Genetic engineering of enhanced vaccine cell lines to eradicate poliovirus and other vaccine preventable diseases

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All viruses utilize host genes and machinery to replicate. At the same time, infected cells including vaccine cell lines, express gene products to interfere or resist virus replication. The purpose of this project is to increase production of polio virus vaccine, and other vaccine cell lines to address vaccine preventable diseases by silencing non-essential virus resistance genes in a vaccine cell line thereby reducing costs and increasing vaccine availability. This project directly addresses the post-eradication challenge of the high cost of IPV manufacturing. The central hypothesis is that genome-wide small interfering RNA libraries that target individual genes in the host genome can be used to identify host genes that when silenced result in fold-increases in viral replication. Once identified, the target gene(s) are permanently silenced, e.g. CRISPR in approved vaccine cell lines. In this presentation, data will be shown for gene knockdown events that enhance poliovirus vaccine production where polio virus replication is increased by up to 30-fold. The poliovirus derived from modified and unmodified vaccine cells is antigenically equivalent, and studies show that gene knockdown events that increase Sabin-2 titers also elevate Sabin-1 and Sabin-3 production. Moreover, based on results we have obtained in analogous screens employing other viruses (influenza, measles) we have high confidence that this approach represents a sustainable technology platform that can be applied to a wide range of vaccine-preventable diseases, a feature that may allow for eradication of some important human diseases.

Biography

Ralph A Tripp received his doctorate in 1989 from Oregon State University, was awarded a National Research Service Award, and studied adenovirus mechanisms of immune evasion at Emory University as a post-doctoral fellow. He then studied as a senior fellow with 1996 Nobel Laureate Professor Peter C. Doherty at St. Jude Children’s Research Hospital determining the mechanisms of T cell memory to influenza virus. Following this, he led a research team in vaccine studies for respiratory viral diseases in the Respiratory and Enteric Viruses Branch at the CDC in Atlanta, GA. He now is at the University of Georgia, studying vaccine and antiviral drugs countermeasures for emerging infectious diseases.

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