MICROBIOLOGIE, INFECTIOLOGIE ET IMMUNOLOGIE

Université de Montréal

CONFÉRENCE

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Functions and evolution of the E3 ubiquitin ligase assembled by the adenoviral proteins E4orf6 and E1B55K.

E4orf6 and E1B55K are two early adenoviral proteins that assemble during infection to perform several functions. Together they promote nuclear export of the late viral mRNAs, block export of the cellular mRNAs, and degrade several specific cellular proteins, including p53. Our group was the first to demonstrate that Ad5E4orf6 assembles a Cul5-based E3 ubiquitin ligase that binds E1B55K and ubiquitinates p53 leading to proteasome-mediated degradation. Other known substrates include Mre11, DNA ligase IV, integrin α3, and Bloom's helicase, although almost certainly other targets exist, presumably to optimize viral replication and perhaps to facilitate persistence or latency. Although human adenovirus type 5 (Ad5) has been widely studied, relatively little work had been done on other adenoviruses. We now have shown that although the ability to form the viral ligase complex is conserved among adenovirus species, heterogeneity exists in both composition of the complex and in substrate identity. Following the identification of key motifs in E4orf6 for the assembly of the ligase complex, we have done a systematic analysis concerning the conservation of these motifs throughout all human and non-human species of adenoviruses and have drawn some interesting conclusions about the evolution of this function throughout Adenoviridae. Finally, we have recently observed that expression of E4orf6 and E1B55K in the absence of E1A is able to induce a limited viral replication cycle. This effect seems to occur through the activation of E2F, the same factor targeted by E1A, and possible mechanisms will be discussed.

Jeudi 19 décembre 2013 à 11h30
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