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Fiber mediated receptor masking in non-infected bystander cells restricts Adenovirus cell killing effect but promotes Adenovirus host co-existence

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The outcome of viral replication is dependent on the interplay between viral and host genomes. Whereas viral genome strives to re-direct host cell gene expression in favor of viral replication, host cell genome initiates defense mechanisms counteracting viral replication. The mechanisms on viral propagation and spread are however poorly clarified. By studying the propagation kinetics of conditionally replicating adenoviruses consequence (CRAD), we have identified a novel viral mechanism controlling the equilibrium between adenovirus propagation and host cells existence. CRAD as oncolytic agents is conceptualized that progenies from each infection round will efficiently disperse and infect surrounding cells, and subsequently exponentially expand. However, we found that CRAD infection at low multiplicity of infection (MOI) was inefficient in cancer cell killing. Excessive production of fiber molecules from initial round of CRAD infection in only 1 to 2% cancer cells and their release prior to the viral particle itself, caused a tropism-specific receptor masking in both infected and non-infected bystander cells. Consequently, this resulted in inefficient CRAD propagation. Further, fiber overproduction correlated closely with the restricted adenovirus spread in xenograft cancer therapy models. Fiber overproduction and resulting receptor masking are thus key factors limiting CRAD functionality. Besides the CAR-binding Ad5, infection with CD46-binding Ad35 and Ad11 also caused receptor masking. These findings suggest that fiber overproduction and its resulting receptor masking are evolutionally conserved among many adenovirus serotypes. Our observations give important clues for understanding mechanisms underlying natural infection course of various adenoviruses, and potentially also other viruses.

Biography

Xiaolong Fan graduated from Shanghai Medical University in 1997. He was then trained for doctoral and postdoctoralstudies at University of Greifswald, Germany between 1989 and 1997 in the field of human genetics and bacterial infection biology. Following a move to Lund University in Sweden, he developed own research projects on cancer cell biology and the exploration of adenovirus as a tool for gene transfer into hematopoietic stem cells, or as cancer therapy agents. Since 2009, Dr. Fan is a professor at Beijing Normal University in China.