

## **Interferon gamma allows long-term maintenance of VZV-infected neurons in vitro**

**Baird NL; Bowlin JL; Cohrs RJ; Gilden D**

### **Abstract**

Varicella zoster virus (VZV) is a neurotropic alphaherpesvirus. During primary infection, VZV causes varicella (chicken pox), after which the virus goes latent in ganglionic neurons along the entire neuraxis before reactivating decades later to cause zoster (shingles). Interferon gamma (IFN $\gamma$ ), produced during viral infection, stimulates transcription of genes that mediate antiviral responses. Herein, it was tested whether IFN $\gamma$  treatment of human neurons inhibits VZV infection of human neurons in vitro. Infected neurons not treated with IFN $\gamma$  developed a cytopathic effect in 4 weeks, during which time VZV DNA increased 7-fold and viral RNA accumulated. Infected neurons cultured in the presence of IFN $\gamma$  for 8 weeks or infected neurons cultured in IFN $\gamma$  for 4 weeks followed by cytokine removal for an additional 4 weeks had only a 2.8- and 3.6-fold increase of viral DNA, respectively in the 8 weeks post-infection. Furthermore, levels of VZV transcripts did not increase between 4 and 8 weeks post-infection when IFN $\gamma$  was removed at 4 weeks post-infection, and even began to decrease when the cultures were maintained in IFN $\gamma$  for the entire 8 weeks. In accordance with reduced DNA accumulation and mRNA levels when infected neurons were maintained in IFN $\gamma$ , less CPE was evident at 8 weeks post-infection compared to cultures which had IFN $\gamma$  removed at 4 weeks post-infection.

### **Keywords:**

Replication of VZV DNA and transcription of viral genes was inhibited by IFN $\gamma$  and the extent of virus gene expression in IFN $\gamma$