TRANSCRIPTION REGULATION OF ADENO-ASSOCIATED VIRUSES

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ABSTRACT

The small genome size of adeno-associated viruses demand efficient gene regulation achieved by various strategies. This research compared these strategies from AAV2, AAV5 and bovine-AAV, and found that AAV2 capsid promoter P40 has a low basal level and is activated by its non-structural Rep in the presence of adenovirus while AAV5 capsid promoter P41 has a higher basal level and is not further activated by Rep. The difference of the activation ability between AAV2 and AAV5 Rep resides in the amino terminus of the protein. The higher basal level of P41 is at least partially contributed to the AP1 and CRE transcription factor binding sites upstream. Although BAAV, a closer relative to AAV5, has both sites, its capsid promoter activity is still low and can be further activated by both its own Rep and AAV5 Rep. This study not only enriched our understanding of the basic molecular biology of these viruses, which potentially would benefit gene therapy vector design, but also provided clue of the evolution migration between the animal and human AAVs.