Gilead Biomarkers

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Biomarker Sciences Mission

Employ biomarker and translational research to further our understanding of specific aspects of biology, inform research, development and pipeline decisions, and advance the effectiveness of available therapies in appropriate patient populations

"We generate insights for the Project Team to deliver the right drug at the right dose to the right patient"

Biomarker Sciences engages pre-clinically & supports through all stages of development

How Biomarker Sciences Impacts Drug Development

Pre-NME

- Determine target modulation and disease impact partnered with Biology
- Develop new assays or utilize existing assays for use in clinical trials
- Evaluate and onboard relevant technologies

Ph 1-4

- Generate project and program biomarker strategy with stakeholders
- Lead cross-functional Biomarker Sub-Team to execute strategy
- Results inform Project Team, provide feedback to Research and support Commercialization

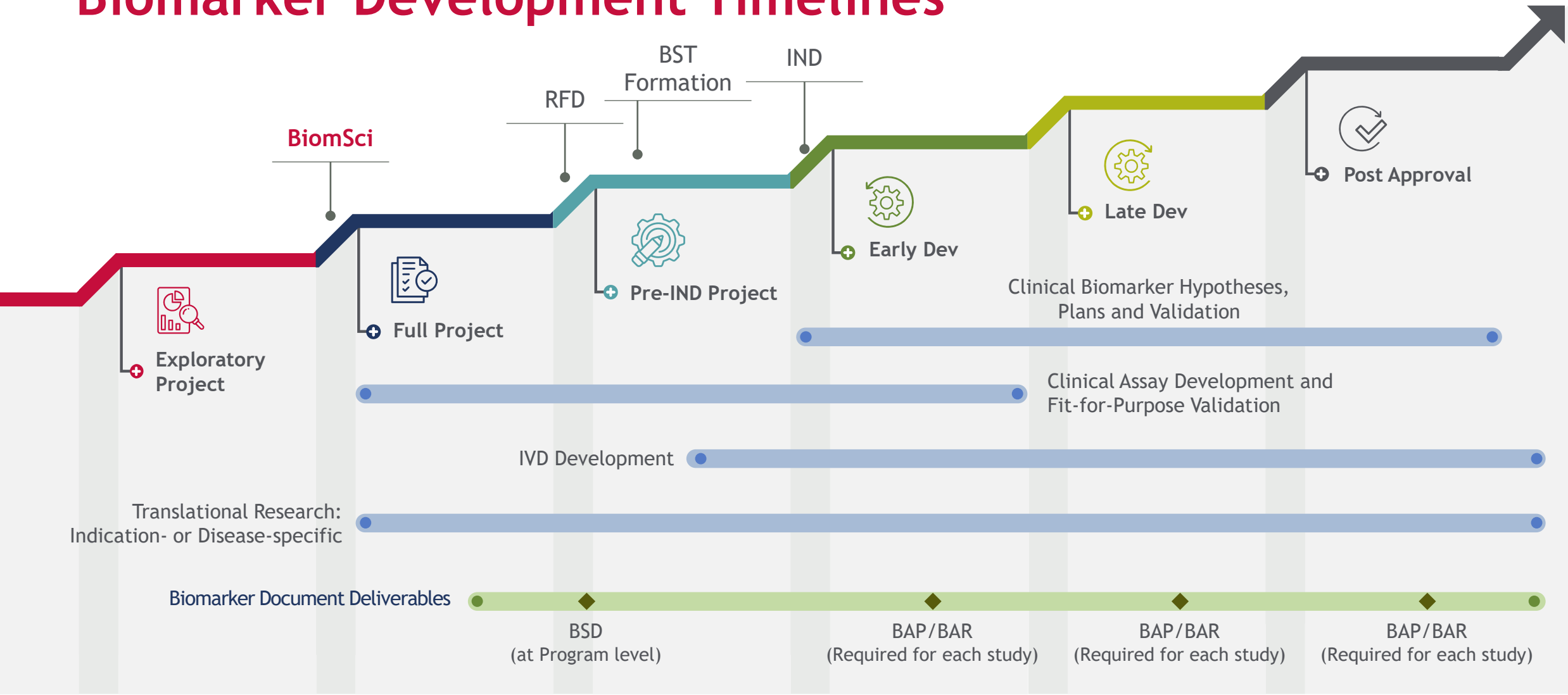
In Vitro Diagnostic (IVD)

- Determine biomarker to IVD transition potential
- Identify and establish IVD partner and lead collaboration through regulatory clearance/approval
- Support global roll-out of IVD by partnering with Development/Commercial

Translational

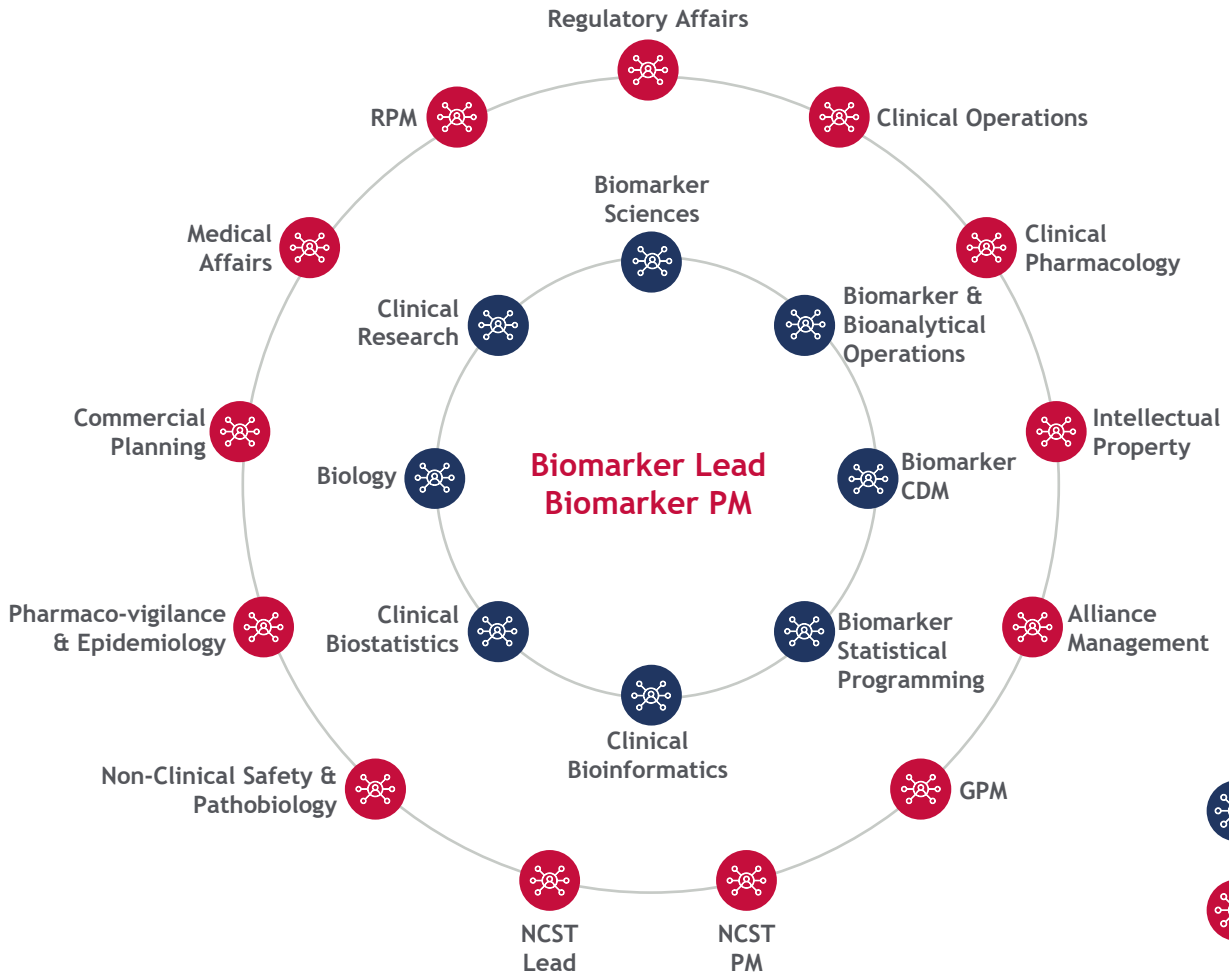
- **Data-based (Mol Epidemiology Group)** Leverage Real World Data for correlates of response to SoC, patient journey, diagnostics used (partner R&D)
  Sample-based: With R&D, establish targeted translational projects for deeper exploration of pathobiology
- Partner with academic groups to address R&D aims

Biomarker Development Timelines



Biomarker Sub-team (BST)

- Cross-functional collaborative matrix team
- Support biomarker work that enables clinical development
- Consists of core and extended team members
- Co-led by Biomarker Lead and Biomarker PM



Core members: Expected to attend and contribute to all meetings

Extended members: Receive meeting invitations and materials; attendance is agenda-driven

- *One example of BST; membership is program-dependent and determined by BL and BPM*
- *Refer to slide 23 for abbreviations*

Biomarker Categories

Disease related biomarkers

Therapy related biomarkers

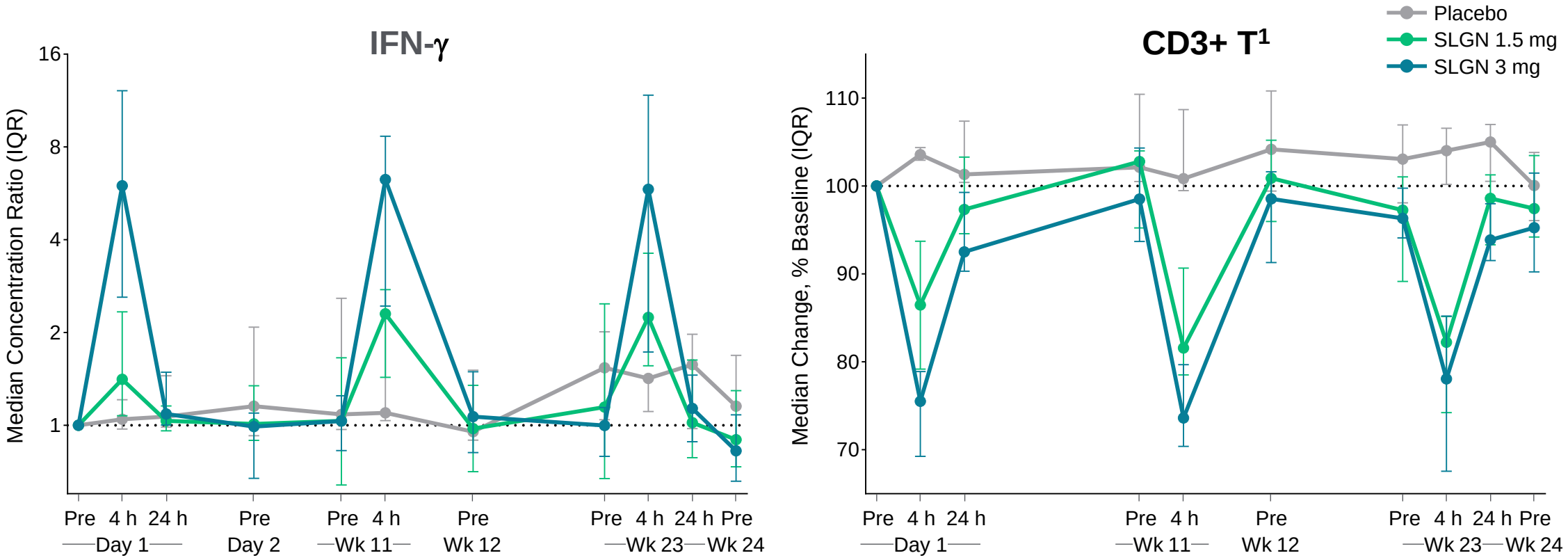
Prognostic/ disease covariates	Surrogate endpoint	Disease monitoring	Pharmaco - dynamic	Mechanism of action	Predictive	Mechanism of resistance	Safety
Predict probable disease progression	Early read - out clinical efficacy	Monitor disease progression/ recurrence	Enable dose selection	Confirm expected mechanism of action	Predict likely response or adverse event	Enable RX decisions/ inform future targets	Monitor adverse event/ toxicity

Clinical trial design/ patient stratification

Dose / therapy adaptation

Therapy selection

Change in Peripheral Cytokines and Immune Cell Populations With SLGN Dose

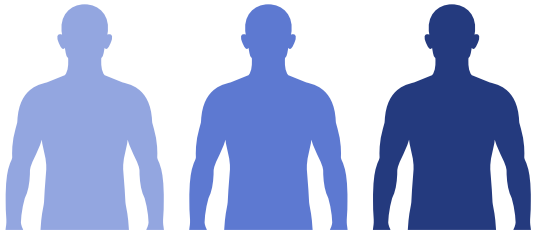


- Similar to IL-12p40 and IL-1RA, IFN-γ responses were dose-proportional and no tachyphylaxis
- SLGN treatment induces transient margination of T cells

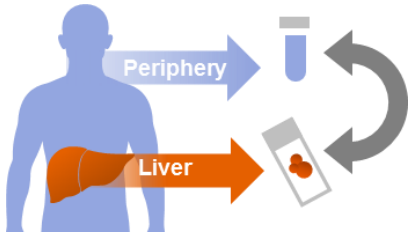
IQR, interquartile range. 1. Dunbar R, et al. AASLD 2019.

HBV/HDV Translational Efforts

Clinical Development

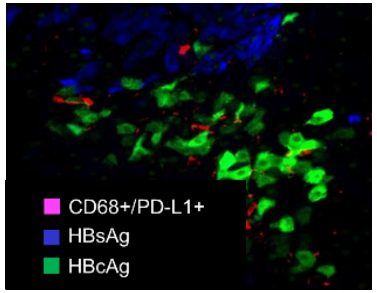


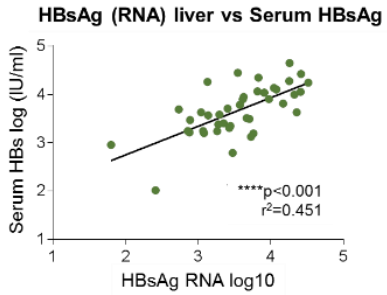
Patient Selection



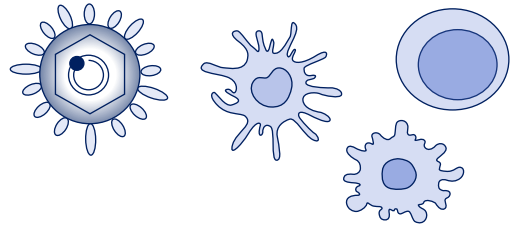
Predictive Biomarkers

Translational Programs

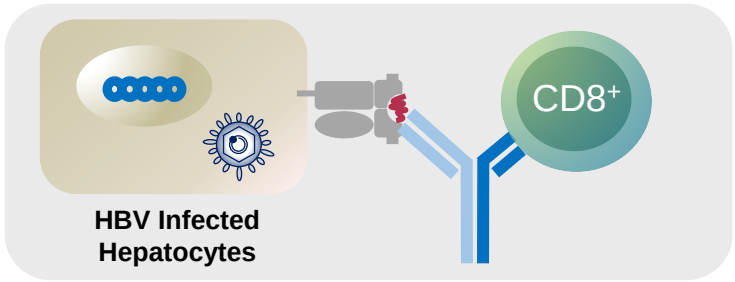




Research

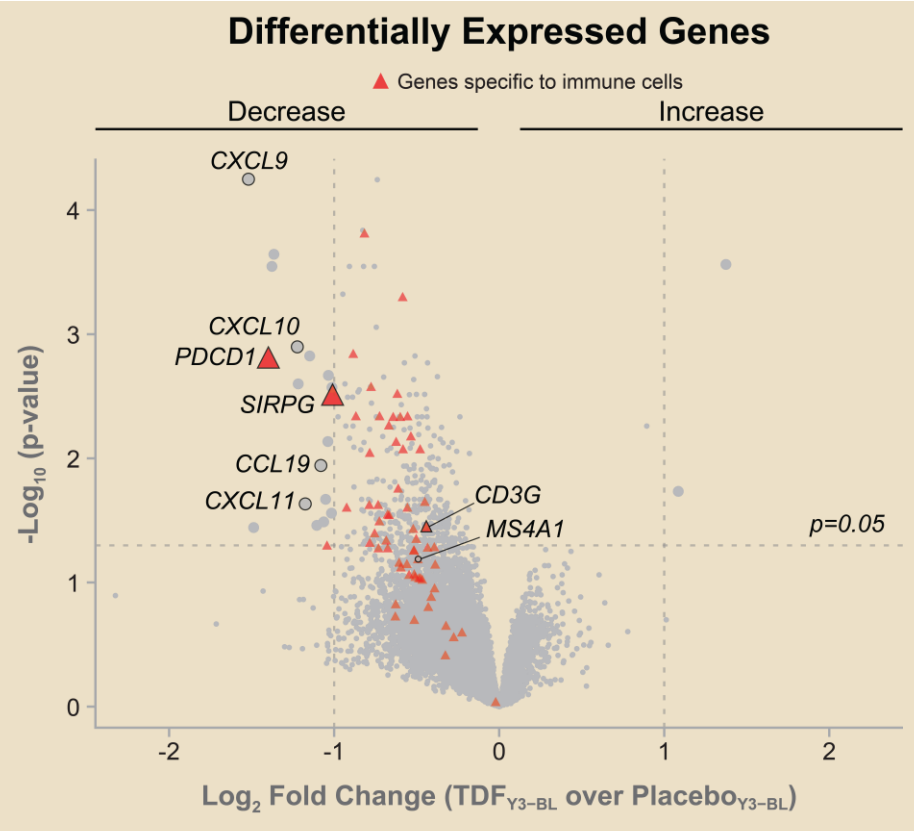


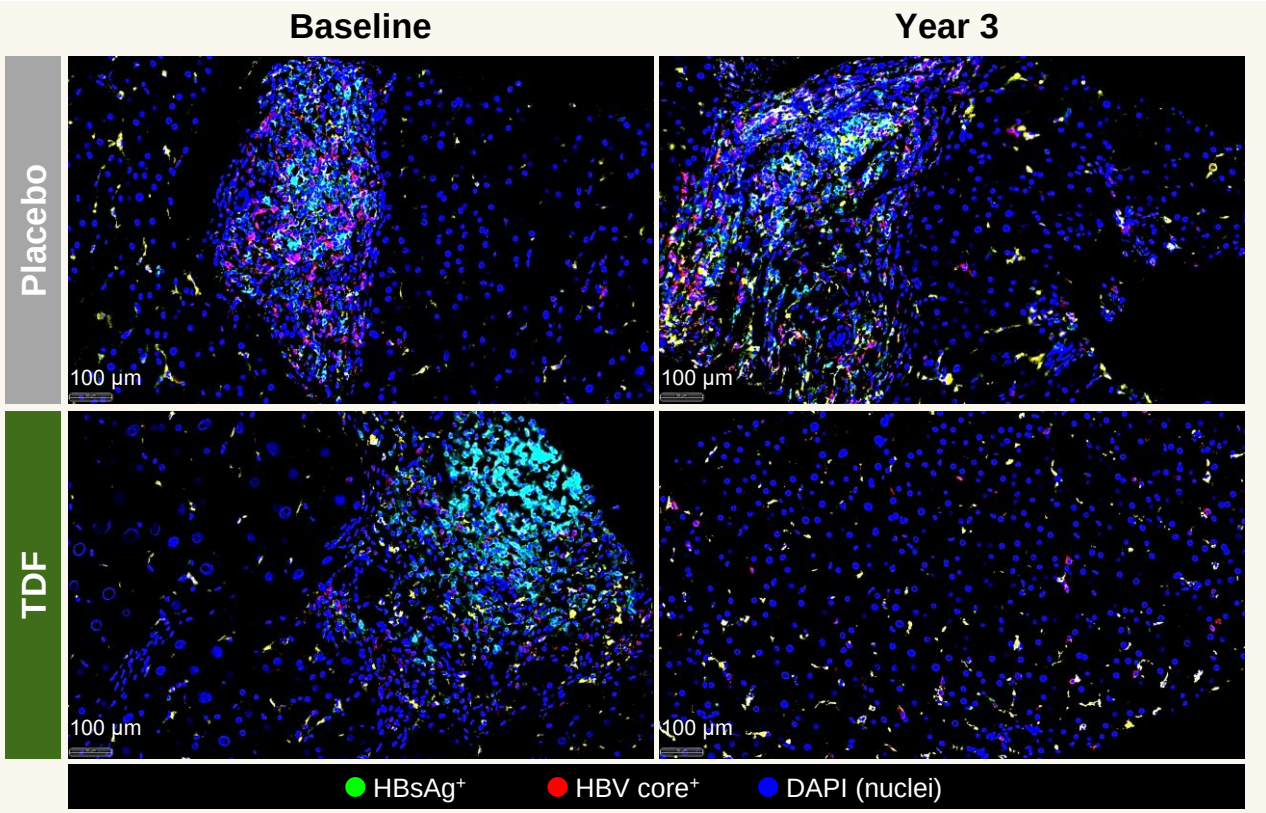
Relevance of Pathways



Novel Biology

NUC Treatment Significantly Suppressed Intrahepatic Inflammation*



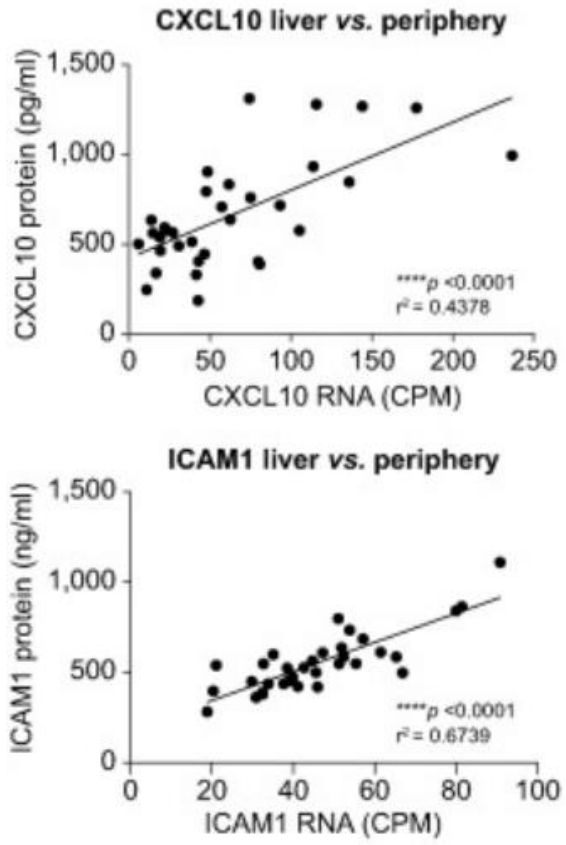


- Differential gene expression analysis of TDF vs placebo treatment showed a significant reduction in expression of genes encoding chemokines and genes enriched in immune cells
- Liver immune microenvironment analysis by mIF showed reduction in liver inflammation with 3 years of TDF treatment compared with placebo

*p-values were derived by moderated t-test and adjusted for false discovery rate (FDR) using Benjamini-Hochberg procedure. DAPI, 4′,6-diamidino-2-phenylindole; Y3–BL, change from baseline to Year 3.

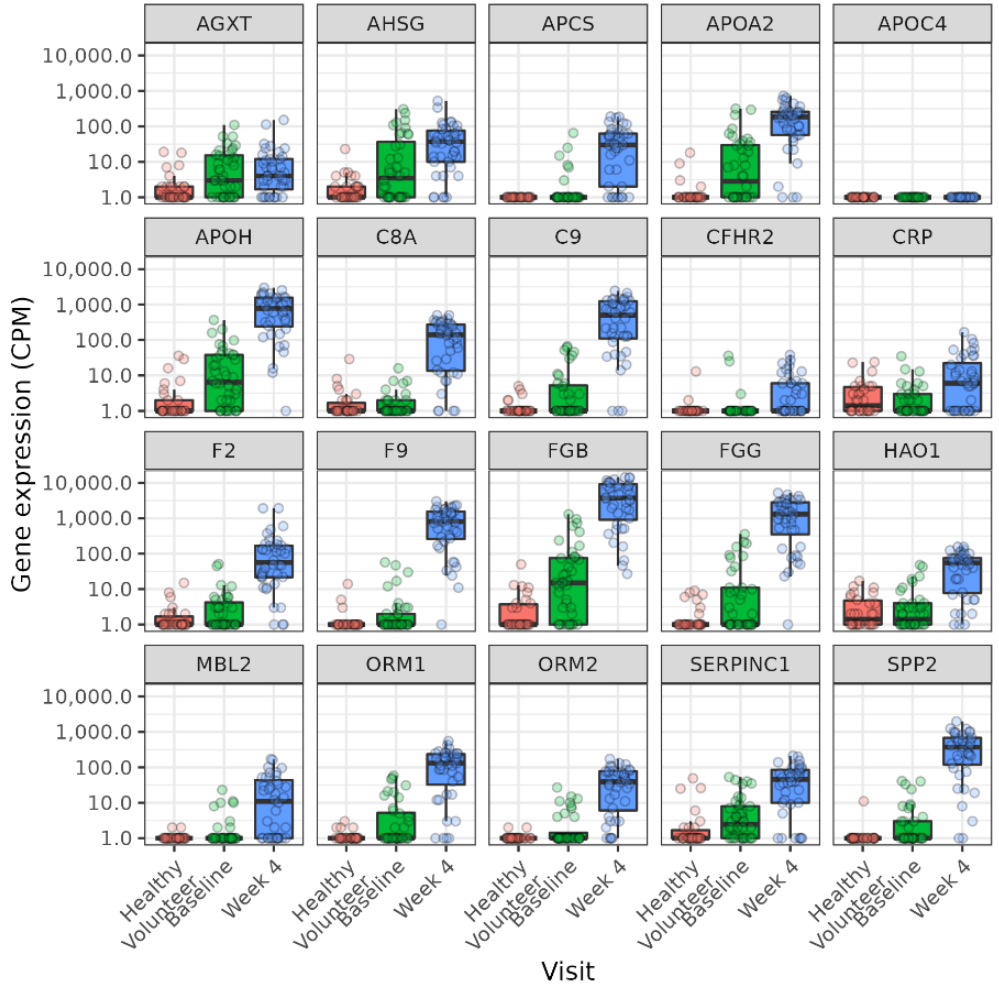
Peripheral Markers of HBV Infected Liver?

Correlation of liver gene expression with peripheral protein readouts



Van Buuren et al., J Hep Rep 2021

Liver specific genes upregulated in exosomes following PEG treatment



Cortese et al, Keystone, 2022