The adaptor protein Disabled-2 mediates hepatitis C virus entry and is a potential target for modulating viral infectivity

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Abstract

The entry of hepatitis C virus (HCV) into host cells is a multi-step process that involves receptor binding and internalization. Despite that clathrin-dependent endocytosis has been demonstrated to play a pivotal role in mediating HCV entry, little is known regarding the component of the cargo-specific adaptor protein that modulates the assembly of clathrin-coated pits at plasma membrane upon HCV entry. In this study, we investigated whether the cargo-specific adaptor protein Disabled-2 (DAB2) that is involved in various receptor-mediated and clathrin-dependent endocytosis modulates HCV entry. Accordingly, the Huh7.5 cells were stably transfected with a expressing construct encoding the short hairpin RNA of DAB2 (shDAB2) followed by infection with the HCV pseudotype virus (HCVpv). Our data revealed that the HCVpv infectivity for DAB2 knockdown cells was approximate 50% of the vector control cells. Consistent with these observations, the decrease in the HCV infectivity was reversed by overexpression of DAB2 but not another cargo-specific adaptor protein autosomal recessive hypercholesterolemia (ARH). Notably, the deletion of DAB2 N-terminal phosphotyrosine binding (PTB) domain but not the C-terminal proline-rich domain served as a dominant negative mutant and diminished further the entry of HCVpv in the DAB2 knockdown cells. Taken together, DAB2 mediates HCV enter into host cells and could be a molecular target for modulating HCV infectivity.