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BIOCHEMICAL AND STRUCTURAL CHARACTERIZATION OF A HOST PROTEIN THAT BINDS EBOLA VP30

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Ebola and Marburg viruses are negative sense RNA viruses that can cause high case fatality rates during outbreaks. Approximately 19 kb genome encodes for seven open reading frames. During virus replication, 7-10 multifunctional proteins are expressed, but viral replication and pathogenesis also require numerous cellular proteins. While the need for host factors in virus replication and pathogenesis has been long appreciated, our understanding of key host-virus interactions during filoviral infection and replication remain incomplete. In order to address this limitation, our collaborators recently performed a proteomic analysis, which identified RBBP6, an E3 ubiquitin ligase, as a cellular interactor of Ebola VP30 (eVP30). eVP30 is a viral protein critical for transcription initiation. In this study, we generated a series of recombinant RBBP6 and eVP30 truncation constructs. We performed in vitro pull-down assays to validate the initial proteomic identification of the eVP30/RBBP6 protein-protein interaction and defined key regions within RBBP6 that are critical for eVP30 binding. Furthermore, using purified eVP30 protein, we generated initial crystals with a RBBP6 binding peptide (RBBP6BP) and are currently refining X-ray diffraction data to develop a molecular model for RBBP6 interaction with eVP30. At the completion, we expect to define a key host-viral interface that modulates viral pathogenesis and define a novel target for potential development of antiviral therapeutics that target filoviruses.