

## Novel Cell-Targeted Approaches to Adenovirus Keratoconjunctivitis

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**Purpose:** Cell signaling is a process by which cellular enzymes transmit signals from the cell surface to effect specific patterns of gene expression. The role of cell signaling in the pathogenesis of ocular adenovirus infection has now been partially elucidated. We describe the potential for cell signaling-based approaches to the therapy of adenovirus keratoconjunctivitis.

**Methods:** Cultured corneal cells and C57BL/6j mice corneas were infected with purified human adenovirus type 19 (HAdV-19) or HAdV-37. Chemical and molecular inhibitors of protein kinases were used to block specific signaling cascades. Viral replication, pro-inflammatory chemokine expression, and clinical keratitis were assessed.

**Results:** Activation of multiple kinases by adenovirus infection, including Src, PI3K, Akt, p38, JNK, and ERK were shown *in vitro* and/or *in vivo*. Inhibition of specific kinase pathways reduced viral replication and chemokine expression in cell culture and clinical keratitis in infected mice.

**Conclusion:** Cell signaling cascades present novel therapeutic targets in ocular adenovirus infection. Targeting host cellular molecules in viral infection represents a potential paradigm shift in antiviral therapy.