

The role of epidermal growth factor receptor in the viral life cycle of the hepatitis E virus.

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Although hepatitis e virus (HEV) is a common cause of acute viral hepatitis, prevention and treatment options remain scarce. Our recent work has identified cholesterol metabolism as druggable target to combat viral infection by interfering with the viral release pathway. We aimed to dissect metabolism-regulating signaling cascades, focusing on the epidermal growth factor receptor (EGFR) signaling. Kinome analyses of persistently HEV-infected A549 cells reveal activation of EGFR, associated with a decrease in EGFR levels and a delay in the response to EGF. To determine the role of EGFR in the viral life cycle, it was modulated by siRNA-based knockdown or erlotinib-mediated inhibition. We observed an increase in released infectious viral particles, which coincided with higher levels of extracellular and intracellular HEV genomes. Using a subgenomic luciferase reporter assay, we noted enhanced viral genome replication. In addition, endolysosomal structures and actin cytoskeleton are affected by erlotinib. Kinome profiles indicated a modulation of focal adhesion-related pathways, which are linked to actin cytoskeleton organization, a key viral structure for initiation, maintenance and spread of infection. This study highlights EGFR as a novel HEV host factor. As its inhibition results in favorable conditions for viral spread, it may be a counter-indication in patients receiving EGFR inhibitors. Modulation of EGFR signaling could be a strategy to interfere with HEV life cycle.

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Yes, I am a Junior Scientist.

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