Structural Transformation Begets Multiple Functions in the Viral Life Cycle

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Proteins, particularly viral proteins, can be multifunctional, but the mechanism(s) behind this trait are not fully understood. Here, we illustrate through multiple crystal structures, biochemistry and cellular microscopy that the VP40 matrix protein of ebolavirus rearranges into different structures, each with a distinct function required for the virus life cycle. A butterfly-shaped VP40 dimer trafficks to the cellular membrane. There, electrostatic interactions trigger rearrangement of the polypeptide into a linear hexamer. These hexamers construct a multi-layered, filamentous matrix structure that is critical for budding and resembles tomograms of authentic virions. A third structure of VP40, formed by a different rearrangement, is not involved in virus assembly, but instead uniquely binds RNA to regulate viral transcription inside infected cells. These results provide a functional model for ebolavirus matrix assembly and the other roles of VP40 in the virus life cycle, and demonstrate how a single, wild-type, unmodified polypeptide can assemble into different structures for different functions.