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Title: Improvement of oncolytic adenovirus vectors through genetic capsid modifications

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Improvement of Oncolytic Adenovirus Vectors through Genetic Capsid Modifications

1. The capsid protein IX of human adenovirus type 5 (HAdV-5) is a suitable locale for the attachment of tumor targeting polypeptides. (*This thesis*)
2. HAdV-5 can be targeted to cancer-testis antigens presented on tumor cells by incorporating single-chain T cell receptors in the viral capsid. (*This thesis*)
3. The attachment of a tumor targeting polypeptide to protein IX of HAdV-5 results in targeted transduction of tumor cells with varying efficiencies, depending on the polypeptide fused. (*This thesis*)
4. The absence of protein IX in the virus capsid results in enhanced activation of peripheral blood mononuclear cells, which suggests a biological function of protein IX in diminishing the immune response against HAdV-5. (*This thesis*)
5. Oncolytic vectors based on blood-borne virus types may display improved systemic delivery to tumor sites as compared to adenoviral vectors which require complex modifications to prevent rapid clearance from the circulation.
6. Preclinical studies with oncolytic viruses in animal models can be misleading as a result of differences in the anatomy or physiology between humans and animals.
7. Advances in our understanding of the molecular genetics of cancer suggest that the complexity of the heterogeneity of human malignancy both between patients with one disease type arising at a particular site as well as between cancer cells within one patient, is such that population-based unselected approaches have major limitations for the development of novel cancer therapeutics. J.S. de Bono and Alan Ashworth (Nature 2010; 467:543-549).
8. The recognition that oncolytic viruses can induce anti-tumor immune responses allows renaming of these therapeutic agents as 'therapeutic vaccines', which may facilitate their public acceptance and translation to the clinic.
9. Where all is but dream, reasoning and arguments are of no use, truth and knowledge nothing. John Locke (1632-1704).
10. It is the weight, not numbers of experiments that is to be regarded. Sir Isaac Newton (1643-1727).
11. We reveal ourselves in the metaphors we choose for depicting the cosmos in miniature. Steven Jay Gould, *Full House: The Spread of Excellence from Plato to Darwin* (New York: Three Rivers Press, 1996; 7).