Instituto de Medicina Molecular João Lobo Antunes

Master Project Proposal

Title: Targeting SARS-CoV-2, Zika, and other viruses in the brain to prevent neurological damages

Synopsis:

Frequently viruses reach the brain and cause neurological damages. Classical antiviral drugs have two typical limitations:

1) They specific for one viral species, only, so they cannot account for co-infections with more than one viral species simultaneously
2) They cannot translocate from blood to brain therefore not targeting brain-resident viruses

We are tackling both problems at the same time by developing broad spectrum antivirals that translocate over the wall of brain arteria.

The efficacy of the innovative molecules we are developing against SARS-CoV-2, Zika virus, HIV, and Dengue virus is being tested.

We are seeking for enthusiastic and focused students with determination to help to develop this new generation of disruptive antivirals.

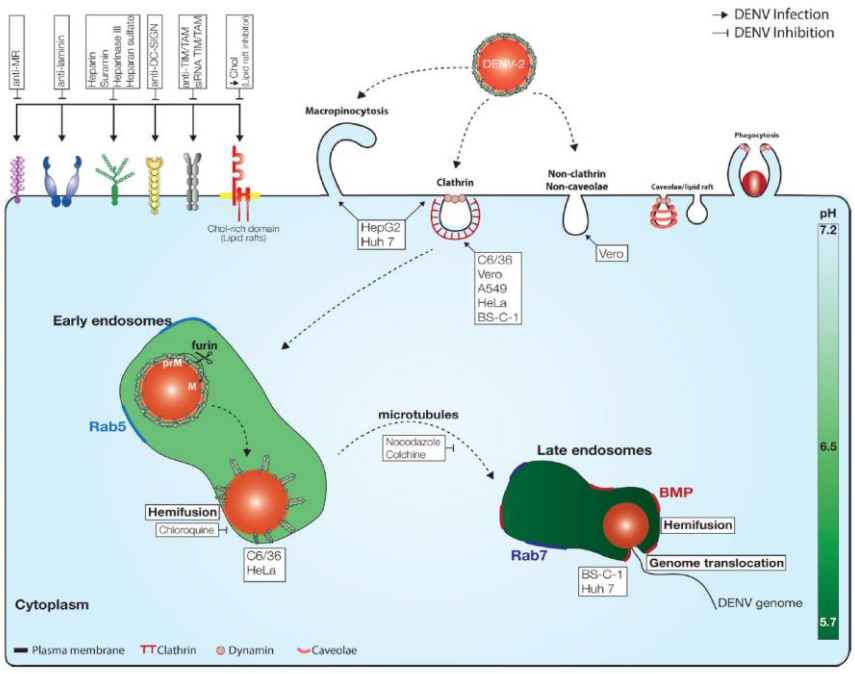

Figure 2. DENV entry pathways into its host cells. DENV attaches to the host cell surface through a myriad of receptors identified by different experimental approaches, such as the use of receptor analogues as inhibitors, antibodies, receptor gene silencing by siRNA or pharmacological inhibition of lipid raft formation. Virus particle is internalized through distinct routes, which include clathrin-mediated endocytosis, non-classical clathrin-independent endocytosis or macropinocytosis, depending on the cell host and virus serotype. During endocytic trafficking, the pH of the endosomal medium is acidified, triggering E protein conformational changes that induce hemifusion between viral and endosomal membranes. Depending on the cell type, virus fusion occurs in early or late endosomes, being in this latter case dependent on BMP, an anionic lipid specific of these organelles. The TGN protease furin may also be located in early endosomes, where it may promote immature virus particle maturation by cleaving prM. In some cases, microtubule depolymerization inhibits fusion and/or genome release into cytoplasm, suggesting that virus trafficking from early to late endosomes involves the transport through intraluminal vesicles.

Supervisor: *Miguel Castanho, Miguel Castanho Lab, macastanho@medicina.ulisboa.pt*
Co-Supervisor: *Ana Salomé Veiga, Miguel Castanho Lab, aveiga@medicina.ulisboa.pt*
Webpage of the group

Bibliography:

https://www.noviruses2brain.pt/