# Abstract

Dengue virus (DENV) is a major pathogen of concern globally. Infection with this mosquito-borne virus causes debilitating acute febrile disease that occur in over 128 countries putting more than 3.9 inhabitants to be at risk of the infection. If left untreated, the fatality rate for severe dengue can reach 20%. A vaccine that effectively prevents infection with all four types of DENV is thus highly desirable. However, despite years of effort, an efficacious dengue vaccine remains elusive. Moreover, the reason behind why past efforts to develop live attenuated dengue vaccines, which is arguably the most potent form of vaccine available, have mostly been unsuccessful remains undefined. Lack of detailed knowledge on why such previous attempts failed to generate a safe and effective vaccine hampers future vaccine development; the likelihood of repeating past mistakes are thus high. The goal of this project is thus to reconstruct DENV3 infectious clones carrying mutations that produces attenuating features. The reverse genetics derived viral strains will be tested *in vitro* for their replicative efficiency and ability to evade innate immune responses in susceptible cells. This project will dovetail into several other studies examining clinical and epidemiological fitness of DENV.



Keyword: *DENV*, *Vaccine Development, Reverse Genetics*