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Gene therapy is considered one of the most important developments in medicine today. The ability to modify a specific cell type or tissue by gene therapy is based on the ability to deliver, incorporate, and express a therapeutic gene in the target cell. The delivery of such genes into cells is accomplished by the use of vectors. Both viral and non-viral vectors are used. A particular viral vector for use in gene therapy is the Adeno-associated virus (AAV). This viral vector is known to be one of the safest vectors and has been identified as the only site specific vector in use today. The AAV vector is being investigated for use in treating many well known diseases including cancer.

The wild type Adeno-Associated Virus contains a small single stranded DNA[(1)] with a small size of 4.68kb[(2)]. The single stranded DNA molecule contains two genes. The Rep gene codes for proteins that control viral replication, gene expression, and integration into the host genome[(3)]. The Cap gene codes for capsid structural proteins[(3)]. At each end of single stranded DNA are 145 bp terminal repeats[(3)]. When used as a vector, the Rep and Cap genes are replaced by the trans gene or therapeutic gene[(3)]. However, removal of the Rep gene removes the site specific activity of the Adeno-Associated Virus vector.

very good Summary of the reader.

The Rep gene codes for four proteins[(2)] based on a single reading frame. The four proteins are Rep78, Rep68, Rep52, and Rep40[(2)]. The proteins are translated from two different translation codons due to alternate RNA splicing of RNA products[(2)]. Both Rep78 and Rep68 proteins exhibit strand and site specific endonuclease activity and DNA-DNA/ DNA-RNA helicase activity[(2)]. These activities are specific to sites located on human chromosome 19[(4)]. Therefore, the Adeno-associated Virus is able to integrate into a specific site in the human genome. The Adeno-associated Virus is the only

Eukaryotic Virus with this site specific integration[4]. This mechanism is one of two that the Adeno-associated Virus uses for genomic integration.

The Adeno-associated Virus is of the *Dependovirus* genus that contains the four paroviridae family genuses[1]. Of the four, the Adeno-associated Virus is the only virus that requires a helper virus to replicate[1]. After infection with a helper virus, replication of Adeno-associated Virus can occur. The helper virus is typically the adenovirus[2] hence the name Adeno-associated Virus, but the herpesvirus is also a known helper virus[2]. No disease associated with the Adeno-associated Virus has been identified in humans[5]. The nature of the Adeno-associated Virus to only replicate in the presence of a helper virus[5] makes it a very safe viral vector for use in human gene therapy. Also, laboratory handling of the Adeno-associated Virus is at a Biosafety level of 1 (BL-1) when not associated with the adenovirus which is a Biosafety level 2 (BL-2)[6]. These safety issues make the Adeno-associated Virus ideal for use in gene therapy applications and research.

The Adeno-associated Virus has several serotypes. Of which, AAV-2 is one of five distinct serotypes that have been characterized and is used in gene therapy[1]. The primary receptor for AAV-2 is heparan sulfate proteoglycan[1], which are cell surface molecules associated with a wide range of cells of vertebrate[7]. AAV-2 enters the cell nucleus by means of motor proteins and endosomal routes all in the matter of seconds[1]. These physical characteristics are what make the Adeno-Associated Virus an ideal vector for treating disease using gene therapy. One disease being targeted with Adeno-Associated Virus is cancer.

Research is being conducted that utilizes the specific physical characteristics of the Adeno-Associated Virus particularly the Rep78 protein product to fight cancer. The Rep78 protein is directed to inhibit E2F-1 transcription and to stabilize pRB-E2F-1 complex in cells[8]. The E2F-1 is one of four transcription factors and pRB is Retinoblastoma tumor suppressor protein[9]. The interaction of pRb with Ef2 transcription factors gives control of the cell cycle by regulating expression of genes[9]. Treatment with Rep78 could stabilize the formation of the pRB-E2F-1 complex[8] and would be very useful in the treatment of cancer[8].

Though the Adeno-Associated Virus is only one of many vectors for use in gene therapy, it is certainly showing promise for use in fighting serious diseases like cancer. Other diseases being targeted with the use of the Adeno-Associated Virus vector include cystic fibrosis, hemophilia, high blood pressure, muscular dystrophy, and Parkinson's disease[1]. Among the mentioned characteristics of the Adeno-Associated Virus as a vector, other advantages include transduction of nondividing cells and a mild immune reaction in patients undergoing gene therapy[1].

very good abstract description
Also well written

Exactly what I was looking for.

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