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# SYNAPTIC DEPENDENT AMYLOID- $\beta$ GENERATION IN VIVO IN ALZHEIMER'S DISEASE MOUSE MODEL

Derrick Ogola

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Alzheimer's disease (AD) is the most common cause of dementia and is pathologically characterized by toxic amyloid- $\beta$  (A $\beta$ ) oligomers and plaques. Extracellular accumulation of A $\beta$  peptide in the brain appears to precipitate disease onset and the cognitive AD-associated pathogenic cascade. In humans and transgenic models of AD, brain regions with the highest levels of synaptic activity show the greatest amount of A $\beta$  plaques, suggesting A $\beta$  production is closely linked to synaptic transmission. To determine whether changes in synaptic activity alter the amounts A $\beta$  in the brain, we developed novel micro-immunoelectrode (MIE) technology that detects A $\beta$  in the brain ISF with high temporal resolution in the hippocampus of living mice allowing us to examine rapid A $\beta$  kinetics. We custom designed a 3D-printed adaptor to connect the MIE to an injection port which enables us to measure A $\beta$  and locally deliver drugs directly to the dentate gyrus. With these technologies, we pharmacologically manipulated synaptic activity by delivering excitatory and inhibitory drugs. Here, we show that changes in levels of A $\beta$  are closely related synaptic activity in the brain, where large increases in synaptic activity rapidly brought forth higher A $\beta$  levels in the mouse brain, while inhibition of nonspontaneous synaptic activity decreased A $\beta$  levels *in vivo* in a concentration dependent fashion. These findings highlight a close temporal relationship between synaptic activity and A $\beta$  generation in the brain.