NRC·CNRC

ADENOVIRAL VECTORS

For vaccines and cancer therapy – licensing opportunity L-10890

HIGHLIGHTS

Adenoviruses can be used for antigen delivery in vaccine applications and for the therapeutic treatment of cancer. The NRC has improved the safety and utility of this important class of vectors by creating a vector called adenovirus delta protease. Our experts have manipulated the adenoviral strain to specifically delete the viral protease from the vector's genetic sequence to avoid dissemination to healthy cells, while retaining all the desirable features of the vector, namely efficient delivery and production of antigens and activation of the immune system. Complementary cell lines facilitate amplification of non-replicating, non-disseminating vectors for optimal safety of antigen delivery, as well as replicating, non-disseminating vectors for greater transgene production and enhanced tumour cell killing.

TECHNOLOGY TRANSFER

- Commercial exploitation licence
- R&D agreement for development

MARKET APPLICATIONS

- Antigen delivery vector for vaccines against viral and bacterial infections
- Cancer therapy

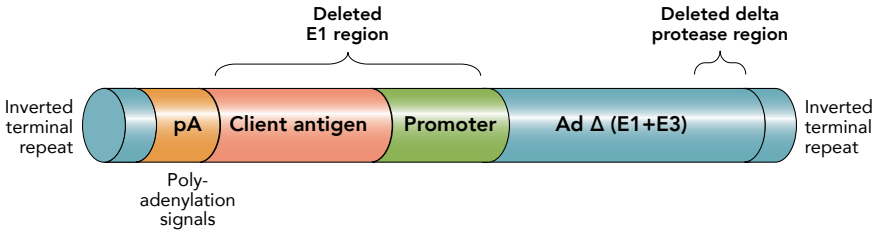

Figure 1A: Non-replicating, non-disseminating vector

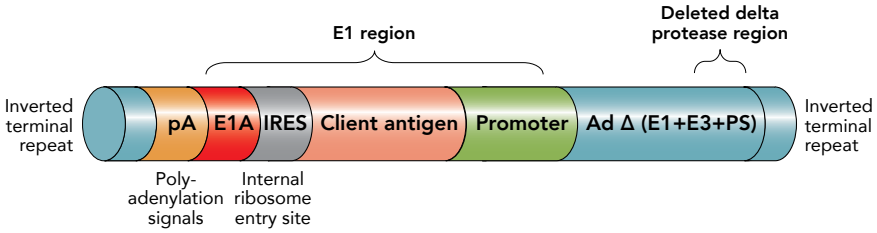

Figure 1B: Replicating, non-disseminating vector

HOW IT WORKS

Vaccines against viral and bacterial infections: Non-replicating, non-disseminating vector (Figure 1A)

The NRC's vector can be used by clients seeking to increase immune response to a given antigen. Our vector specialists insert the antigen's genetic code (ex. Hepatitis C) into the vector, whose viral protease and E1 region have been deleted. Then, they produce recombinant plaques of the virus, amplify the vector using a complementary cell line, and purify it. When injected, the vector enters targeted cell tissue and produces high levels of the antigen. Because of the absence of E1 and protease, the vector cannot replicate nor disseminate to other cells, thus greatly increasing its safety. Transient high-level production of the antigen by the infected cells generates a strong and durable protective immune response (humoral and cellular) against the infectious agent from which the antigen is derived.

Highly potent vaccines and cancer therapy: Replicating, non-disseminating vector (Figure 1B)

The NRC's vector can also be used by clients to develop more powerful vaccines against infectious agents, or therapeutic vaccines against cancer. For infectious agents, our specialists insert the antigen's genetic sequence into the vector; for cancer, they insert a tumour-specific antigen sequence (ex. Melanoma). The E1 region is present, allowing the vector to replicate and dramatically increase its cargo copy number.

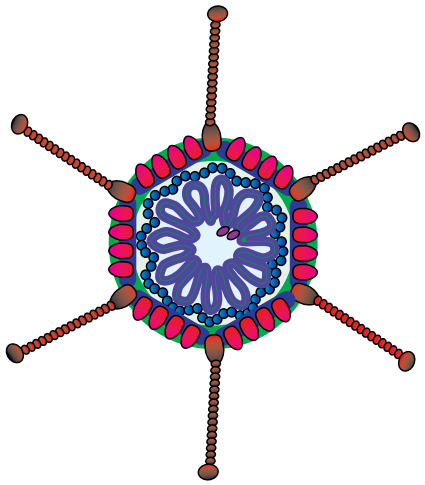

Figure 2: Adenovirus – gene sequence (DNA) coiled inside

Recombinant plaques of the vector are produced and amplified using a complementary cell line.

In vaccines against infectious agents, the vector replicates in the cells of the injected tissue and produces large quantities of the antigen, but does not disseminate, making it both potent and safe. When used for cancer therapy, the vector is injected directly into the tumour mass and begins to replicate, causing cancer cell death. During replication, the vector expresses high levels of tumour-specific antigens and cytokines, which attracts inflammatory cells to the tumor site. This triggers a strong immune response that recognizes and kills other cancer cells of the same type throughout the body.

BENEFITS

- Safe for vaccines and cancer therapy due to deleted viral protease
- Can infect almost all cell types without disseminating to untargeted cells
- Easy to produce and purify

PATENTS

NRC file 10890 (adenoviral vector): Patents issued in Canada and the United States.

NRC file 10624 (A549 cell line for production of adenoviral vectors): Patents issued in Canada and the United States.

NRC File 11225/11648 (cumate switch for virus amplification): Patents issued in Canada, the United States, and Europe.

NRC file 11444 (coumermycin switch for virus amplification): Patents issued in Canada, the United States, Europe, Australia, New Zealand, and Japan.

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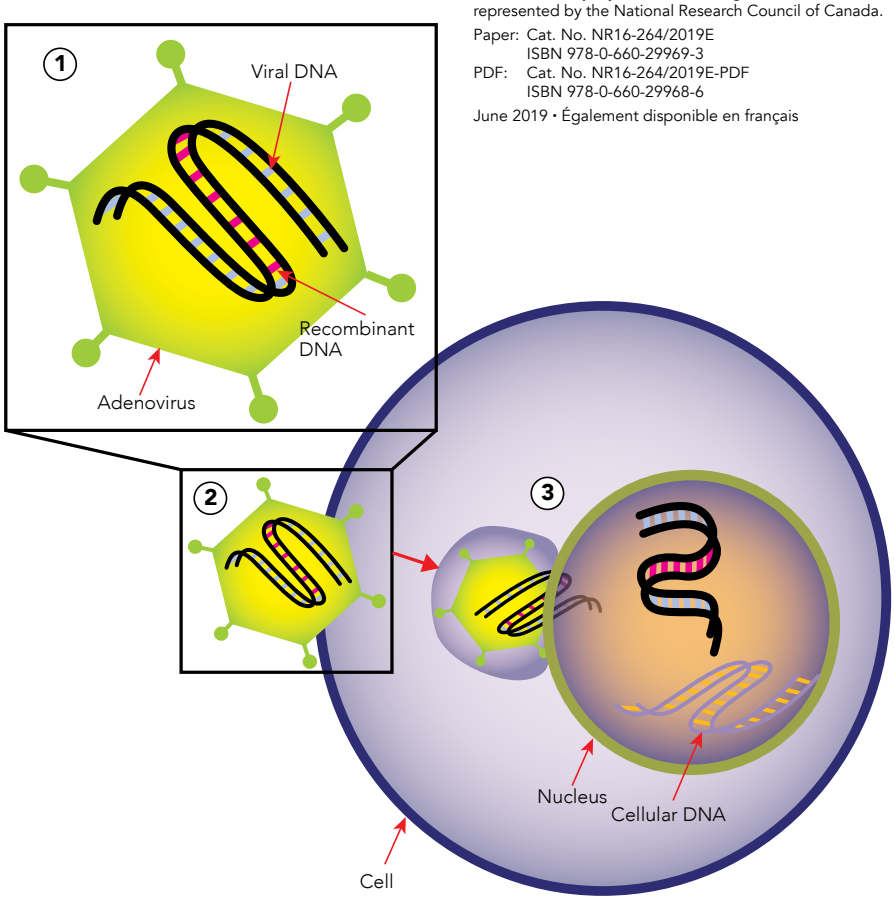

Figure 3: The process of using an adenoviral vector to deliver antigens:

1. Recombinant antigen DNA is inserted into the adenoviral vector.
2. The vector binds to the cell membrane, is packaged in a vesicle, and then injects the antigen DNA into the nucleus.
3. Cell then makes the antigen using the recombinant antigen DNA, while the cell's own DNA remains unaltered.