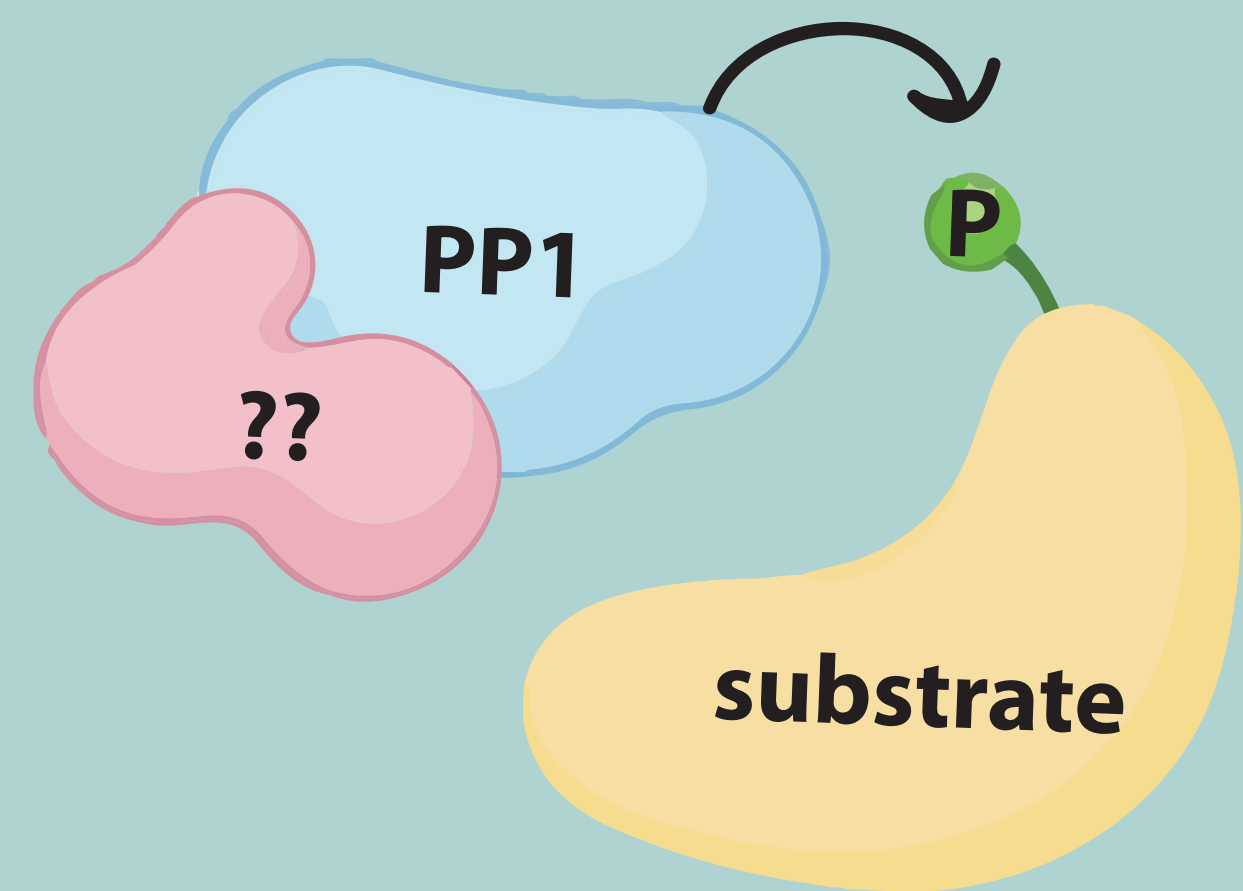


HOW NOT TO BE SEEN

Protein phosphatase dysregulation as a novel immunomodulatory mechanism of Human Cytomegalovirus

Abstract- The phosphorylation state of proteins is tightly controlled by cellular protein kinases and protein phosphatases. More than 70% of all eukaryotic cellular proteins are regulated by protein phosphorylation. The Ser/Thr protein phosphatase 1 (PP1) is responsible for much of the phosphatase activity in eukaryotic cells. Several viruses exploit the importance of PP1 for the host cell, including innate immune signaling, for the benefit of viral replication by the expression of viral PP1 binding proteins or inhibition of PP1 activity. In contrast, Human Cytomegalovirus (CMV) activates PP1 expression in target cells and additionally carries cellular PP1 in its virion for a rapid supply of the enzyme after viral entry. However, the mechanism and consequences behind CMV-mediated PP1 activation remain unknown.

1 WHICH PROTEINS DOES PP1 BIND TO?



Through bioinformatic analyses, mammalian2hybrid assays and Co-Immunoprecipitation we will determine the binding partners of PP1. We hypothesize that the interaction is dependent on binding the "RVXF" motif binding pocket of PP1.

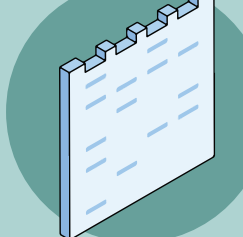
in silico



2hybrid



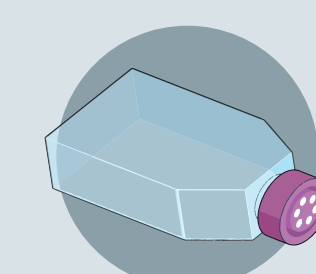
Co-IP



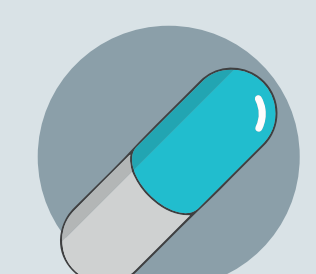
WHAT I DO FOR A LIVING?
I infect children's foreskin cells with herpes!

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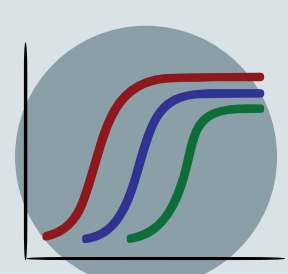
2 CAN PP1 INHIBITORS STOP CMV INFECTION?



CMV infection

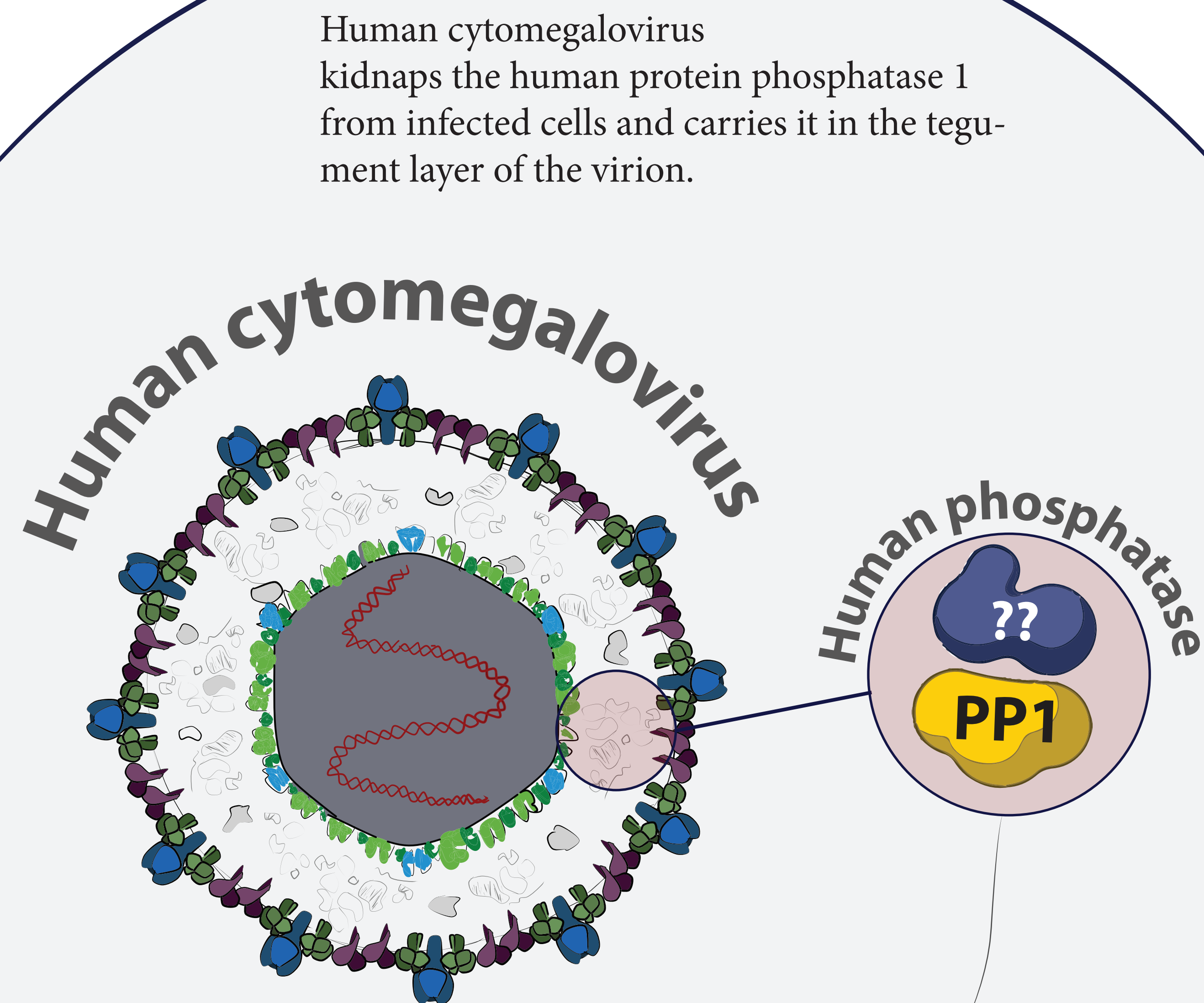


PP1 inhibitor



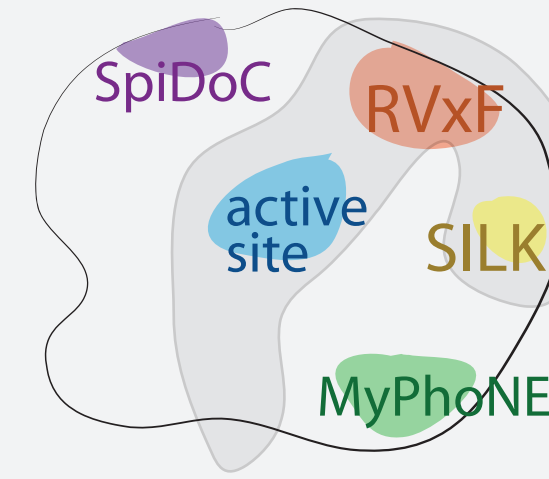
gene expression

Using a novel approach specifically targeting the regulatory "RVXF" binding site of PP1 rather than catalytic activity, we aim to inhibit the virus without harming the cell. All life stages of the virus are investigated (qPCR, Western blot, plaque assay) to see which stage is specifically targeted by the inhibitor.

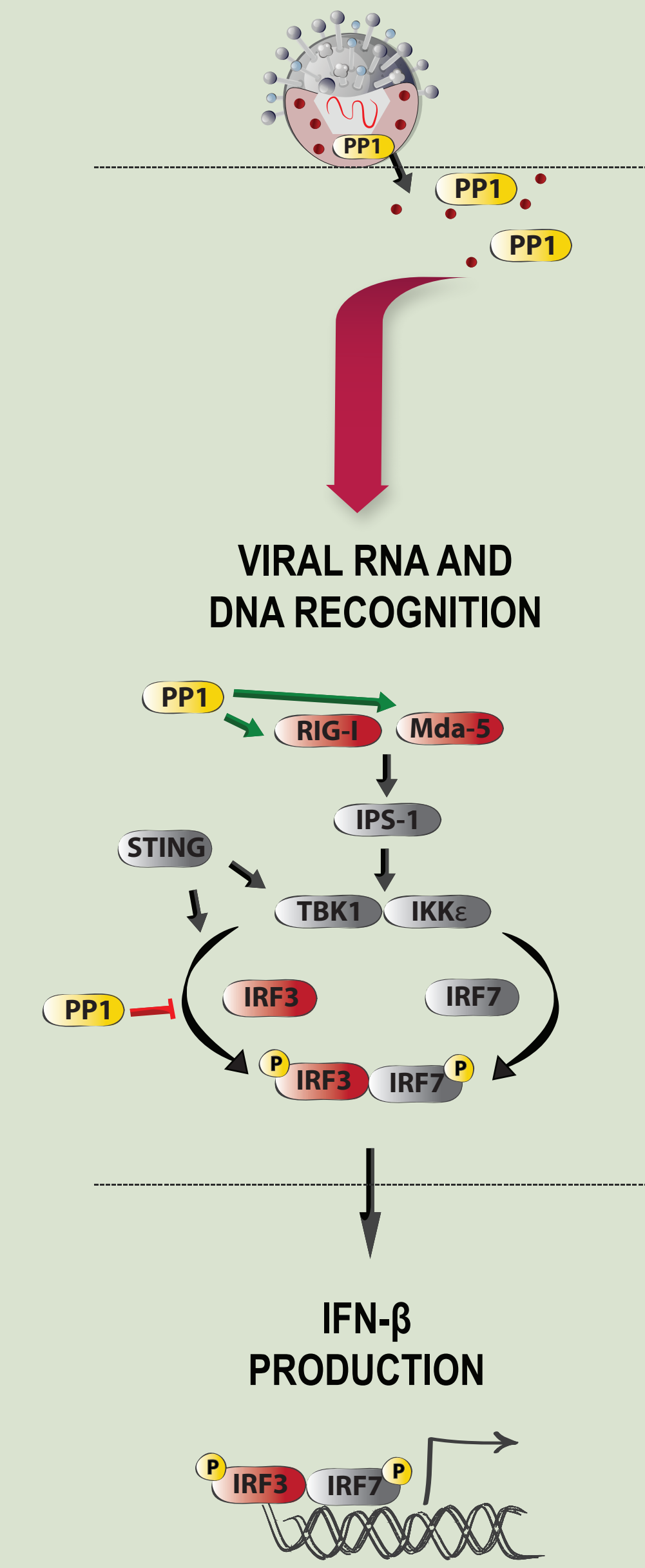


Human cytomegalovirus kidnaps the human protein phosphatase 1 from infected cells and carries it in the tegument layer of the virion.

PP1 has different binding sites, the most important of which is the hydrophobic pocket binding to the "RVXF" motif present on almost all PP1-binding proteins.

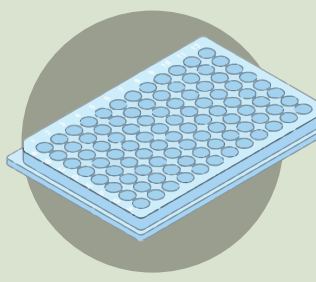


3 HOW DOES PP1 REGULATE INNATE IMMUNITY?



PP1 is known to play an ambivalent role in innate immune signaling pathways. We study whether cytomegalovirus derived PP1 is targeted to inhibit innate immune signaling.

ELISA



phospho Western



reporter assays



ÖAW ÖSTERREICHISCHE AKADEMIE DER WISSENSCHAFTEN

MEDIZINISCHE UNIVERSITÄT WIEN