Background:

Amyloid β (Aβ) plaques are hallmarks of Alzheimer’s disease (AD). Aβ40 and Aβ42 are the two main type of Aβ polymers that have direct role in plaque formation, Aβ42 is less abundant, highly insoluble but severely neurotoxic. In addition, the entorhinal cortex is traditionally the first area affected in AD, and more specifically the lateral entorhinal cortex (LEC).

The authors of the paper set up an optogenetic experiment to show that levels of brain interstitial fluid (ISF) Aβ42 in the APP Tg mice (a transgenic mice that overexpresses APP) were significantly higher that the levels observed in the wild-type mice.

The authors of this paper injected the two types of mice with two different fluorescent activatorss under control of the CAMLIIα promoter:

* The APP Tg mice are injected with an adeno-associated virus (AAV) expressing SSSFO-EYFP. Stable step-function opsin (SSFO) is a mutated version of channelrhodopsin (hChR2(C128SS)) that puts neurons in a state of excitability up to 30mins after activation by a pulse light. The last effect can be reversed by a brief pulse of a deactivation light.
* An AAV expressing EYFP is injected into wild type mice.

<https://www-ncbi-nlm-nih-gov.proxy1.library.jhu.edu/pmc/articles/PMC2795712/>

cfos labeling

The proto-oncogene c-fos, an immediate early gene, is expressed in neurons in response to various stimuli. The protein product can be readily detected with immunohistochemical techniques leading to the use of c-FOS detection to map groups of neurons that display changes in their activity.

In the brain, the perforant path or perforant pathway provides a connectional route from the entorhinal cortex to all fields of the hippocampal formation, including the dentate gyrus, all CA fields (including CA1), and the subiculum.

https://en.wikipedia.org/wiki/Entorhinal\_cortex

<http://www.scholarpedia.org/article/Entorhinal_cortex>

LEC: lateral entorhinal cortex

OML: outer molecular layer of Dentate Gyrus

The dentate gyrus, like the hippocampus, consists of three distinct layers: an outer molecular layer, a middle **granule cell layer**, and an inner polymorphic layer