

## **RSV VACCINES: ENGINEERING IMMUNOGENICITY**

Marty Moore, Emory University, USA

Respiratory syncytial virus (RSV) is a leading cause of infant hospitalization and there remains no pediatric vaccine. Achieving an effective balance of attenuation and immunogenicity has proven challenging for RSV live attenuated vaccines (LAV). We engineered RSV LAV strains with enhanced immunogenicity using a multifaceted, rational mutagenesis approach. We sought to enhance expression of the pre-fusion conformation of the RSV fusion (F) protein. Genetic mapping identified F protein residues that correlate with pre-fusion antigen maintenance and thermal stability of infectivity, and we introduced these residues into LAV candidates. We codon-optimized non-essential genes associated with virulence, including the non-structural (NS1 and NS2) genes and the attachment (G) gene. We increased antigen expression by deletion of the upstream small hydrophobic (SH) gene. The novel RSV LAV candidates exhibited elevated pre-fusion antigen levels, thermal stability, immunogenicity, and efficacy despite being highly attenuated in cotton rats.