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The role of tight junction proteins during Dengue virus entry

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Which more than one-third of the world's population living in areas at risk of infection, dengue disease becomes a huge public health burden around the world. Considerable molecular, biochemical and structural virology information have been accumulated for Dengue virus (DENV), however, our understanding on its entry process remains ambiguous. We reported here that a group of cell surface proteins, including tight junction proteins claudin-1 and occludin, were involved in DENV entry process. In Huh 7.5 cells with claudin-1 or occludin knockdown, the amount of DENV entering into the cells was reduced. Consequently, the virus progeny productions were decreased and DENV-induced CPE/apoptosis were prevented. Furthermore, resuming the expression of claudin-1 in claudin-1-knockdown and occludin in occluding-knockdown cells facilitated DENV entry in respective cells. Using pulldown assay, we showed that claudin-1 interacted with DENV prM/M protein and occludin interacted with the E protein, respectively. Mutations on essential domains in claudin-1 and occludin disrupted such interactions. The critical domain and amino acids in claudin-1 were determined using various deletion mutations and point mutations, especially mutations on the extracellular loops (ECL) of claudin-1 and occludin. Since host and viral factors involving in virus entry are very promising therapeutic targets, and entry inhibitors may provide attractive therapeutics against DENV. Thus, the results reported will provide significant insights of DENV entry mechanisms and will lead, eventually, to the ability to describe completely the entry process and to moderate or inhibit it at will.

Biography

Dr. Qianjun Li received his Ph.D. degree at the age of 27 years at Beijing Agricultural University (1993), and had postdoctoral training at Carnegie Mellon University and University of Florida at Gainesville. He is currently an assistant professor at Division of Infectious Diseases, Department of Medicine, University of Alabama at Birmingham. Dr. Li has published more than 30 papers in reputed journals, and has served on the editorial board of several scientific journals, and on the advisory panels of academic and government institutions, including the USDA and NIH.

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