Use of Constitutive Transport Elements to Control the Host Range of Retroviral Vectors

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Technology description

The major host range determinant for retroviruses and for retroviral vectors is the envelope glycoprotein. However there is a second element, the constitutive transport element, or CTE, that also plays an important role in determining host range. In order to replicate, retroviruses must transport both spliced and unspliced RNAs from the nucleus to the cytoplasm. For simple retroviruses, transport of the unspliced RNA requires an interaction between the CTE -- which is small element in the viral RNA -- and host factors. The CTE of avian sarcoma/leukosis viruses (ASLV) does not function in mammalian cells. As a consequence ASLV, and vectors derived from ASLV, will not replicate in mammalian cells even if the host/virus system is modified so that the entry of the ASLV into mammalian cells is efficient. This invention demonstrates how this barrier to viral replication is overcome by introducing sequences from an amphotropic murine leukemia virus (MLV) into a modified ASLV vector. The resulting vector can replicate in mammalian cells if the host cell/vector system is designed to provide compatibility between the envelope of the virus and the receptor on the host cell. The resulting ASLV vector should be useful for experimental applications both in cultured cells and in animal models. In addition to being able to extend the host range of retroviruses by modifying their CTEs, it is also possible to restrict their host range.

Application area

A modified MLV virus that replicates only in avian cells, not in mammalian cells has been developed.

Advantages

This virus can be used to develop a new generation of safer MLV-based vectors. Therefore, this invention provides the advantages of being able to restrict or extend the ability of retroviral vectors to replicate in defined hosts by manipulating their CTEs. This will be useful in the development of a new generation of retroviral vectors that are both safer and more useful than those currently available.

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