G protein-coupled receptor kinase 2 promotes flaviviridae entry and replication. [1]

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Abstract	Flaviviruses cause a wide range of severe diseases ranging from encephalitis to hemorrhagic fever. Discovery of host factors that regulate the fate of flaviviruses in infected cells could provide insight into the molecular mechanisms of infection and therefore facilitate the development of anti-flaviviral drugs. We performed genome-scale siRNA screens to discover human host factors required for yellow fever virus (YFV) propagation. Using a 2×2 siRNA pool screening format and a duplicate of the screen, we identified a high confidence list of YFV host factors. To find commonalities between flaviviruses, these candidates were compared to host factors previously identified for West Nile virus (WNV) and dengue virus (DENV). This comparison highlighted a potential requirement for the G protein-coupled receptor kinase family, GRKs, for flaviviral infection. The YFV host candidate GRK2 (also known as ADRBK1) was validated both in siRNA-mediated knockdown HuH-7 cells and in GRK(-/-) mouse embryonic fibroblasts. Additionally, we showed that GRK2 was required for efficient propagation of DENV and Hepatitis C virus (HCV) indicating that GRK2 requirement is conserved throughout the Flaviviridae. Finally, we found that GRK2 participates in multiple distinct steps of the flavivirus life cycle by promoting both entry and RNA synthesis. Together, our findings identified GRK2 as a novel regulator of flavivirus infection and suggest that inhibition of GRK2 function may constitute a new approach for treatment of flavivirus associated diseases.
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[1] https://www.cienciapr.org/es/g-protein-coupled-receptor-kinase-2-promotes-flaviviridae-entry-and-replication [2] https://www.cienciapr.org/es/user/garci001 [3] https://www.cienciapr.org/es/biblio?f%5Bauthor%5D=556 [4] https://www.cienciapr.org/es/biblio?f%5Bauthor%5D=557 [5] https://www.cienciapr.org/es/biblio?f%5Bauthor%5D=558 [6] https://www.cienciapr.org/es/biblio?f%5Bauthor%5D=559 [7] https://www.cienciapr.org/es/user/13/biblio [8] http://dx.doi.org/10.1371/journal.pntd.0001820 [9] https://www.ncbi.nlm.nih.gov/pubmed/23029581?dopt=Abstract