Virus panel classification: a strategy toward delineation of plasma bnAb activity

300

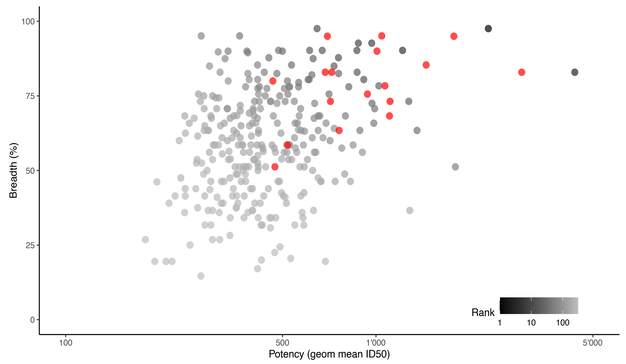
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Background

- Dissecting broadly neutralizing antibody (bnAb) specificity in polyclonal plasma in HIV-1 infection and post vaccination remains challenging.
- Current delineation methods fail to resolve the presence of multiple bnAb specificities or novel bnAb types
- We report on the **virus panel classification**, a novel delination method to overcome these limitations
- We evaluate multi-specificity in the XbnAb cohort, a large cohort of bnAb inducers (N=304) identified in the Swiss 4.5K Screen (Rusert et al. 2016).
- To prove the validity of the prediction **we characterized bnAbs from 17 individuals** with either single or multiple specificity prediction.

XbnAb cohort
304 bnAb inducers with diverse breadth and potency

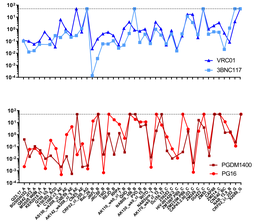


We developed virus panel classification, a new neutralization fingerprinting method to assess multi-specificity of plasma bnAb activity and confirmed the method by bnAb cloning.

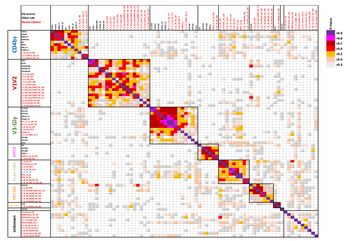
The virus-panels method: a versatile fingerprinting strategy that predicts dominant and multi-specific neutralization activity

1 Measure neutralization activity of known bnAbs against a virus panel of choice (N=40) in TZM-bl assay

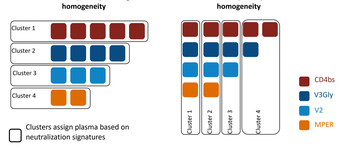
Neutralization fingerprint



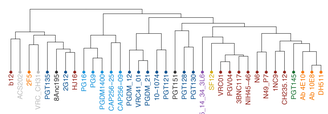
2 Conventional Spearman-based fingerprint using full virus panel



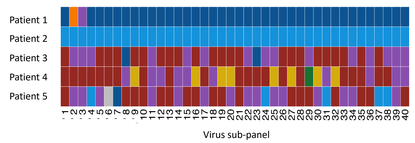
3 Compute from same data homogeneity of bnAb specificity prediction for 65'000 smaller-sized (N=10-35 viruses) random virus sub-panels



4 Select 40 sub-panels with highest homogeneity (best predicting)



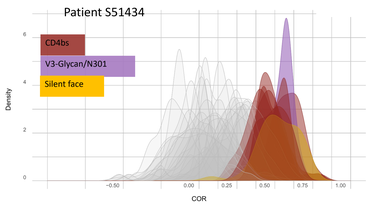
5 Measure plasma against the identical virus panel as in Step 1 and compile maximum Spearman values for all virus sub-panels



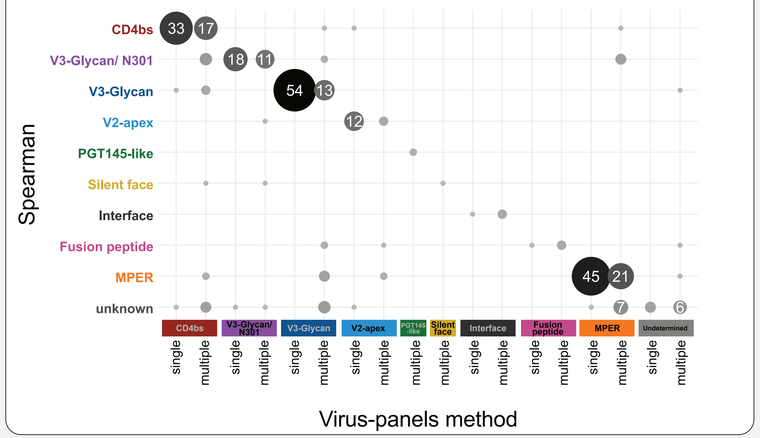
6 Compute for each plasma the percentage of epitope prediction across all 40 virus sub-panels. Epitope predictions are called at percentage > 20%



7 Obtain for each plasma correlation distributions with all bnAb specificities across the 40 virus sub-panels. Epitope predictions are called at mean correlation ≥ 0.4

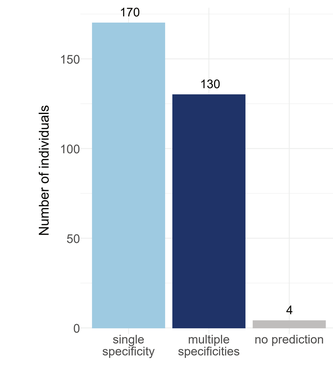


Good agreement between original fingerpring and panel method

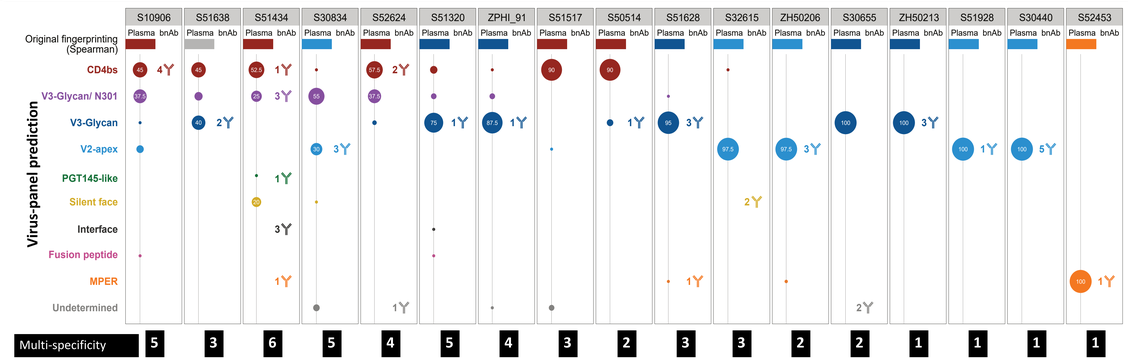


Virus-panels method

High frequency of multi-specificity in the Xbnab cohort (43%)



bnAb cloning confirms prediction of bnAb specificity in plasma by the virus-panels method



Conclusion

- The virus-panels method creates a new possibility to assess multi-specificity of plasma bnAb activity
- The panels method can be continuously expanded and refined by adding additional bnAbs to the analysis
- Validity of the virus-panel predictions is confirmed by bnAb cloning
- Data from the XbnAb cohort show that multi-specificity bnAb activity is common
- Vaccine immunogens should be explored for their capacity to induce multi-specific bnAb activity

Acknowledgments

Supported by the Swiss National Science Foundation, the Swiss HIV Cohort Study, and the SHCS research foundation.

University of Zurich[UZH]
USZ Universitäts Spital Zürich
FNSNF Fonds National Suisse Schweizerischer Nationalfonds Fondo Nazionale Svizzero Swiss National Science Foundation
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