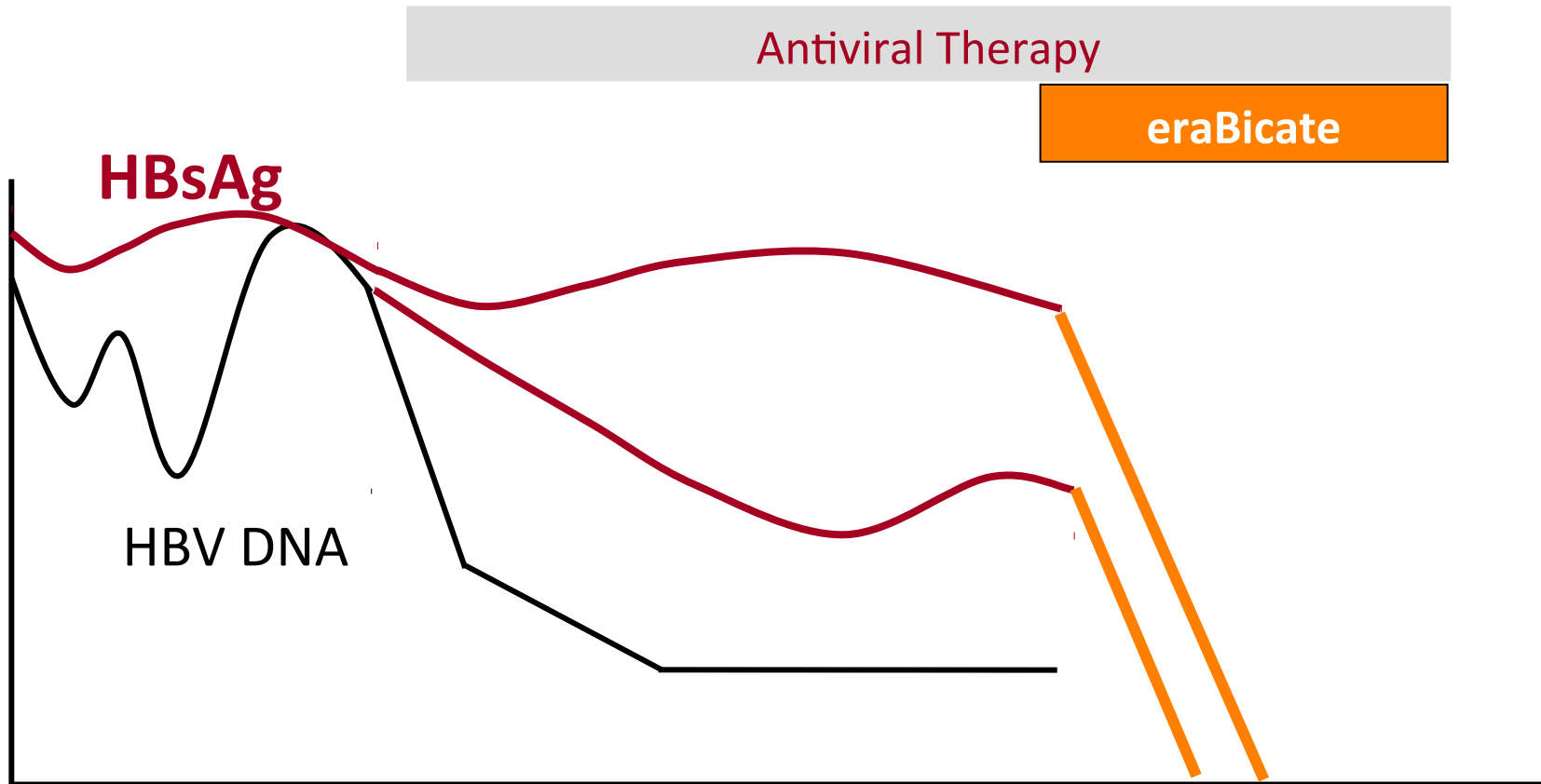


# Different Patterns of HBsAg during antiviral therapy

Antiviral Therapy

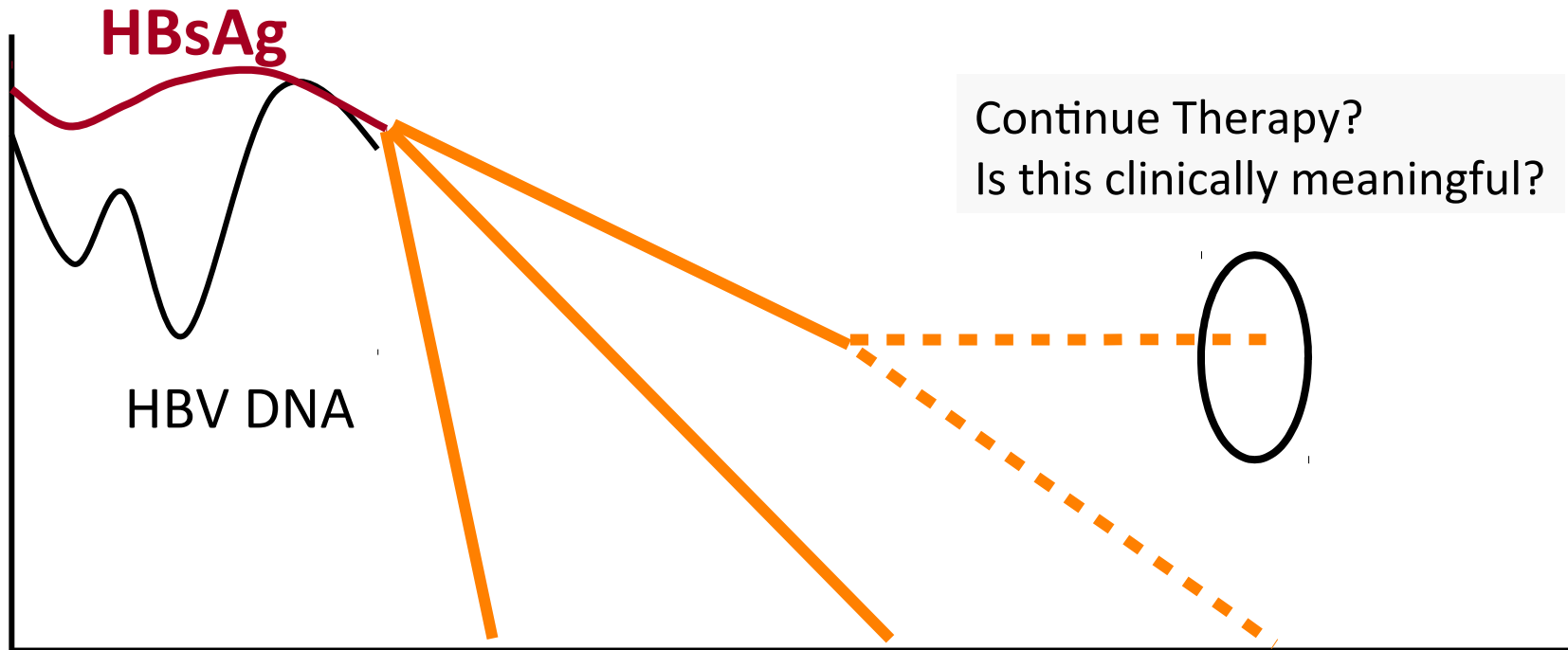


# HBsAg kinetics have to be considered in the development of novel curative therapies

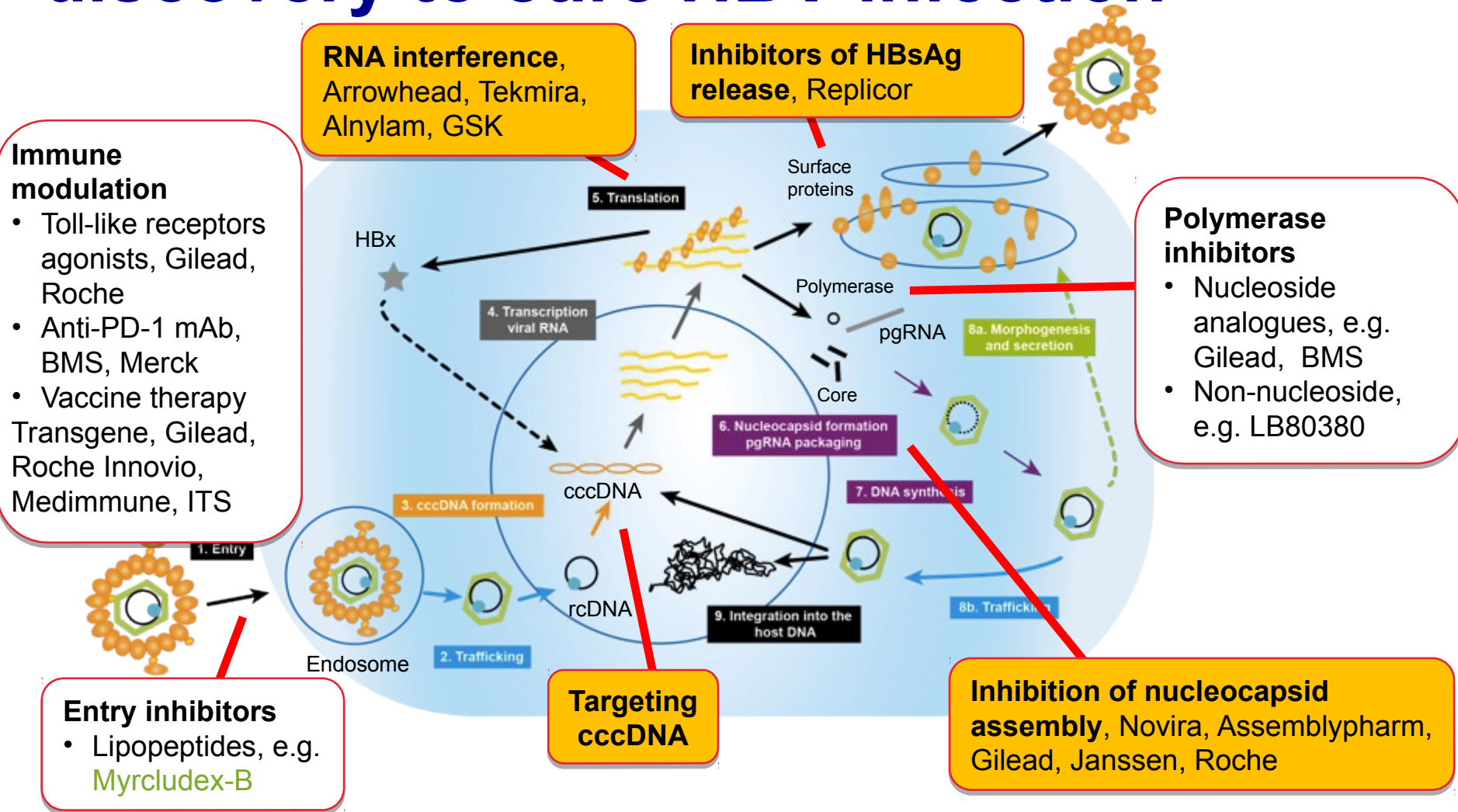


# Novel curative therapies as first line treatment?

eraBicate



# Future directions: target & drug discovery to cure HBV infection



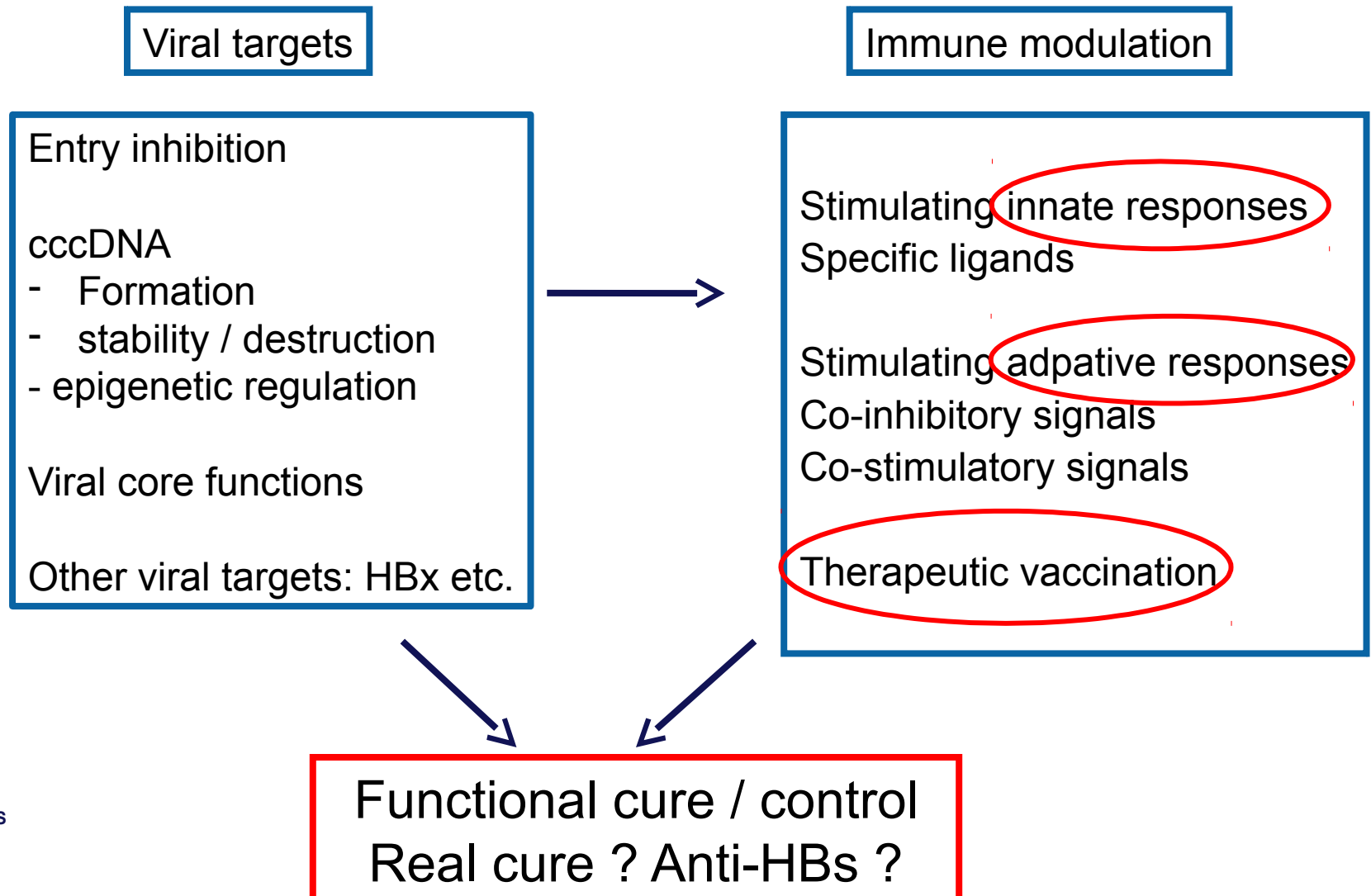
Development stage: **preclinical**, **clinical**

Zoulim F, et al. Antiviral Res 2012;96(2):256–9; HBF Drug Watch, Available at:

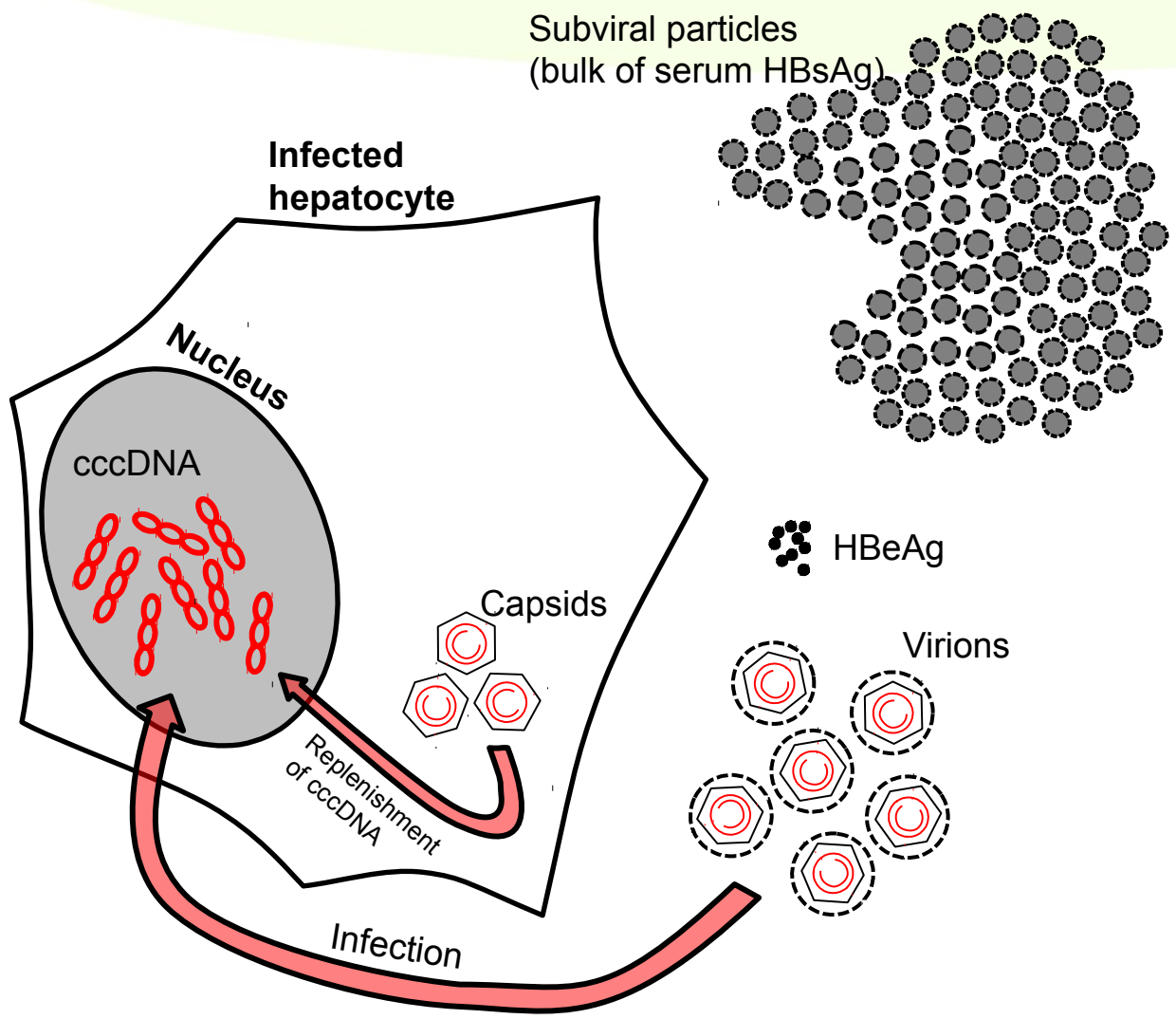
[http://www.hepb.org/professionals/hbf\\_drug\\_watch.htm](http://www.hepb.org/professionals/hbf_drug_watch.htm)



# The concept of combination therapy



# The immunological disorder in chronic HBV infection is caused by HBsAg

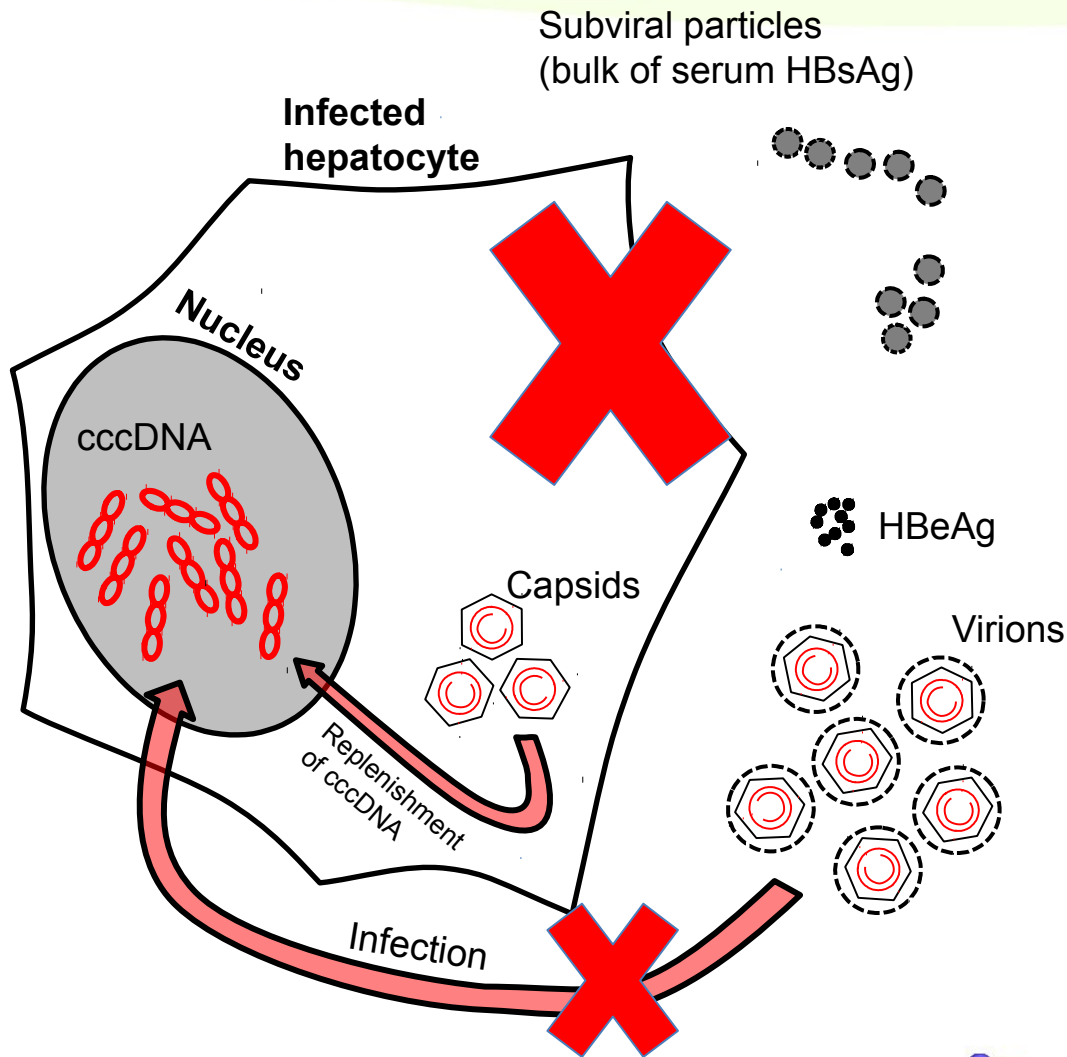


**HBsAg is the key:**

- Sequesters anti-HBs
- Suppresses innate immunity
- Suppresses T-cell proliferation
- Suppresses cytokine signaling
- Suppresses immunotherapy**

**HBsAg removal will be required to achieve high SVR rates**

# NAPs block the release of subviral particles (replicor)



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**HBsAg removal  
will be required  
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# REP 2139-Ca + short duration immunotherapy in HBV infection: serum HBsAg

REP 102 study: 12 patients treated, 2 non responders, 1 with 1.1 log reduction in HBsAg

9 patients with HBsAg clearance

Immunotherapy added  
in combination for the last  
12-26 weeks of treatment

Patient	Serum HBsAg (IU / ml)		Log reduction
	Start	Lowest observed	
1	70050	0.03	6.37
2	13400	0.01	6.13
3	3450	0.03	5.06
4	50994	0.03	6.23
5	87690	0.01	6.94
6	72968	0.02	6.56
7	17988	0.03	5.78
8	125000	0.02	6.80
9	1504	0.02	4.88

Dosing: 500mg once weekly by IV infusion **(2 hours, no tolerability issues)**

# Synergistic activation of immunotherapy in the absence of serum HBsAg

Serum anti-HBs production in an indicator of immune stimulation

REP 2139-Ca  
(HBsAg clearance)

REP 2139-Ca + immunotherapy  
(Pegasys® or Zadaxin®)



**anti-HBs level observed in 6%  
of patients after 48 weeks of  
Pegasys® alone**

**CURED !?**

**YES WE CAN !!!**