Interferon (IFN) is a cellular protein produced as part of the innate anti-viral response. Many viruses have evolved mechanisms by which they bypass the cell’s ability to activate this antiviral response, thereby allowing a productive infection to occur. The main research focus in our laboratory is to understand the mechanisms used by Vesicular Stomatitis Virus (VSV), the prototype member of the Rhabdovirus family, to block activation of the IFN response. It is known that the viral matrix (M) protein nonspecifically suppresses IFN gene expression by inhibiting global host transcription. Preliminary studies indicate that VSV may also specifically control induction of the IFN gene by regulating activation of a cellular transcription factor called NF-κB. Once activated, NF-κB translocates to the nucleus and becomes part of an enhanceosome complex responsible for IFN gene induction. The goal of this study was to investigate the viral protein(s) responsible for NF-κB activation. L929 cells (mouse fibroblast) were infected with wild type VSV or mutant virus strains that contain a defective M protein. After various times post infection, NF-κB nuclear localization was monitored by immunofluorescence and confocal microscopy. Preliminary results indicate that the M protein is involved in the regulation of NF-κB activation.