Counteracting a host factor allows adenovirus infection to progress to new virus production

Viruses use the cells of another organism to reproduce and spread. Although very variable in size, the genetic material of a virus is usually tiny in comparison to that of its host and so cannot specify very many proteins. Consequently, viruses depend for their reproduction on many of their host's own processes and so have evolved many different strategies to adapt host cell processes to their own benefit. Equally, the host organism mounts numerous responses to an invading virus, with the aim of preventing or containing its reproduction. Thus, studying the interactions between virus and host components is key to understanding the outcome of infection.

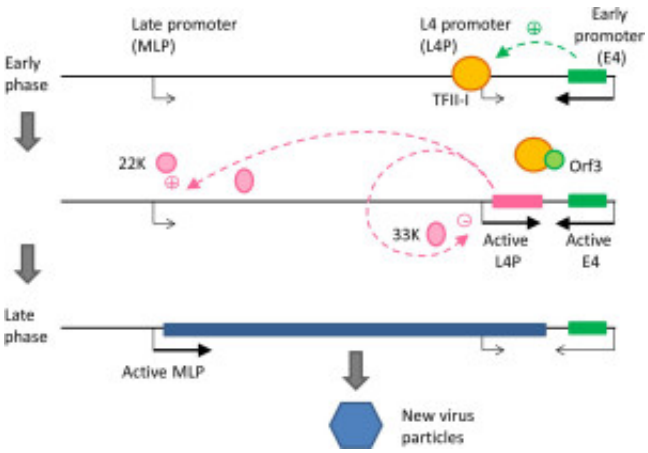

Fig. 1. Adenovirus 5 infection progresses from early phase (top) to late phase (bottom) via a burst of L4P activity (middle), which produces proteins that both activate late genes and inhibit L4P itself.

Human adenoviruses classified in species C, such as adenovirus 5, commonly infect our airway in early life with usually only mild symptoms, but establish a long-lived inapparent infection in adenoids and tonsils. When studied in laboratory cell cultures, this virus uses its genes in a series of stages, firstly producing proteins that adapt the host environment and counteract antiviral responses, then secondly proteins that provide the machinery for reproducing the genetic material and finally the proteins needed to form new virus particles. This last period is known as the late phase of infection. Since the switch from the early to the late phase represents the point where the cell becomes committed to making new virus (and probably therefore to being killed by the infection), we have been studying how this transition is controlled.

We found in 2009 that production of two proteins crucial for transition to the late phase was controlled by a novel adenovirus promoter (a piece of the genome that determines the timing and amount of expression of a gene), which we termed L4P. In this new work, we examined the

detailed structure and regulation of L4P. We found that it is kept inhibited by a host protein, known as TFII-I, until a viral protein termed Orf3 accumulates sufficiently to counteract that protein and remove it from the promoter. At that point, L4P becomes active and the virus can produce proteins known as 22K and 33K which switch on the full late phase. In turn, one of these proteins then switches off L4P again once the late phase is established. In other words, the virus uses a combination of host proteins and its own proteins to generate a brief blip of L4P activity (Fig. 1.). This stage in the life cycle of adenovirus therefore represents a potential control point at which the outcome of infection can be determined.

Publication

The Human Adenovirus Type 5 L4 Promoter Is Negatively Regulated by TFII-I and L4-33K.
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