Transcriptional States of B cells Producing Broadly Neutralizing Antibodies that target HIV-1 Envelope

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INTRODUCTION

Broadly neutralizing antibodies (bnAbs) target the HIV-1 envelope (env) on multiple different HIV strains and are attractive targets for HIV-1 vaccines (Figure 1). Previous studies have shown that HIV-1 bnAb induction is disfavored by host immunity, given their genetic properties and auto-polyreactive nature. The transcriptional programs of HIV-1 Env bnAb B cells may provide insights into the nature of these B cells and inform future vaccine strategies to harness them.

MATERIALS & METHODS

• Broadly neutralizing antibodies (bnAbs) target the HIV-1 envelope (env) on multiple different HIV strains and are attractive targets for HIV-1 vaccines (Figure 1).
• Previous studies have shown that HIV-1 bnAb induction is disfavored by host immunity, given their genetic properties and auto-polyreactive nature. The transcriptional programs of HIV-1 Env bnAb B cells may provide insights into the nature of these B cells and inform future vaccine strategies to harness them.

RESULTS

Figure 2: UMAP projections of the B cell clusters from HIV+ and HIV- individuals.

Figure 3: Identification of bnAb B cells and the transcriptional overlap of bnAb clusters

Table 2: Summary of the cohort and number of B cells studied to define transcriptional states of bnAb B cells elicted by HIV-1 infection

Table 3: Summary of the HIV- and HIV+ cohort used in this study, and for the future COVID-19 dataset that will be integrated with care to better understand B cell dysfunction in the context of HIV-1 infection. Dynamically analyse for each single cell dataset: B cell receptor signaling pathway, Th17 cell differentiation, interferon-gamma signaling pathway, and chemokine signaling pathway. To better understand B cell dysfunction in the context of HIV-1 infection.

CONCLUSION

• HIV-1 Env bnAbs and autologous NAb B cells are produced by B cells within transcriptionally-distinct B cell subsets that are expanded in HIV-1 infected individuals.
• The transcriptional co-clustering of bnAbs and autologous NAbs suggests that bnAbs may not require the expression of specialized transcriptional programs in order to achieve their neutralization breadth.
• The transcriptional profile of B cell clusters with the highest number of bnAbs B cells implicate loss of B cell regulation bnAb B cells implying loss of B cell regulation bnAb B cells may lead to anergy.
• These data raise the hypothesis that appropriate immunogens may be needed to rescue anergic B cell cells and select improbable mutations to achieve bnAb status.

FUTURE STUDIES

Future studies seek to integrate our HIV- single-cell dataset with other infections, including COVID-19, to better understand if B cell dysfunction is unique to HIV-1 infection, and/or may be manipulated during HIV-1 vaccination.

REFERENCES


Evangelou T, et al. (2021). Integrated analysis of multimodal single cell transcriptomes to two dimensions by Uniform Manifold Approximation and Projection (UMAP). Cells were clustered using a graph-based approach to create a single-cell map of cell clusters.

Table 1: Genes involved in the B cell receptor signaling pathway

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