Introduction
- Lifelong latent infections of herpes simplex virus type 1 (HSV-1) are characterized by periodic reactivation, during which newly produced virions may also reach the central nervous system (CNS).
- Epidemiological and experimental findings suggest that HSV-1 might contribute to the pathogenesis of Alzheimer’s disease (AD).

Aims
- What is the role of herpes viral infection in promoting the formation of neurotoxic APP fragments that can contribute to the development of Alzheimer’s disease?
- What are the effects of productive HSV-1 infection on APP processing in neuronal cells?

Methodology
- Measure PRV growth kinetics in Neuro-2a neuroblastoma cells to identify early and late timepoints to examine AD proteins (APP, nicastrin, BACE-1, AB 1–40, AB 1–42).
- Visualize and quantify AD protein levels in PRV-infected Neuro-2a cells via ELISA and WB.

Results
- Growth curve indicates that 9h, 12h, 24h timepoints may be promising for comparison of APP processing in Mock, PRV, HSV-1 infected cells.
- Western Blot data shows that full length APP greatly reduced at 24h, suggesting cleavage activity resulting in the formation of intermediate products (45-55 kDa) and AB peptide (4 kDa).
- Interestingly, while there is a negative correlation between infection duration and the amount of full length APP in HSV infected cells, full length APP appears to increase upon duration of infection in PRV infected cells.
- The ELISA data provides additional support for the idea that APP levels are decreasing in HSV1 infected cells, possibly due to increased cleavage activity.

Legend
- PRV180 growth curve in Neuro2a cells,
- Western Blot of APP showing cleavage products,
- ELISA data of intracellular APP,
- Red capsid PRV180 visualization

Conclusions
- These findings demonstrate that HSV-1 infection of neuronal cells can generate multiple APP fragments with well-documented neurotoxic potentials.
- It is tempting to speculate that intraand extracellular accumulation of these species in the CNS resulting from repeated HSV-1 reactivation could, in the presence of other risk factors, play a co-factorial role in the development of AD.

Future Directions
- I intend to repeat the ELISA data to increase statistical power and reduce inter-trial variability.
- The next goal is to obtain brain tissue from normal and Alzheimer’s Diseased mice and see if ex vivo analysis corroborates the preliminary findings in vitro.
- Lastly, an HSV-1/Neuro2a growth curve should be assayed to ensure that proper timepoints are being selected for analysis.

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