260f A Viral/Non-Viral Hybrid Gene Delivery Vector

Josh Ramsey and Daniel W. Pack

A number of challenges remain to be overcome in order for gene therapy to become common practice. The development of safe and efficient vectors is a primary focus for many in the field of gene therapy. Viral vectors exhibit high efficiency but suffer from problems such as immunogenicity, pathogenicity, and limited stability. While non-viral vectors may avoid such problems, they are significantly less efficient than viral vectors and typically are limited to transient expression of the therapeutic gene.

We are developing a hybrid vector based on Moloney murine leukemia virus particles lacking envelope protein ("bald viruses") and synthetic transfection reagents including cationic lipids and polymers. Unlike non-viral vectors, this hybrid vector delivers genes that are integrated into the target cell genome. Since the vector lacks viral envelope protein, it may exhibit reduced immunogenicity and improved stability over enveloped viral vectors. In addition, the vector can be targeted to non-native cells via ligands conjugated to the transfection reagent. For example, hybrid vectors comprising bald MLV and Lipofectamine 2000 transfect NIH-3T3 cells with approximately 10% the activity of enveloped virus (~$2x10^3$ cfu/ml compared to ~$2x10^4$ cfu/ml). This presentation will discuss the effects of various transfection reagents on physical properties of vector complexes (particle sizing, TEM) and transfection efficiency and stability.