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In-vitro and in-vivo gene delivery into vertebrate cells by recombinant baculoviruses.

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Despite widespread use for protein expression in insect cells, the application of recombinant baculoviruses for gene transfer into vertebrate cells is rather rare, although the so-called BacMam technology which uses modified baculoviruses carrying vertebrate cell-active regulatory elements has proven to be a versatile and efficient approach for transient gene expression. Based on the Bac-to-Bac system (Invitrogen) we constructed novel baculovirus transfer vectors for single, dual and inducible expression of proteins in mammalian, avian and piscine cells, and for gene silencing by shRNA. Protocols were developed for effective transduction of cells which are resistant to other gene transfer techniques. High-level synthesis of biologically active foot-and-mouth-disease virus (FMDV) 3C-protease in transduced cells demonstrated expression of cytotoxic proteins from transduced baculoviruses. Advantages of BacMam viruses as gene delivery vectors for vertebrate cells are that they: 1) can be easily isolated and produced, 2) have an extensive range of permissive cells, 3) cause no observable cytopathic effect, 4) are safe because they do not replicate in vertebrate cells, 5) have a large insert capacity (about 40 kbp) for simultaneous delivery of multiple genes, 6) have a broad application spectrum, 7) are cost effective (virus from 1 ml culture supernatant can transduce 10exp9 cells). In addition, inoculation experiments with mice and rabbits showed that BacMams containing the P1-2A+3C coding regions of FMDV or the rabbit haemorrhagic disease virus (RHDV) VP60-encoding gene induce a B- and T-cell response against the respective target protein which in the case of VP60 protects against a lethal RHDV challenge infection.

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