Determining the Patchwork Lattice of Ebola and Marburg Virus Matrix Layers Using Cryo-Electron Tomography

William Wan¹, Mairi Clarke², Michael Norris³, Larissa Kolesnikova⁴, Alexander Koehler⁴, Zachary Bornholdt⁵, Erica Saphire³, Stephan Becker⁴ and John Briggs⁶

¹Vanderbilt University, United States, ²University of Glasgow, United States, ³La Jolla Institute for Immunology, United States, ⁴Philipps-Universität Marburg, United States, ⁵Mapp Biopharmaceutical Inc, United States, ⁶MRC Laboratory of Molecular Biology, United Kingdom

Filoviruses, such as Ebola and Marburg viruses, cause severe hemorrhagic fevers with high mortality rates in humans. Filoviruses form filamentous particles that bud from host cells; this process is driven by the assembly of the viral matrix protein VP40, which binds and curves host cell membranes to form filamentous membrane envelopes. When expressed alone, VP40 spontaneously buds filamentous viruslike particles, indicating that membrane localization, matrix assembly, and membrane curvature are all intrinsic properties of VP40 independent of other viral assemblies like the nucleocapsid.

While a number of crystal structures of VP40 have been determined, there are no structures of the assembled VP40 matrix with viruses or virus-like particles available. Here we present structures of Ebola and Marburg VP40 matrix layers within virus-like particles and within Marburg viruses determined by cryo-electron tomography and subtomogram averaging. We find that VP40 dimers assemble into extended chains, which then stack to form patches of locally ordered 2D lattices below the membrane surface. These form a patchwork assembly across the membrane surface that mediate the budding of filamentous membrane envelopes.

References

William Wan, Mairi Clarke, Michael Norris, Larissa Kolesnikova, Alexander Koehler, Zachary Bornholdt, Stephan Becker, Erica O. Saphire, John A.G. Briggs. Ebola and Marburg virus matrix layers are locally ordered assemblies of VP40 dimers. *eLife*. (2020) 9: e59225