Single-cell virus sequencing of influenza variants that trigger innate immunity

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Abstract The outcome of viral infection is extremely heterogeneous at the cellular level, and many viruses trigger innate immunity in only a fraction of infected cells. Here we develop an approach to determine how the genetic variation inherent in viral populations contributes to this heterogeneity. We simultaneously determine the cellular transcriptome and full sequences of all viral genes in hundreds of influenza-infected cells. Infections that trigger immunity are enriched for several features: absence of the gene encoding the virus's primary immune antagonist, internal deletions in viral polymerase genes, and mutations in viral proteins involved in replication and nuclear export. However, immune activation remains stochastic in cells infected by viruses with these genetic lesions, and sometimes occurs even in cells infected with fully wildtype virions. Overall, our work shows that viral genetic variation substantially contributes to but does not fully explain heterogeneity in infection outcome and immune activation.

Introduction

(***Russell et al., 2018***)

Results

Subsection

Figure 1 and ***Figure 1–Figure Supplement 1*** and ***Figure 1–source data 1***

Discussion

Add text

Methods and Materials

Add text

Acknowledgments

Add this

References

Russell AB, Trapnell C, Bloom JD. Extreme heterogeneity of influenza virus infection in single cells. eLife. 2018; 7:e32303.

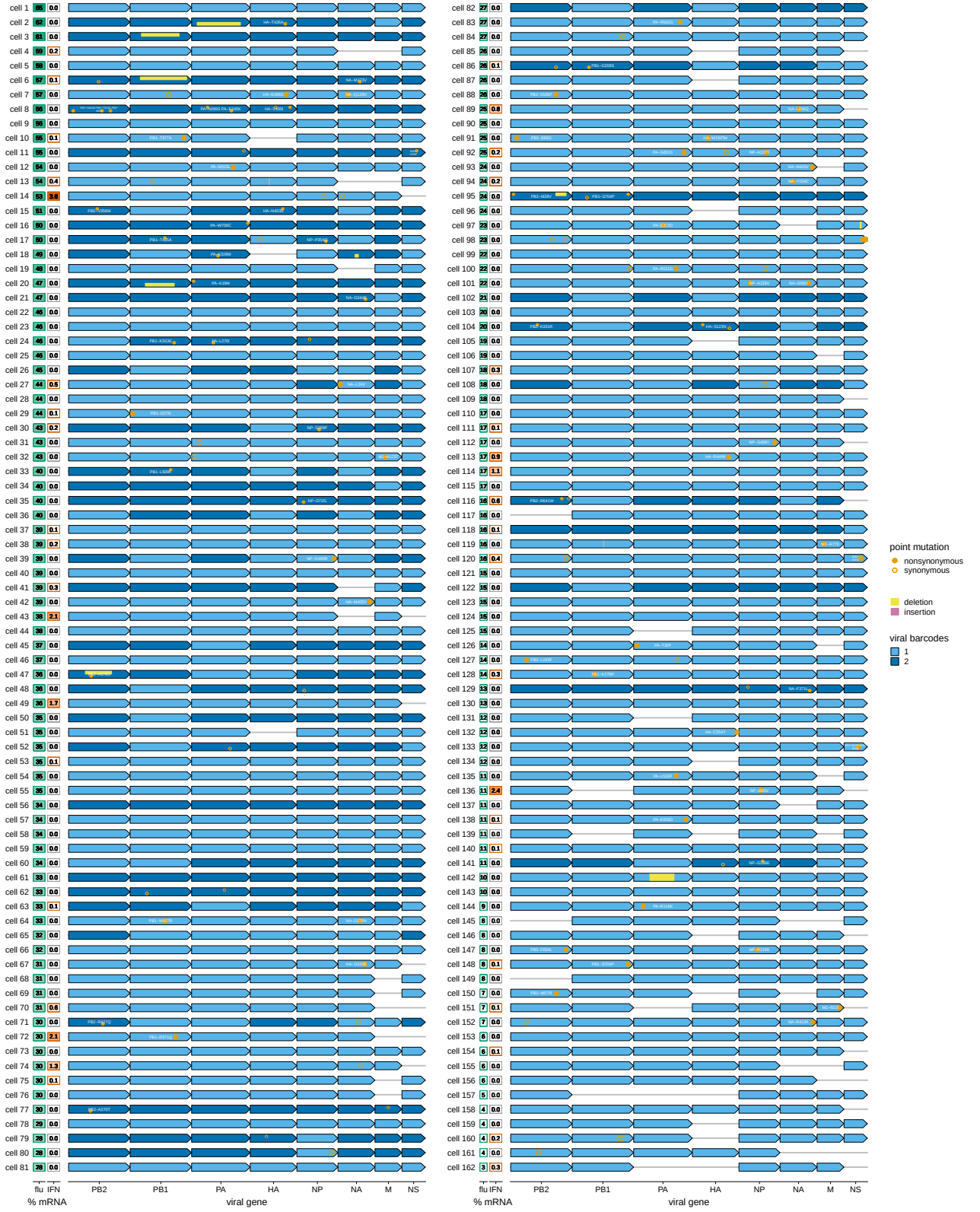

Figure 1. Viral genotypes and infection outcomes in single cells.

Figure 1–Figure supplement 1. Genotypes and infection outcomes plotted separately for IFN+ and IFN- cells.

Figure 1–source data 1. A CSV file giving the genotypes is in `figures/genotypes.csv`.

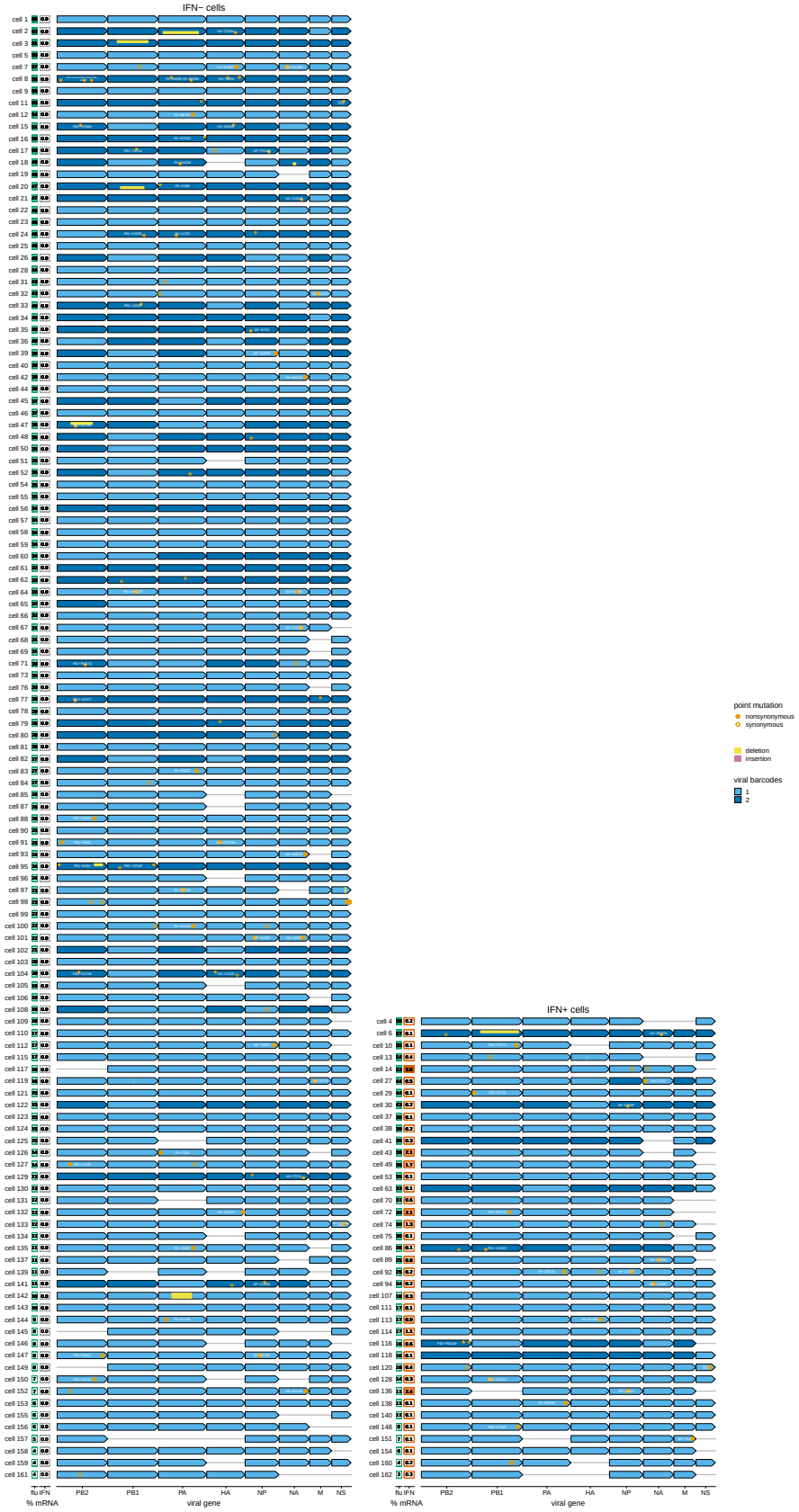

Figure 1–Figure supplement 1. This plot shows the same data as **Figure 1**, but with cells separated into columns based on whether they are IFN- or IFN+.