Rift Valley fever virus (RVFV) is an arbovirus, endemic in sub-Saharan Africa, that causes severe disease in ruminants and humans. Despite its potential pathogenic and economic impact, there are currently no FDA approved drugs or vaccines to prevent the global spread of the RVFV. The nonstructural small (NSs) protein is the primary virulence factor of RVFV that suppresses the host's antiviral innate immune response and thereby an important target for countermeasure development. A combination of computational-, structural-, biophysical-, molecular biology-, and virology-based techniques are being utilized to uncover critical NSs interacting partners that mediate viral replication and pathogenesis. The implications of these findings for antiviral development and vaccine efforts will be discussed.