



**THE FORUM**  
For Collaborative Research<sup>SM</sup>

# HBV Forum Immune Monitoring Working Group (IMWG)

## Co-chairs

**Adam Gehring and Sara Ferrando-Martinez**

HBV Forum 5 – Vienna, April 10<sup>th</sup>, 2019

**Berkeley** Public  
Health

# Presentation overview

- Presentation of the group – IMWG members
- Presentation of the group – IMWG concept and objective
- IMWG first steps

# IMWG members

- **Ryan Anderson**, MS, MPH – PM, HBV Forum
- **Andre Boonstra**, PhD – Erasmus MC
- **An De Creus**, PhD – Janssen
- **Eric Donaldson**, PhD – US FDA
- **Sara Ferrando-Martinez**, PhD - AstraZeneca
- **Robert Fontana**, MD – U Michigan
- **Adam Gehring**, PhD – TCLD
- **Georg Lauer**, MD, PhD – MGH
- **Mala Maini**, PhD – U College London
- **Veronica Miller**, PhD – HBV Forum
- **Poonam Mishra**, MD – US FDA
- **Kirsten Richter**, PhD – Roche
- **Kathleen Whitaker**, PhD – US FDA
- **Teresa Wright**, MD – Consultant, clinical trial designs

# IMWG concept

- ❖ With the goal of finding a cure for CHB, novel agents are being developed targeting both the virus and the host
- ❖ Boosting HBV-specific immunity of CHB patients is a promising approach to therapy, but has been proven difficult
- ❖ A combination of therapeutic modalities will be required to meaningfully change treatment response rates in CHB
- ❖ Successful HBV therapies will likely have an immunological component – there is a growing need to improve immunological measurements

# IMWG – Goal

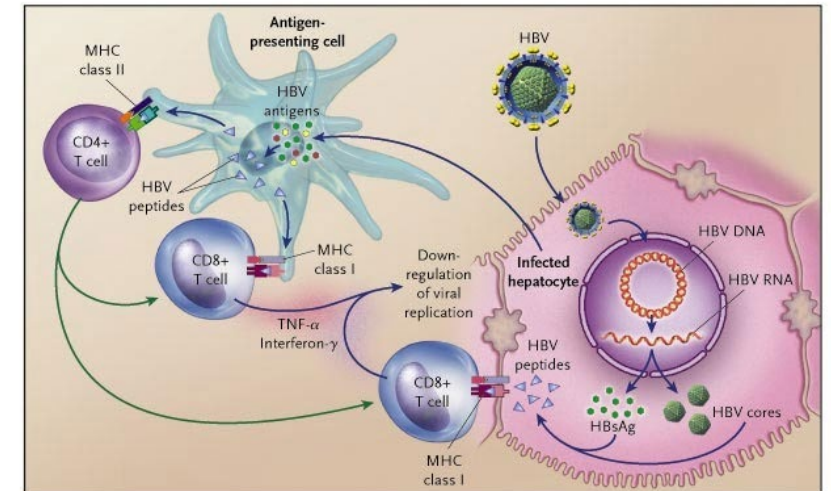
The **long-term** goal is to identify *immune biomarker(s)* that

- predict **effective viral control** and/or **toxicity** in
- identify patients more likely to **respond** to

therapies including immune-based interventions

# IMWG concept

- ❖ Immunology can support clinical trials but there are challenges
  - ❖ Most informative immunological assays are complex and difficult to standardize (standardization and clinical validation will be a must for clinical trials)
  - ❖ Reproducibility can depend on the volume of sample
  - ❖ HBV-specific T cells are extremely rare
  - ❖ Peripheral blood is more accessible but we don't know (yet) to what extent it represents the immune responses within the liver



# IMWG – Objectives

## Acknowledging the challenges involved, the IMWG will work towards:

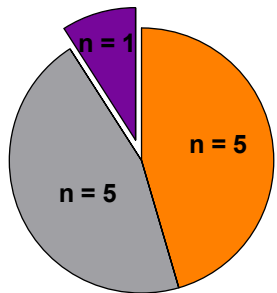
- Identifying a minimum set of basic assays, and the protocols to implement them, to facilitate cross-trial and cross-study comparison
- Consider to what extent assay standardization recommendations can be made (complementing the work of ICE-HBV for reagents)
- Join forces to use standardized assays to identify biomarkers for immune-based interventions that predict:
  - **Effective immunological control**
  - **Toxicity**
  - **Patients more likely to respond**

# IMWG – First steps

Develop a **white paper** to identify all the immune-based assays currently used by the HBV community: standardization, strengths and deficiencies

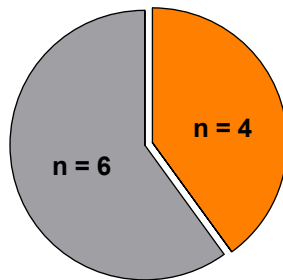
- Gather information about common assays from the forum members

Phenotypic analysis



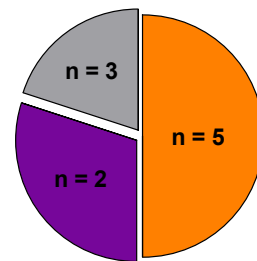
■ Ex vivo Multimers  
■ Expanded Multimers  
■ CyTOF Multimers

T cell activation



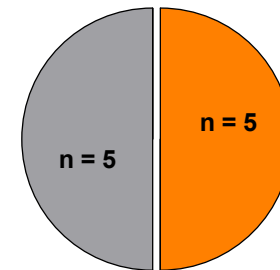
■ Described synthetic peptides  
■ Overlapping libraries  
■ Recombinant antigen / proteins

Functional assays (I)



■ Ex vivo ELISpot  
■ Expanded ELISpot  
■ Ex vivo FLUOROSpot  
■ Expanded FLUOROSpot

Functional assays (II)



■ Ex vivo Flow  
■ Expanded Flow  
■ CyTOF

*NK assays*  
*Cytotoxicity (NK and T cells)*  
*Proliferation*  
*Gene expression*  
*Single cell RNAseq*  
*Transcriptomics*  
*Luminex (...)*



# IMWG – First steps

Develop a **white paper** to identify all the immune-based assays currently used by the HBV community: standardization, strengths and deficiencies

- Gather information about common assays from the forum members
- Determine which working group members have most knowledge of each assay, and assign sections accordingly
  - Make sure we cover non T cell based immune assays
  - Look for external collaborators for assays that forum members are not familiar with?

# IMWG – First steps

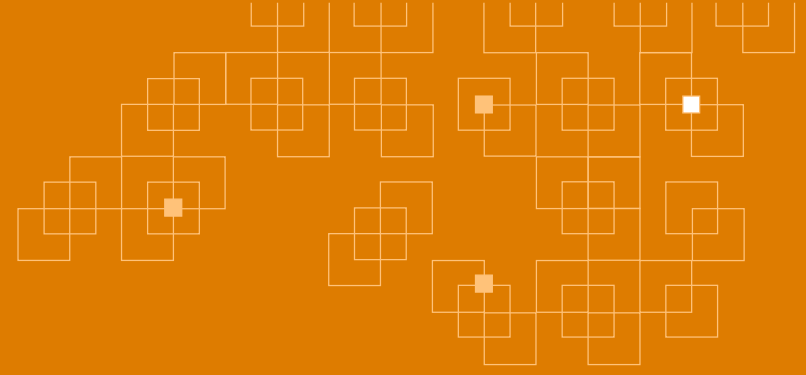
Develop a **white paper** to identify all the immune-based assays currently used by the HBV community: standardization, strengths and deficiencies

- Gather information about common assays from the forum members
- Determine which working group members have most knowledge of each assay, and assign sections accordingly
- Include a section about FDA requirements for these assays to be recognized as part of an IND (FDA CDRH and FDA DVAP forum members)

# Immune Monitoring Working Group



**Ready to start!**



**Thanks!**