SARS-CoV2 transmission and the emergence of new variants

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As SARS-CoV-2 has evolved from ancestral lineages to variants of concern (VOC) it remains unclear how some mutations and evolutionary patterns lead to novel phenotypes. Several hypotheses may have been put forth to explain VOC evolution, including changes in viral replication rates at the port of entry and egress, binding affinity to and location of ACE2 receptors, natural and vaccine-induced immune escape, and the ability of the variants to overcome innate immune responses. We have established a household transmission cohort to understand SARS-CoV2 transmission. This created an opportunity to examine the kinetics of transmission and evolution of SARS-CoV2 using a collection of samples gathered over a period of three years. To link epidemiological data with a molecular and cellular understanding of virus transmission, we developed a model system using air-liquid interface (ALI) cultured primary nasal epithelial cells (HNE). We discovered that the virus uses motile cilia, microvilli, and mucociliary-dependent mucus flow as critical for virus replication efficient in nasal epithelia. Our studies revealed that Omicron variants have evolved to replicate faster nasal epithelia. The overall goal is to validate and optimize mathematical and tissue culture models to elucidate the molecular determinants of SARS-CoV-2 transmission and anticipate the emergence of new variants of concern, which underpin our ability to develop effective preventive and therapeutic strategies.