Unit Assessment – Module 9 Case Study: Neurdogeneration (II) – Randy Maysaud

Referring to figure 1, it displays the difference of two AAV vectors in both the Lateral entorhinal cortext and the Dentate Gyrus. One vector is the SSFO vector and the other is the EYFP vector. Both AAV vectors have a promoter of CaMKIIa and is tailed by the WPRA-pA. In the SSFO vector it uses the optogenetic SSFO (Stabilized Step-Function Opsin) with the EFYP (Enhanced Fluorescent Yellow Protein), while the EFYP vector only has the EFYP gene. The use of the EFYP is to follow the virus expression mark of the CaMKIIa gene. The SSFO will be used for optogenetics allowing the controlled activation of CaMKIIa, the EYFP will be used to measure the activity. Therefore, the EFYP vector is used to measure the control mice group while the SSFO vector will be used on the experimental mice group. This experiment takes measurements of the CaMKIIa output from the EFYP vector as well as the neural activation from c-Fos, the images were labeled using Immunofluorescence labeling, red is the neural activation, and the green is the CaMKIIa output. The images taken were from the ipsilateral and contralateral side of both the lateral entorhinal cortex and the dentate gyrus. This represents the perforant pathway which is a large neuronal connectional route from entorhinal cortex to the dentate gyrus. With this information I can conclude that the authors are experimenting optogenetics in the CaMKIIa of mice, this experiment is used to view if the optogenetics can support in Alzheimer's Disease. Alzheimer's Disease relates to perforant path fiber loss which results in cognitive impairment. [1] Also the if the promoter gene CaMKIIa is dysregulated it can become a modulator for toxicity within Alzheimer's Disease. [2]

The result of this research is interesting if we view the neural activity between the SSFO vector and the EYFP vector in the ipsilateral side of both the dentate gyrus and the lateral entorhinal cortex we can view that there is a greater amount of neural activity. The green represents the activation of the CaMKIIa gene, as we can see there is an increase in the CaMKIIa activation as well, this result is from the use of optogenetics from the SSFO vector which allows for opening and closing of calcium gates which activate the CaMKIIa gene with the use of light. Since the gates can be manually opened allowing for a greater activation of the gene, the gene in return increases the neural activity. Therefore, it shows a correlation between neural activity and the activation of the CaMKIIa gene. However, looking at the contralateral side there is not an increase in neural activity in SSFO, however there is also no CaMKIIa activation as well which further proves the correlation between the CaMKIIa activation and the neural activity. Referring to figure 2, the SSFO vector had a higher level of Aβ42 than the mice with the EFYP vector. In Alzheimer's Disease, Aβ42 can have lower level in dementia from type DAT, therefore SSFO vector can be a solution to help combat low Aβ42 levels. [3]

References:

[1] Burke, S. N., Turner, S. M., Desrosiers, C. L., Johnson, S. A., & Maurer, A. P. (1AD, January 1). Perforant path fiber loss results in mnemonic discrimination task deficits in Young Rats. Frontiers. Retrieved October 31, 2021, from https://www.frontiersin.org/articles/10.3389/fnsys.2018.00061/full.

[2] Ghosh, A., & Giese, K. P. (2015, November 24). Calcium/calmodulin-dependent kinase II and alzheimer's disease. Molecular Brain. Retrieved October 31, 2021, from https://molecularbrain.biomedcentral.com/articles/10.1186/s13041-015-0166-2.

[3] Fagan, A. M., Head, D., Shah, A. R., Marcus, D., Mintun, M., Morris, J. C., & Holtzman, D. M. (2009, February). Decreased Cerebrospinal Fluid Abeta(42) correlates with brain atrophy in cognitively normal elderly. Annals of neurology. Retrieved October 31, 2021, from https://www.ncbi.nlm.nih.gov/labs/pmc/articles/PMC2763631/.