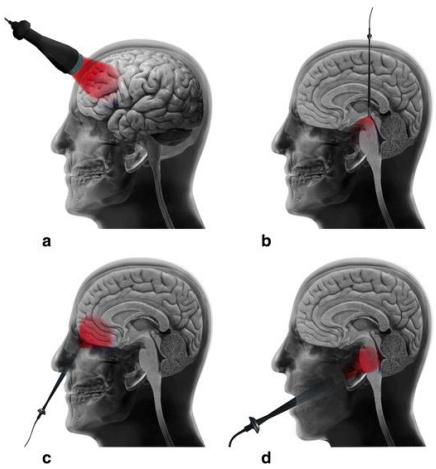
# The application of photobiomodulation therapy on Alzheimer`s disease: studies from *C. elegans* models

Daniela Bejan[1], Domenica Caponio[1], Maria Jose Lagartos-Donate[1], Kjetil Liknes[2], Evandro Fei Fang[1,2]
[1]Department of Clinical Molecular Biology, University of Oslo and Akershus University Hospital, 1478 Lørenskog, Norway
[2]The Norwegian Centre on Healthy Ageing (NO-Age), Oslo, Norway

**Abstract**
Alzheimer's disease (AD) is a neurodegenerative disorder. AD represents the most common cause of dementia, and it is characterized by memory loss, difficulties in language and problem-solving, and limited ability of movement. The deterioration of the brain is the result of neuronal death caused by the accumulation of beta-amyloid (Aβ) plaques and tau tangles. Apart from some treatments that can slow down the progression of the disease, there is no cure for AD at the present. Here we propose that photobiomodulation (PBM) therapy could serve as a non-invasive treatment for AD. We performed pilot experiments using the roundworm *C. elegans* models of AD. In-depth studies are in progress.



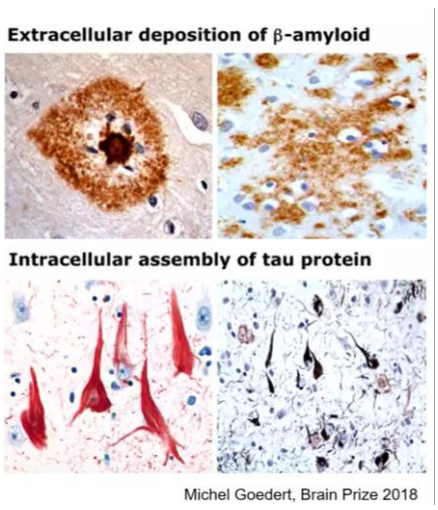




**Fig. 1. Schematic working model.** We propose that photobiomodulation therapy could be serve as a non-invasive treatment for AD via reducing Abeta and Tau pathologies. Upper image (ref. 1).

**Aim of the project**
To test PBM with different frequency of light and administered for different intervals of time to find the most efficient combination to improve memory in the AD C. *elegans* models.

**Mechanism of PBM**
The theory for the mechanism of action of PBM therapy is based on the ability of photons to interact with the brain tissue.
While most of the light is either absorbed by surrounding tissues or reflected or scattered, 10% of the light reaches the neurons. The photons delivered by the light are absorbed by the chromophore group present in the cytochrome c oxidase protein on the internal membrane of the mitochondria. The chromophore region responds to different types of light, with highest affinity for the near infrared range of frequency.
The complete biochemical mechanism is not yet fully understood.
The light used is non-ionizing, non-thermal and therefore safe.

**Methods**
Two strains of C. *elegans* were used for the study, a wild type (N2) strain and a strain with human mutant tau P301L (CK12) for AD model.

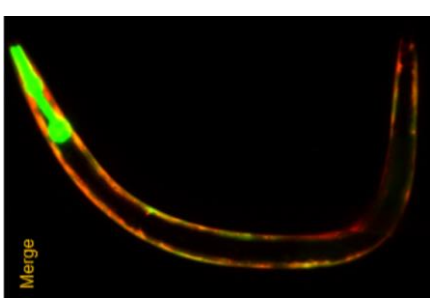



**Fig. 2.** A C. *elegans* with fluorescence. Image: the Fang lab.

**Memory Assay**
A chemotaxis-based simple associative memory assay was used.

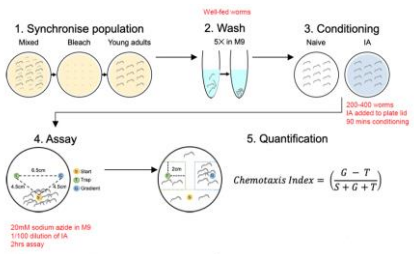



**Fig. 3.** Schematic representation of the chemotaxis-based memory experiment used in *C. elegans*. Image: Fang lab.

**Results**

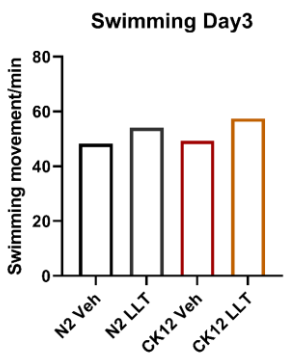
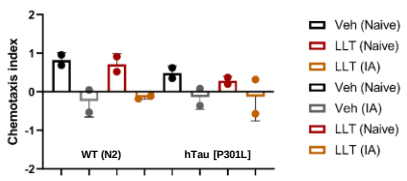



**Fig. 4. LLT shows a trend to increase healthspan in the AD tau worms.** The swimming test was performed with one biological repeat (n =30 worms).

**a 250 Hz for 1 minute, 4 doses**




**b 250 Hz for 1 minute, 2 doses**

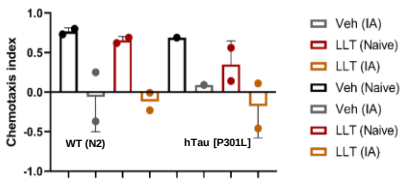



**Fig. 5. Effects of LLT on chemotaxis-based memory in the AD tau worms.** Due to high variaitons of data, the results obtained could not confirm our hypothesis. More data are needed to prove the efficiency of the therapy.

**Conclusion**
We have optimized the condition of PBM for the *C. elegans*-based memory assay. More tests should be carried out to identify the best frequency of light and the interval of time the light is applied. In-depth studies are in progress.

**References**
1.Salehpour, F. et al. Brain Photobiomodulation Therapy: a Narrative Review. Mol Neurobiol (2018).
2. Fang, E.F. et al. Mitophagy inhibits amyloid-beta and tau pathology and reverses cognitive deficits in models of Alzheimer's disease. Nat Neurosci 2019.
3.Xie, C. et al. Amelioration of Alzheimer's disease pathology by mitophagy inducers identified via machine learning and a cross-species workflow. Nat Biomed Eng (In press).