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**Title:** Linking Viral Genotype and Infected Cell Phenotype of Non-polio Enteroviruses at Single-Cell Resolution

**Abstract:** Like all biological populations, viral populations exist as networks of genotypes connected through mutation. Mapping the topology of these networks and quantifying population dynamics across them is crucial to understanding potential pathways of adaptation, and the robustness of populations to changes in their selective environment. The influence of mutational networks in viral populations is especially profound. RNA viruses, like the Enteroviruses (EVs), rapidly explore their mutational neighborhood via high mutation rates to navigate the dynamic and heterogeneous fitness landscapes they encounter throughout their lifecycles. I’ll discuss single-cell sequencing methods we are developing to capture and assemble complete or near-complete viral genomes from hundreds of individual EV-infected cells. Using our method, which we term scRNAseq-Enabled Acquisition of mRNA and Consensus Haplotypes, or SEARCH, we reveal the complex genotypic network that composes the viral population. We obtain these viral genotypes in parallel with corresponding host cell transcriptome information, enabling us to link viral genotype to the host cell transcriptional phenotype. The single-genome resolution provided by SEARCH reveals the genetic structure underlying the adaptive dynamics of enterovirus populations and can be widely adapted to other viruses and biological systems to connect viral infection, evolution, and phenotypic consequence.