

90 kDa ribosomal S6 Kinase 1 promotes endosomal acidification during the early Influenza A virus infection phase

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Influenza A viruses (IAV) activate MAPK/ERK in a biphasic manner to promote viral replication. The family of 90 kDa ribosomal S6 kinases (RSK) belongs to the downstream effectors of MAPK/ERK and is involved in cell growth, proliferation and differentiation. We have previously shown, that the RSK1 isoform mediates the nuclear release of newly produced vRNPs via direct phosphorylation of the viral nucleoprotein during late IAV replication. Within this study, we aimed to identify a so far unknown contribution of RSK1 during the early IAV replication by promoting endosomal acidification and thereby facilitating the cytoplasmic release of viral genomes.

Inhibition of RSK1-3 isoforms with the specific inhibitor BI-D1870 as well as siRNA-mediated knockdown of RSK1 resulted in a decreased internalization of VSV-pseudotyped H1N1 viruses, human IAVs and also HPAIVs. Furthermore, endosomal acidification was reduced upon the missing RSK1 function. Super resolution microscopy (STED) and proximity ligation assays showed that RSK1 interacts with late endosomes. We found colocalization of RSK1 with the v-ATPase, which was confirmed by co-immunoprecipitation of RSK1 with the v-ATPase subunit V1E1. Fusion assays of viral and endosomal membranes revealed that RSK1 manipulation reduced the fusion efficiency between those membranes.

In summary, this work demonstrates for the first time that RSK1 is misused by human IAVs and also HPAIVs to promote the release of viral genomes into the cytoplasm.

Keywords

Professional status of the speaker

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Junior scientist status

Yes, I am a junior scientist.

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