

Investigating the Role of the Novel ESCRT-III Recruiter CCDC11 in HIV Viral Budding: Identifying a Potential Target for Antiviral Therapy

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Acquired immunodeficiency syndrome (AIDS) is a life-threatening condition caused by infection of the human immunodeficiency virus (HIV). Compromising the immune system, HIV reduces the body's ability to fight the organisms that cause disease. In an effort to discover potential targets for antiviral therapies, we explored the role of coiled-coil domain-containing 11 (CCDC11) in HIV-1 budding. CCDC11 plays an important role in ciliogenesis and cytokinesis. During cytokinesis, it recruits the endosomal sorting complex required for transport III (ESCRT-III) membrane scission complex to the midbody to mediate the physical separation of two dividing daughter cells. The ESCRT-III machinery is also integral to the viral budding process of HIV-1 and many other viruses. Therefore, we hypothesized that CCDC11 is also required for viral budding. To investigate this possibility, we established CCDC11-knockout human embryonic kidney (HEK) 293T cells using the CRISPR-Cas9 technology. Indels of the CCDC11 gene were confirmed by DNA sequencing, and protein levels were assessed via western blotting and immunofluorescence staining. To determine the effect of CCDC11-knockout on HIV-1 budding, we employed the Enzyme-linked immunosorbent assay (ELISA) p24 capture assay to indirectly assess viral release by measuring the relative concentration of HIV-1 Gag structural protein (p24) or mutant P7L-Gag in cell media. Our results demonstrate that ectopic overexpression of CCDC11 markedly enhances whereas depletion of CCDC11 in the knockout cells dramatically reduces viral particle release. The defective viral budding in CCDC11-knockout cells was restored when wild-type CCDC11 was re-expressed. Collectively, our data suggest that CCDC11 is critical for efficient HIV-1 budding.

Awards Won:

European Union Contest for Young Scientists Award

First Award of \$3,000

Intel ISEF Best of Category Award of \$5,000