10a Baculovirus as a Tool for Eucaryotic Protein Expression in Mammalian Cells

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Baculovirus has been employed as a gene delivery vector for in vitro and in vivo gene therapy studies. In contrast to previous studies, here we demonstrated the feasibility of adapting baculovirus/mammalian cell system for the production of eucaryotic proteins. To this end, large hepatitis delta antigen (L-HDAg) was chosen as the model protein. We constructed a recombinant baculovirus expressing histidine-tagged L-HDAg under the transcriptional control of CMV-IE promoter. The virus could transduce BHK cells with efficiency over 90% as determined by flow cytometry and resulted in high level expression. The expression level of L-HDAg could be further enhanced 3-fold by the addition of sodium butyrate. The expressed L-HDAg was correctly isoprenylated and localized to the cell nucleus as determined by immunofluorescence double labeling and confocal microscopy, thus confirming the authenticity of the expressed protein. The histidine tags further allowed for the purification of L-HDAg by immobilized metal affinity chromatography. Since L-HDAg requires extensive post-translational modifications, procaryotic cells are not suitable as the host. The expression of L-HDAg in insect cells was also hampered due to the induction of cell cycle arrest. Therefore, the baculovirus/mammalian cell system offers an attractive alternative for the transient expression of proteins that require extensive post-translational modification.