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| Title: | Elucidating the role of GTPase Rab43 in influenza a virus infection |
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| Abstract: | Influenza A virus (IAV) is a global threat as it causes millions of infections worldwide each year. Being a RNA virus, it is more susceptible to mutations which leads to the emergence of new antigenically variable strain of the virus. Also, the genome of the virus can undergo independent assortment leading to the emergence of new strain. Since most of the drugs available in the market target the virus itself, the mutations in the virus leads to the failure of the existing drugs and vaccines. A novel approach to deal with the problem of drug resistance and vaccine ineffectiveness is to target the host cell factors which are manipulated by the virus for its own propagation. IAV uses a variety of the host proteins for getting the access to the host cell machinery and multiplication in the cell. A Genome wide RNAi screen was done in search for the druggable targets in the human genome which are required for IAV infection. Rab43, a small GTPase belonging to Ras superfamily was one of the potential hits in the screen and was showing a significant block in infection (>50%) upon depletion with the siRNA. This work was carried with an objective to elucidate the role of RAB43 in Influenza A cellular entry. Sequential steps of IAV infection were analyzed in a high throughput manner and it was observed that upon depletion of Rab43, IAV vRNP nuclear import is unexpectedly blocked. Following up the preliminary observations, work was done to gain mechanistic insights of the role of Rab43 in promoting vRNP nuclear import. The peculiar upregulation in the levels of early endosome, late endosome and lysosome was observed upon Rab43 depletion. Also, the results suggested that the levels of Rab43 were increased with infection with time dependent progression of infection and it shows a remarkable co-localization with one of the surface protein i.e. HA of the IAV in late stages of infection which indicated the involvement of Rab43 in late stages of infection as well. Together, this works gives preliminary insights of Rab43 as a proviral factor playing critical role in IAV infection. |
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