GENETIC ENGINEERING OF VACCINE MANUFACTURING CELL LINES ENHANCES POLIOVIRUS AND ENTEROVIRUS 71 PRODUCTION

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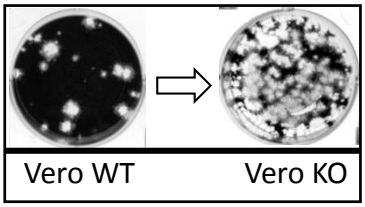

Figure 1 – Plaque Assays. Knockout of individual host genes dramatically enhances poliovirus production

Vaccine manufacturing costs and production limitations represent two fundamental challenges facing researchers, public health officials and vaccine manufacturers committed to global health solutions. To address these issues, we have investigated whether the cell lines employed by vaccine manufacturers can be engineered to enhance vaccine virus production. As a first step in a proof-of-principle study, a genome-wide RNA Interference (RNAi) screen was conducted to identify host gene modulation events that increased Sabin 2 poliovirus (PV) replication. Primary screen hits were validated in a Vero vaccine manufacturing cell line using both attenuated and wild type poliovirus strains. This approach identified multiple single and dual gene knockdown events that increased PV titers >20-fold and >50-fold, respectively. Top candidate genes did not affect virus antigenicity, cell viability, or cell doubling times. Moreover, CRISPR/Cas9-mediated knockout (KO) of the top three targets created stable cell substrates with improved viral vaccine strain production (Figure 1). Interestingly, silencing of several genes that enhanced PV replication also boosted replication of enterovirus 71, a clinically relevant virus for which vaccines are being targeted. The discovery that host gene modulation can markedly increase virus vaccine production identifies a strategy to address current public health and industry challenges.