Determining the Vesicular Stomatitis Virus Components Involved in Interferon Gene Regulation

Riegel, K.R

To help identify the viral component(s) involved in regulation of the host antiviral interferon response, we are comparing the genomic sequence of two strains of Vesicular Stomatitis Virus (VSV) that differ in their ability to produce interferon (IFN). Interferon is a protein that establishes an antiviral state in cells, therefore protecting them from infection. In response, many viruses have evolved ways to shut off the IFN antiviral response. Wild type (Wt) VSV is able to suppress the interferon response, thereby establishing a successful infection. T1026R1 is a mutant strain of VSV that is not able to suppress IFN. Previous results from our lab indicate that VSV may block activation of NF-κB, a transcription factor essential for transcription of the IFN gene. We hypothesize that the viral component responsible for regulation of NF−κB, and therefore suppression of IFN production, is defective in T1026R1. To test this hypothesis, we have sequenced the entire genomes of both Wt and T1026R1 and compared them to each other. We have identified mutations in the G, L and M genes of T1026R1 which result in amino acid changes in the protein of this virus. In previous studies, the M protein has been found to be a responsible for most of the cytopathic effects found in infected cells and is predicted to play a role in IFN gene expression. We have created a series of expression vectors that each encode one of the VSV proteins fused to the green fluorescent protein (GFP). These vectors are now being transfected into mouse L929 cells which allows us to analyze the effect of each VSV protein on NF-κB activation and IFN mRNA production.