EFFECT OF mVP40 MUTATIONS ON MEMBRANE ASSOCIATION AND BUDDING OF MARBURG VIRUS

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ABSTRACT

The Marburg virus (MARV) is a zoonotic virus first identified in a highly fatal hemorrhagic fever outbreak in humans and non-human primates in Marburg, Germany in 1967[1–3]. Since then, there have been several outbreaks around the world, the most recent ones being in Equatorial Guinea and Tanzania in early 2023[4]. Human-to-human transmission can occur through direct contact with bodily fluids. There are no specific treatments or approved vaccines for MVD and supportive hospital care is the only option[3]. However, some repurposed small molecule drugs such as remdesivir and some vaccines are currently under research[1].

MARV is a filamentous negative-stranded virus of the family *Filoviridae*. The genome of MARV encodes 7 genes. VP40 is the 40 kDa matrix protein involved in the budding of the virus and immunosuppression[5]. The N-terminal domain forms the VP40 dimer interface while the C-terminal domain is involved in binding to anionic host cell membrane lipids. VP40 oligomerizes at the membrane which induces membrane curvature and viral budding[5]. When expressed in the absence of other MARV proteins in mammalian cells, VP40 is sufficient to assemble and bud as non-infectious virus-like particles.

Serially passaging MARV in immunosuppressed mice and Vero E6 cells results in a number of adaptive mutations[6]. VP40 is found to adapt very actively while maintaining lethality. Our research involves looking at how some of these mutations (WT or G79S, L96P, E238A, E260A, and E268A) affect plasma membrane localization and virus-like particle (VLP) production from HEK293 cells. For our next steps, we plan to purify these proteins and observe how these mutations affect dimerization. This information will elucidate the sequence-structure relation of VP40. This will help us better understand the oligomerization and budding processes, which are indispensable for the spread of the virus.

References:

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