Analytical and Biophysical Characterization of Oncolytic Viruses

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Oncolytic virotherapy takes advantage of the inability of cancer cells to mount an adequate immune response to viral infections. The basic premise is selective or preferential killing of cancer cells, while healthy cells are typically able to fight off the infection. Several oncolytic viruses (OV) are in pre-clinical or early clinical development and these are engineered recombinant constructs that utilize common DNA and RNA viruses. One OV, known as TVEC, was approved recently for use in melanoma. TVEC contains recombinant HSV and a GMCSF transgene. Our OV platform at MedImmune includes an engineered form of the Newcastle Disease Virus (NDV) and also incorporates GMCSF as a transgene. NDV is a single stranded RNA virus and, in native form, is not a human but an avian pathogen. Genetic engineering was performed to reduce avian pathogenicity and increased virulence against cancer cells. The production of these recombinant viruses requires selection of appropriate host cells, based on yield and quality of the product. In recent years, regulatory agencies have been open to use of human cell lines as host, including HeLa that contains HPV genes. We have compared a few host cell lines for production of NDV-GMCSF. An advantage offered by HeLa cells was incorporation into the virus of proteins known as regulators of complement activation (RCA) that allow a longer half-life of the virus in circulation. However, impurities derived from host cells as well as process conditions must be kept to the lowest levels possible. A thorough analytical and biophysical evaluation of the product includes measurements of (a) infectivity, (b) size distribution and morphology of virus particles, (c) gene sequence and gene copy number, (d) presence of major viral proteins, and (e) contaminants including residual host cell DNA and proteins. Applications of bioanalytical methods and tools to address these areas will be outlined.

Take away messages:

- Oncolytic viruses (OV) are promising as potential front line therapies for many kinds of cancer, with solid tumors being the initial clinical targets
- Production of recombinant and genetically engineered OV requires a thorough bioanalytical characterization of the product to ensure desired efficacy, safety and quality attributes
- Development and applications of analytical and biophysical methods needed to support an OV program will be described using recombinant NDV-GMCSF as an example