Hepatitis C Virus (HCV) infects liver cells and is estimated to infect 3% of the world’s population. HCV is transmitted by contaminated blood and people who are infected with HCV can be asymptomatic. HCV can lead to cirrhosis of the liver and hepatocellular carcinoma. HCV is a single-stranded RNA virus that belongs to the flavivirus family and produces 10 viral proteins. These viral proteins aid in HCV replication and allow HCV to remain undetected by the immune system by inhibiting the production of interferon-beta.

The anti-viral response activates transcription factors such as ATF-2, NFkB, and IRF-3 that translocated into the nucleus and bind to the interferon gene to produce interferon. The HCV viral protein NS3/4A is known to inhibit IRF-3 movement into the nucleus, inhibiting the production of interferon. By blocking the production of interferon, HCV is able to hide from the immune system and establish a chronic infection. HCV viral protein NS5A is known to inhibit the movement of transcription factor NFkB into the nucleus, thus inhibiting the anti-viral response. We are interested to see if NS3/4A inhibits the anti-viral response by blocking the movement of both transcription factors IRF-3 and NFkB into the nucleus.

Hepatitis C Virus makes 10 viral proteins once it infects a cell. Three of these proteins are structural proteins that are essential for virus assembly. Seven of these proteins are non-structural proteins that aid the virus in replication and evading the anti-viral response. NS3/4A is one of these non-structural proteins that are produced by HCV. NS3/4A acts as a protease that cleaves the polymeric strand of viral proteins made following translation of the viral genome. NS3/4A is also known to cleave the protein MAVS. When MAVS is cleaved from the mitochondria, MAVS becomes inactive. By inactivating MAVS, NS3/4A prevents the movement of transcription factor IRF-3 into the nucleus which inhibits the production of interferon. This blocks the ad in evading the anti-viral response as it blocks the movement of transcription factors by cleaving MAVS and inhibiting the production of interferon.

**Hypothesis**

Hepatitis C Virus nonstructural protein NS3/4A blocks the nuclear localization of both transcription factors NFkB and IRF-3 following infection.