

Characterization of prohibitin as a chikungunya virus receptor and its potential in therapeutic treatment

Phitchayapak Wintachai¹, Duncan R Smith¹, Sittiruk Roytrakul²

1 Institute of Molecular Biosciences, Mahidol University, Nakorn Pathom, 73000, Thailand

2 National Center for Genetic Engineering and Biotechnology, National Science and Technology
Development Agency, Pathumthani, 12120, Thailand

Abstract

Chikungunya virus (CHIKV) is a re-emerging mosquito borne alphavirus that recently caused large epidemics around the Indian Ocean, Europe and America. In order to infect a cell, CHIKV uses its envelope protein to promote binding to the host cell surface, which is the first step of infection. This study aimed to identify two CHIKV East Central South African genotypes, E1:A226 and E1:226V, binding proteins expressed on cell membranes of mammalian cells. One-dimensional virus overlay and two-dimensional virus overlay followed by mass spectrometry identified prohibitin (PHB) as a CHIKV binding protein. Colocalization, co-immunoprecipitation, and siRNA mediated infection inhibition studies confirmed a role for PHB in mediating internalization of CHIKV. Flavaglines, a family of natural plant products, were shown to inhibit PHB. This study also determined whether synthetic flavaglines could modulate entry of CHIKV to mammalian cells. Cells treated with each of the flavaglines such as FL3 and FL23 at various concentrations 1-20 nM followed by infection with 10 pfu/cell CHIKV showed that these compounds significantly affected CHIKV infection level nearly 50% reduction. All results were statistically with value of P less than 0.05 for significance using a paired sample test of SPSS analysis. This study identifies for the first time flavaglines as a class of compounds with potential for development as novel anti-CHIKV drugs.