Analysis of Adenovirus - host cell interactions and comparative genomics

Popular Scientific Summary

Oncolytic viruses have the potential to infect cancer cells, multiply selectively within cancer cells and cause death, with the release of new viruses that can infects neighboring cancer cells. Human adenovirus (Ad) is currently being developed as a promising therapeutic candidate for the treatment of cancer. High gene transfer efficiency, relatively simple and efficient purification to large quantities and inherent ability to kill the cell following a completed infection cycle are the characteristics that make adenovirus the virus of choice for many scientists. Consequently, adenovirus is among the most frequently used viral vectors in clinical trials. Tissue and tumor cell specificity, toxicity and host immune responses are the main obstacles for development of novel biological viral cancer therapies. A good animal model is necessary to overcome these issues, but unfortunately, human Ad infection and replication is restricted to human cells. Our lab recently identified a mouse cell line (NMuMG), which shows full susceptibility to infection by human adenovirus serotype 2 (HAdV-2) but not to infection by human adenovirus serotype 12 (HAdV-12). It is not known why some adenovirus serotypes are susceptible while others are not. Nor is it known at what stage the virus infection cycle is blocked during infection with the non-growing Ad serotypes. In this project, we showed that both human adenovirus serotype 3 (HAdV-3) and human adenovirus serotype 11 (HAdV-11) efficiently deliver their genomes into the nuclei of NMuMG cells. However no replication of DNA was found. In order to find differences among adenovirus serotypes, a comparative bioinformatics analysis was performed to identify species-specific genes. We showed that there is a significance genome variation in term of gene content between Ad serotypes and a small number of novel species-specific genes were identified. These results may suggest that specific virus proteins have a functionally important impact on host cell specificity.

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