

Parameters to Guide Detection & Timing of Immunotherapy

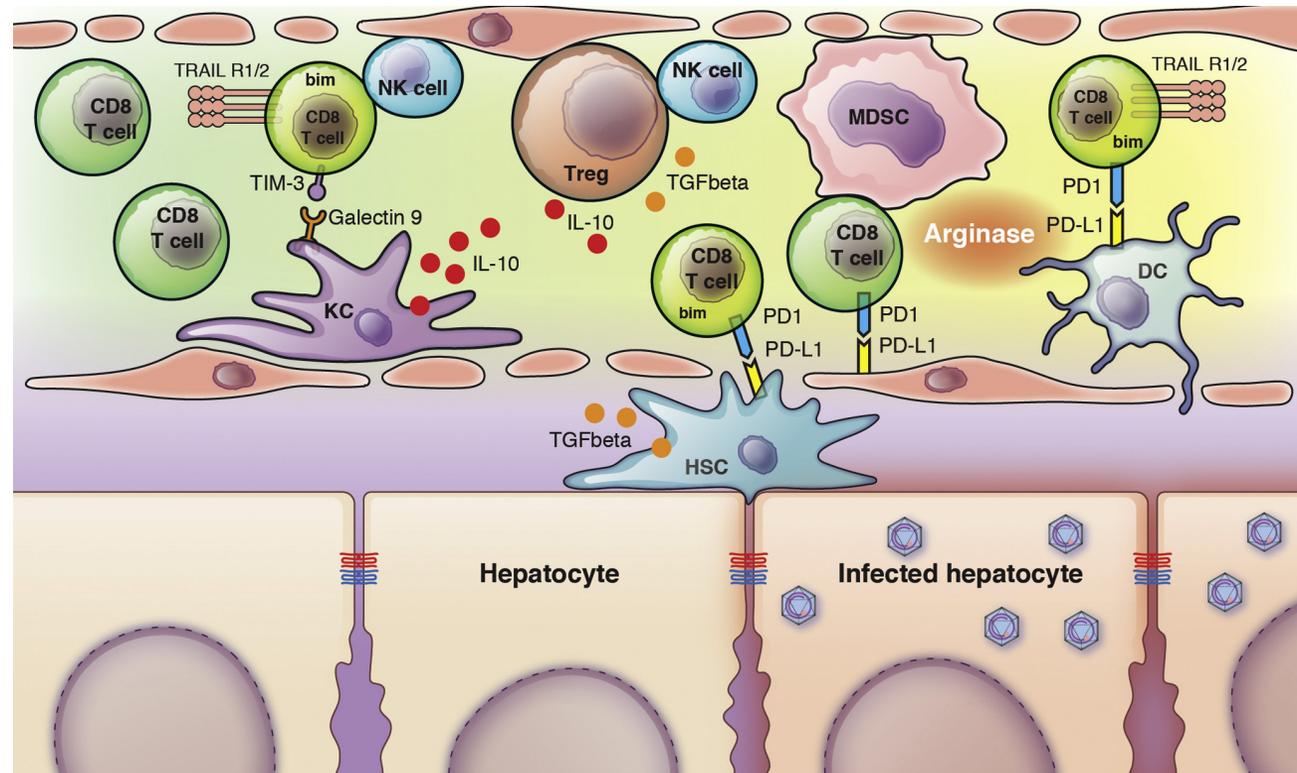
The Case for Immunological Parameters

Kramvis, A. *et al.* A roadmap for serum biomarkers for hepatitis B virus: current status and future outlook.

Nat Rev Gastroentero 1–19 (2022) doi:10.1038/s41575-022-00649-z.

Regulation vs. Prediction of Immunity

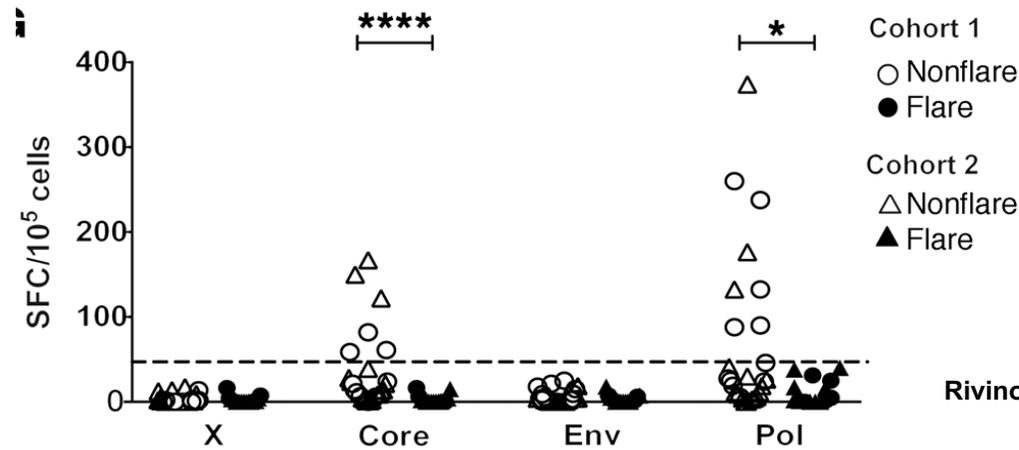
- Wealth of data on mechanisms that regulate immune response in chronic HBV (CHB) patients
- Can we turn that knowledge into a biomarker that can select patients for immunotherapy?



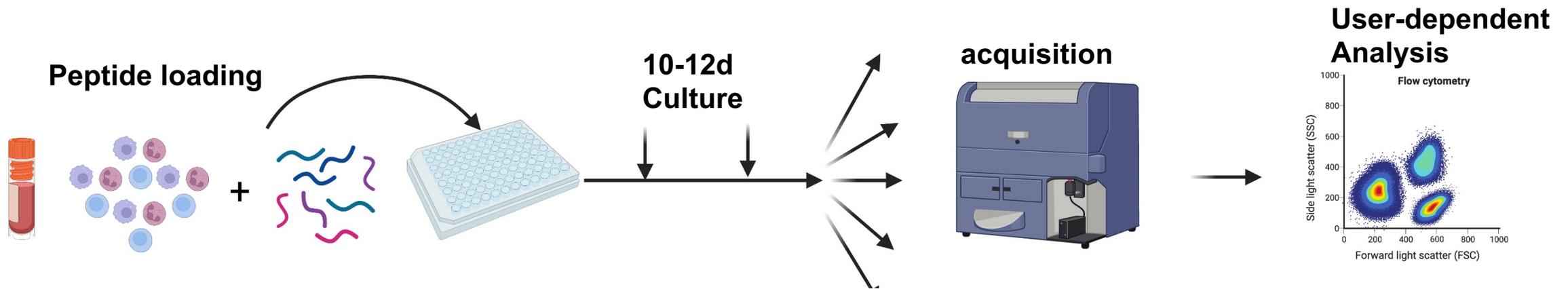
Best Association with Viral Control is the T cell Response

➤ Can existing T cells predict viral control? Maybe

- Patients with more core and polymerase specific T cells did not have flare after stopping Nuc therapy

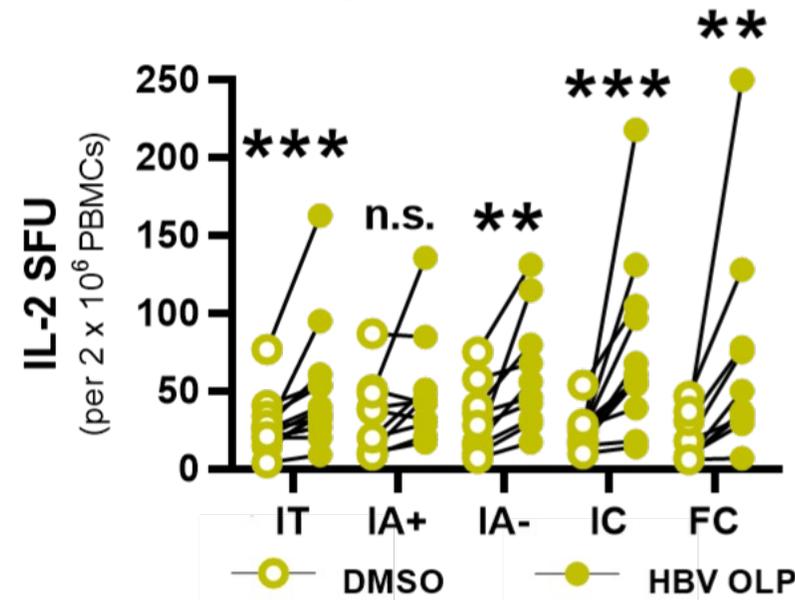
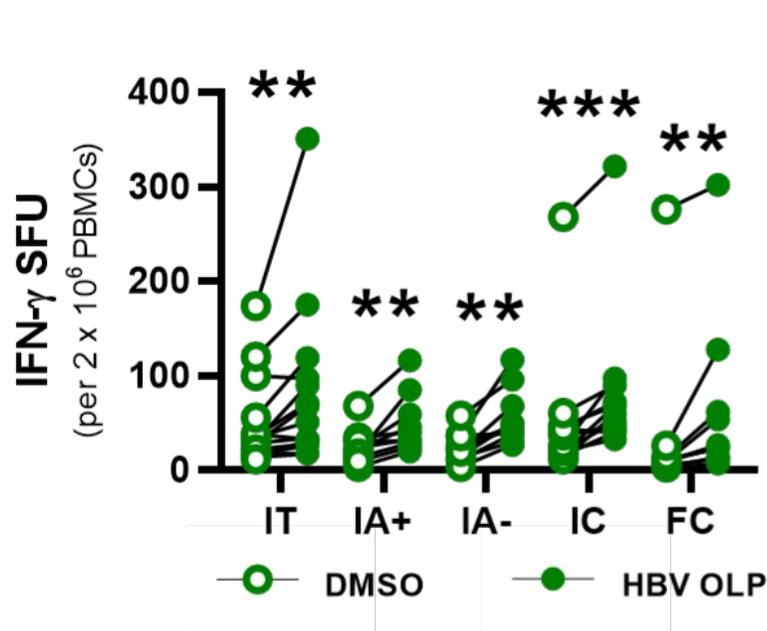


Rivino, L. et al. *J Clin Invest* 128, 668–681 (2018).

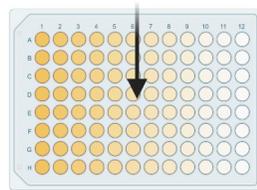
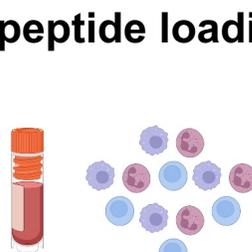


Best Association with Viral Control is the T cell Response

- Can existing T cells predict viral control? Maybe
 - Ex vivo data minimizes handling
 - ELISpot/Fluorospot minimizes user-dependent analysis



Cell + peptide loading

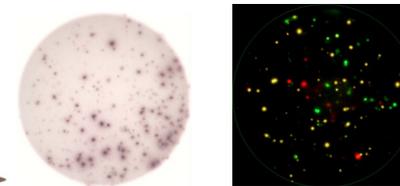


24h

acquisition



count spots



Should we use Pre-existing T cell Immunity to Stratify

Therapeutic vaccines

Patient selection parameters: none

- Highly specific
- Little chance of off-target toxicity

Timing:

- Monotherapy: no time consideration
- Combination therapy (siRNA/ASO): ~3 - 6 months before end of antiviral therapy
 - HBsAg reaches nadir ~6 m
 - Expected peak in T & B cell frequency at therapy termination
- Combination anti-PD-1
 - final vaccine boost

anti-PD-1/PD-L1

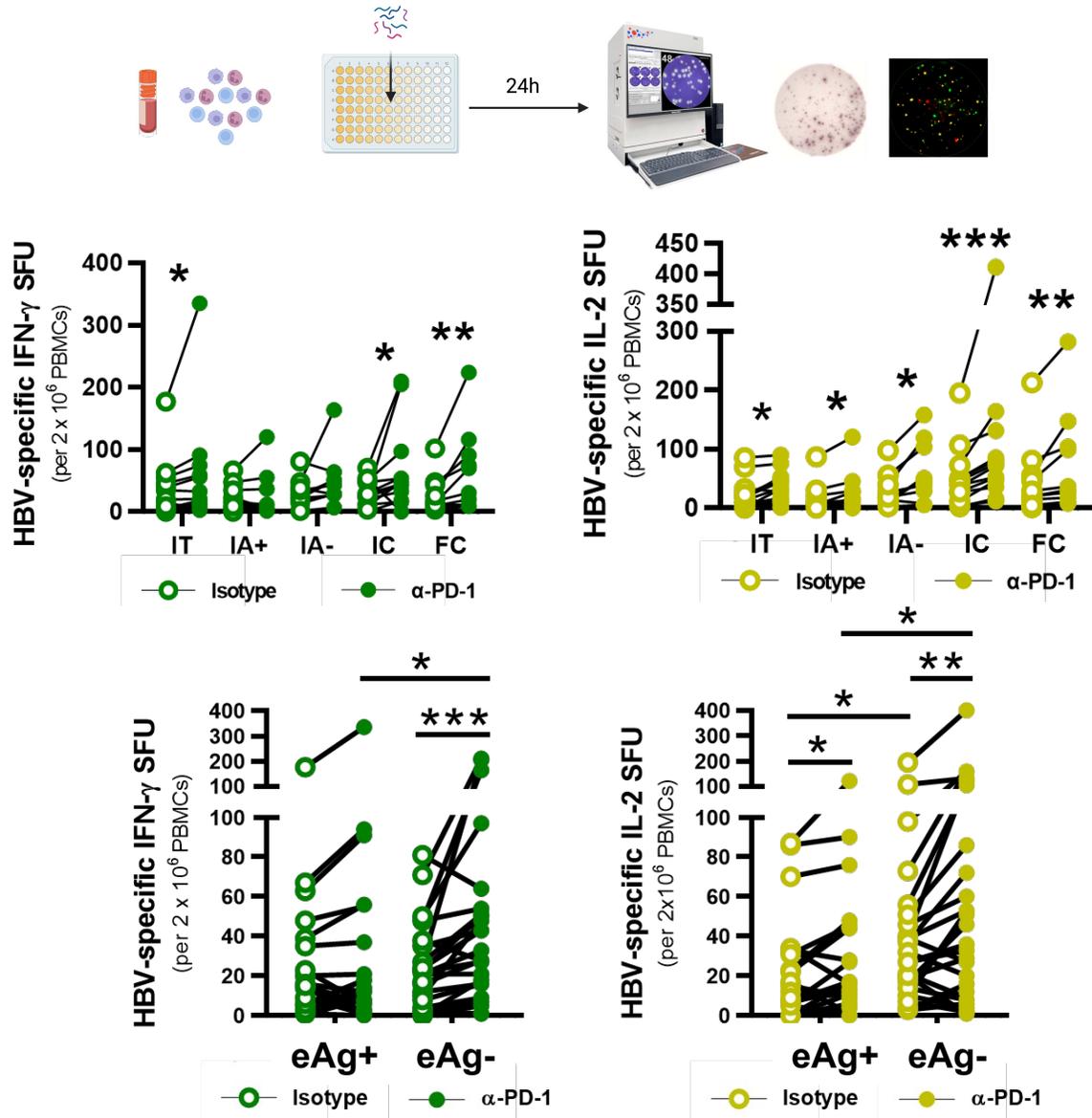
Patient Selection

- Relevant because of immune-related adverse events (irAEs)
- Exclude patient susceptible to autoimmunity: auto-antibody screens
- Include patients likely respond to PD-1 blockade

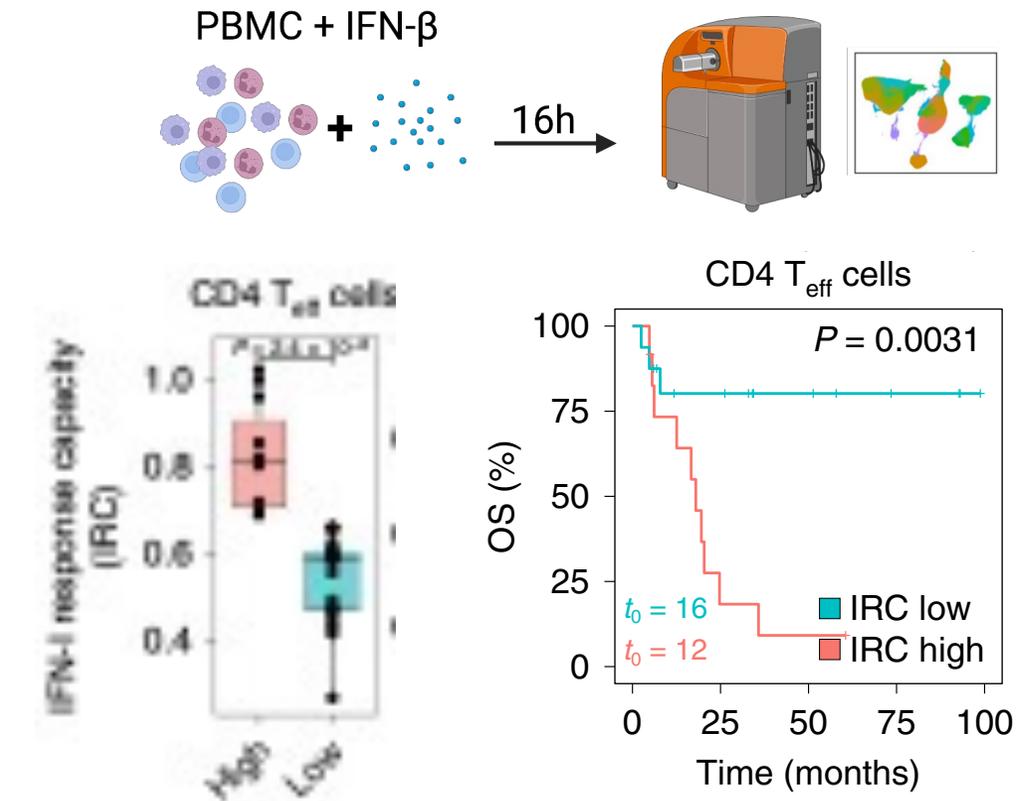
Timing

- Monotherapy – no time consideration
- Combination with ASO/siRNA
 - End of dosing – coincide with viral rebound

Patient Selection for PD-1/PD-L1 Therapy



Non-HBV-specific Responses to Predict Outcome



IFN response capacity predicts overall survival in melanoma patients

Work for HBV?