Utilizing Protein Engineering to Develop a Neurotransmitter Sensor for MRI

You, Faith (School: Hellgate High School)

Functional magnetic resonance imaging (fMRI) has improved our understanding of the brain. However, it cannot distinguish among the discrete signaling pathways of specific neurotransmitters. Many neurological diseases are thought to be caused by imbalances or dysregulation of neurotransmitters. We currently cannot effectively or efficiently track the amount or activity of the neurotransmitters in diseased or healthy brains. The question that was asked was: how can we develop a protein sensor that is sensitive to glutamate? To answer it, two approaches were taken with the aim to engineer a protein sensor that triggers an fMRI signal when glutamate is released by neurons. First, an amino acid mutation was introduced in an effort to disrupt the naturally occurring hydrogen interaction. For the second, a vasoprobe was inserted into different loops of the protein. This project aims to aid in the detection of glutamate and in the mapping of the neural pathways. Previous researchers have developed and tested a range of constructs with various mutations. I tested designs with the N292R mutation and observed that these show promise in disrupting the natural bonds between amino acids. Our sensor does not specifically respond to glutamate at the moment, so our larger future goals are as follows: to find constructs that demonstrate responsiveness to glutamate and to collect a larger batch of data for more reliable conclusions. The second project showed a glutamate-specific response with two different models of a potential protein sensor initially, but further data collection did not support this. Overall, the two projects contribute to the greater understanding of the human brain.

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