

Near-infrared light at 808 nm reduces β -amyloid-stimulated microglial toxicity and enhances survival of neurons in Alzheimer's disease in vitro model

Iuliia Golovynska^{a, #}, Yurii V. Stepanov^{b, #}, Renlong Zhang^{a, #}, Sergii Golovynskiy^a, Liudmyla V. Garmanchuk^c, Tymish Y. Ohulchanskyy^a, Junle Qu^{a, *}



¹ ^a Center for Biomedical Optics and Photonics, College of Physics and Optoelectronic Engineering, Shenzhen University, Shenzhen, 518060, P.R. China

^b Laboratory of Molecular and Cellular Mechanisms of Metastasis, R.E. Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology, NAS of Ukraine, Kyiv 03022, Ukraine

^c Institute of Biology and Medicine, Taras Shevchenko National University of Kyiv, Kyiv, 01601, Ukraine

* Corresponding authors e-mail: jlqu@szu.edu.cn

Equal contributed authors

ABSTRACT

Photobiomodulation (PBM) with 808 nm laser light was applied to microglia cells treated with β -amyloids ($A\beta$). The light irradiation resulted in a metabolic shift from glycolysis to mitochondrial activity in pro-inflammatory microglia affected by $A\beta$, leading to an increase in anti-inflammatory microglia. This process was shown to be accompanied by a decrease in pro-inflammatory cytokines and an activation of phagocytosis. PBM also caused a decrease in the $A\beta$ -induced activity of glucose-6-phosphate dehydrogenase, an enzyme regulating the rate of the pentose phosphate pathway, which activates nicotinamide adenine dinucleotide phosphate oxidases to further produce ROS. During co-cultivation of neurons and microglia, irradiation with 808 nm light was found to prevent the death of neurons, which was caused by ROS produced by $A\beta$ -altered microglia. The obtained data clarify mechanisms of PBM protection against neurodegeneration and support the use of NIR light in the treatment of Alzheimer's disease.

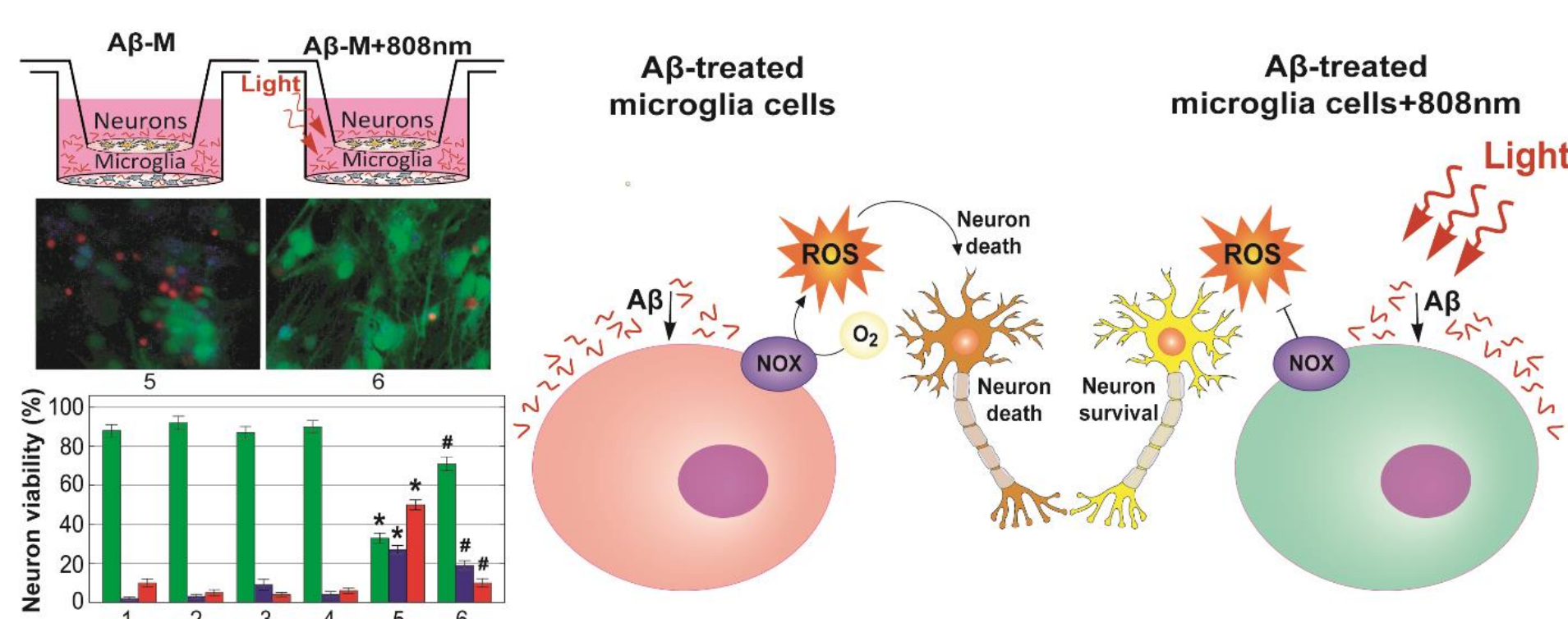


Fig. 1 Schematic diagram of NIR light protection against neurodegeneration in the in vitro model.

METHODS

The studies were carried out using the microglial cell suspension obtained from the hippocampus of healthy mice. $A\beta$ was prepared and used to treat microglia cells. Light irradiation of cells was performed using diode lasers emitting at 808 nm with 30 mW/cm². Mitochondrial membrane potential, ROS level, cell viability, apoptosis and necrosis were assessed using corresponding fluorescent probes and epifluorescence microscopy. Phagocytosis, nitric oxide and H₂O₂ production, arginase and glucose 6-phosphate dehydrogenase activities were measured using standard assays. Cytokines, glucose, lactate, and ATP were measurements with ELISA. As our data were normally distributed, Student's t-test or ANOVA test was used.

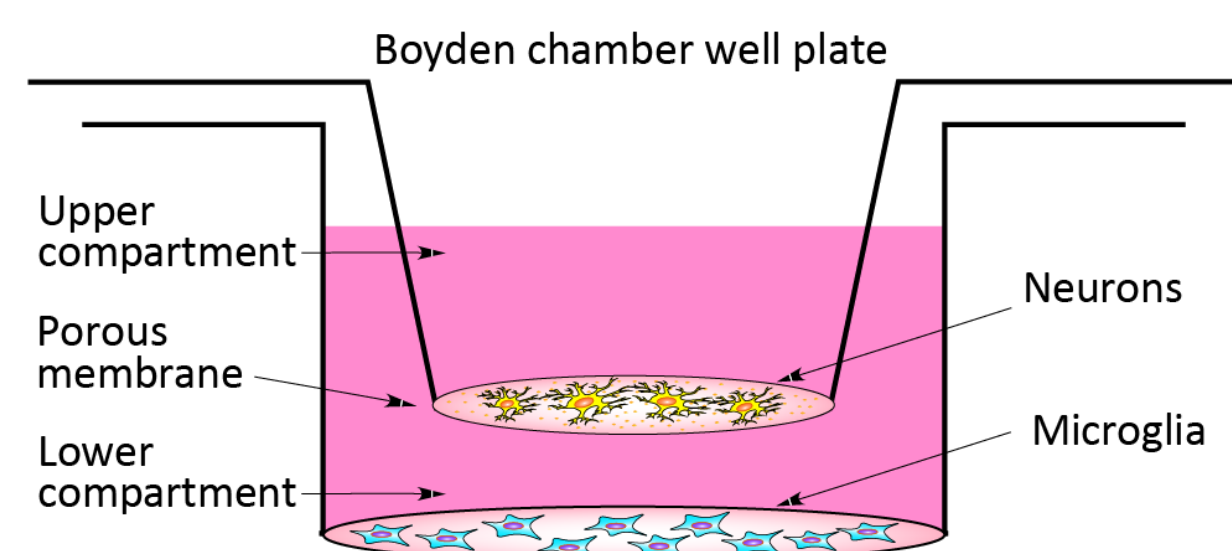


Fig. 2 Schematic illustration of a Boyden chamber with cultured neurons and microglia in two cell medium-filled compartments separated by a microporous membrane.

RESULTS

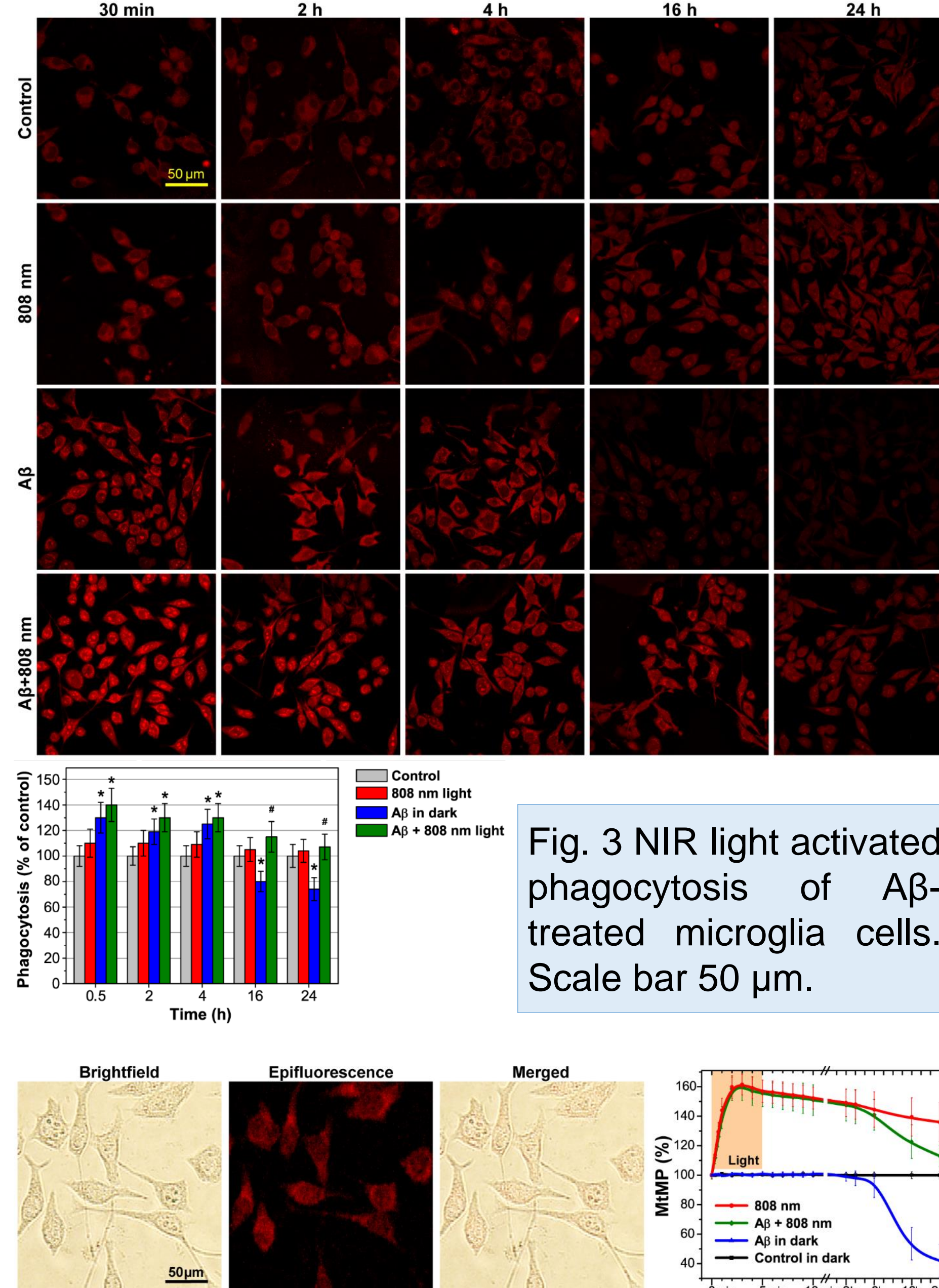


Fig. 3 NIR light activated phagocytosis of $A\beta$ -treated microglia cells. Scale bar 50 μ m.

Fig. 4 Mitochondrial membrane potential activation in microglia cells after $A\beta$ treatment and NIR light irradiation. Scale bar 50 μ m.

RESULTS

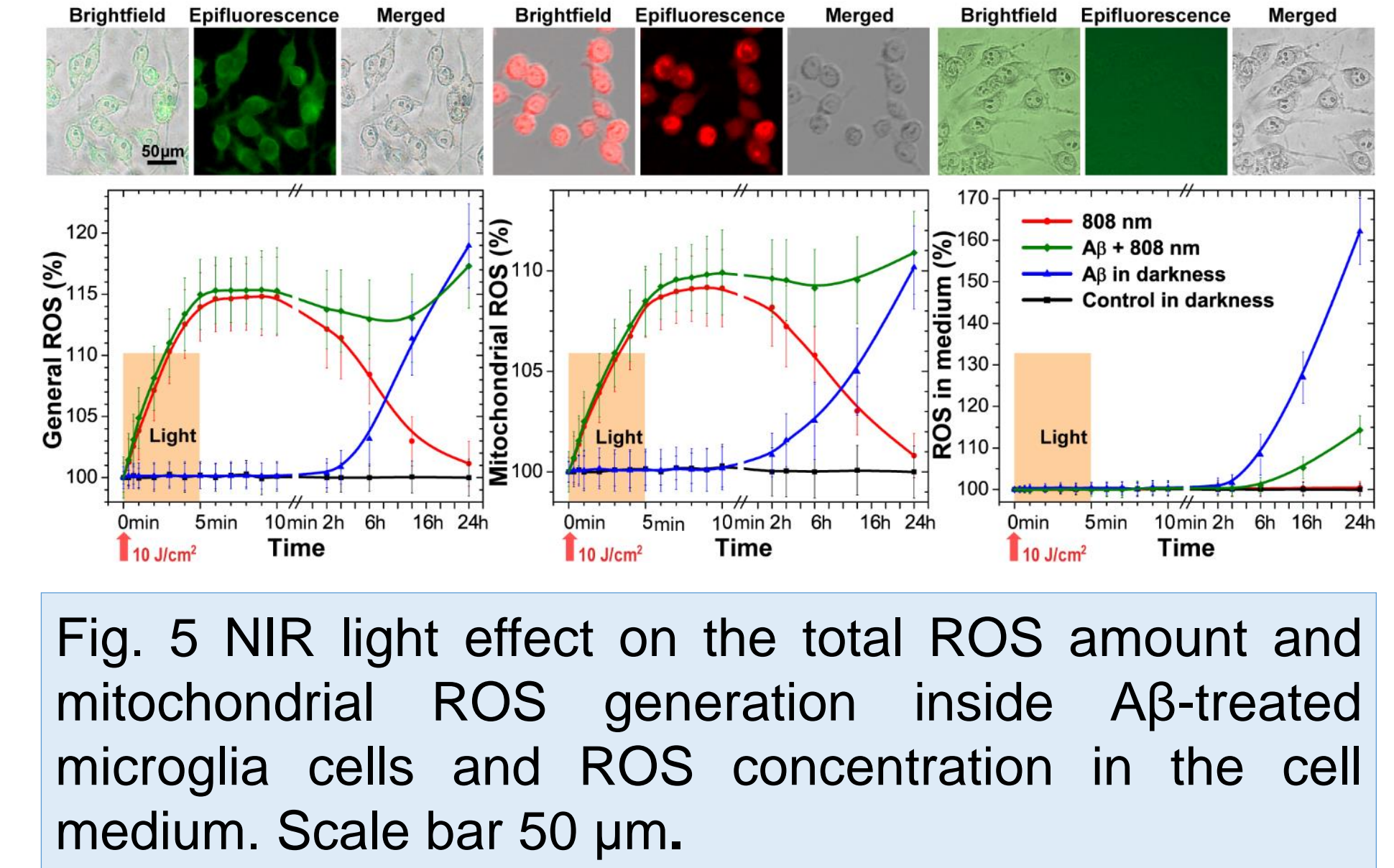


Fig. 5 NIR light effect on the total ROS amount and mitochondrial ROS generation inside $A\beta$ -treated microglia cells and ROS concentration in the cell medium. Scale bar 50 μ m.

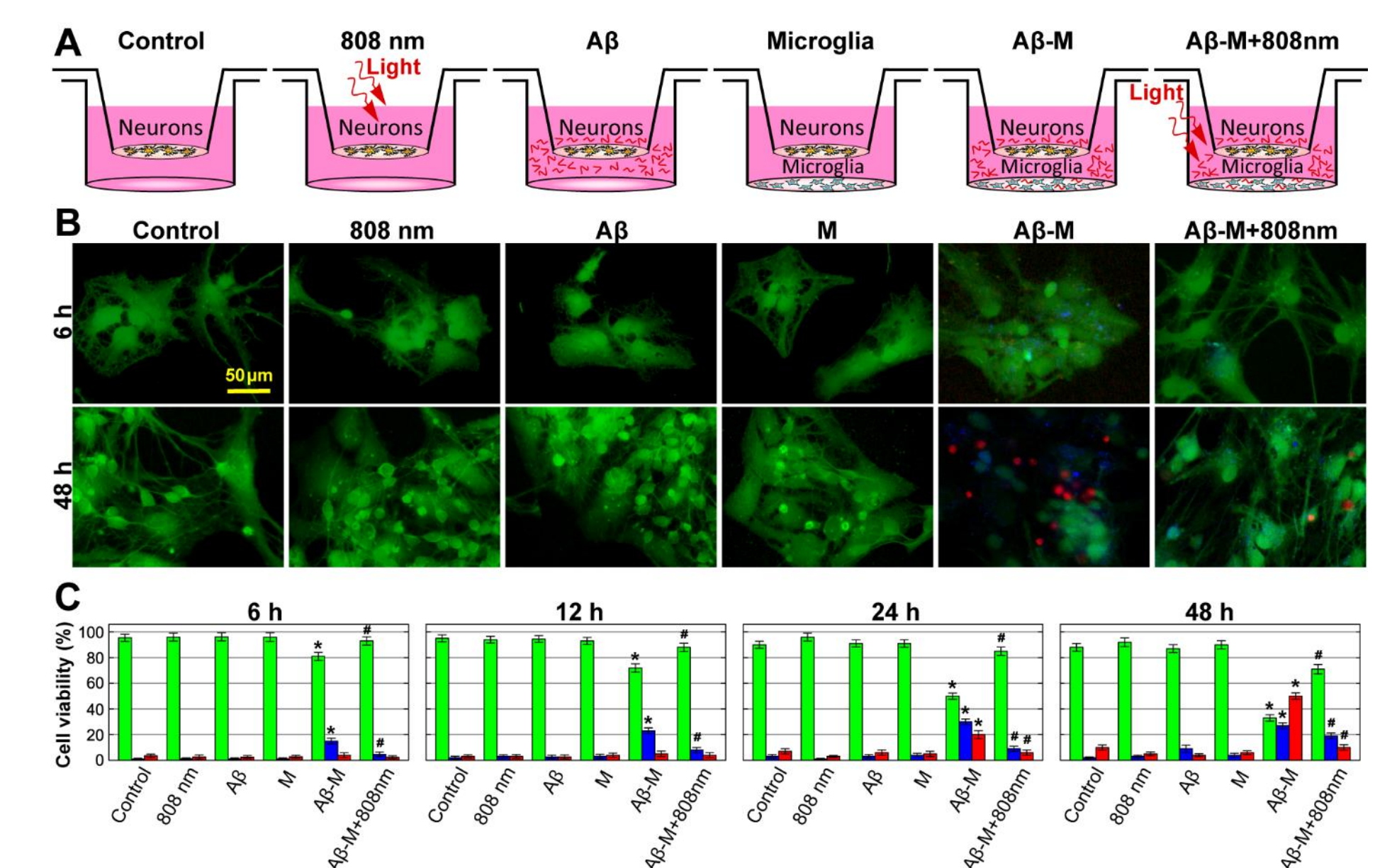


Fig. 6 NIR light induced increased viability of neurons co-cultured with $A\beta$ treated microglia. Scale bar 50 μ m.

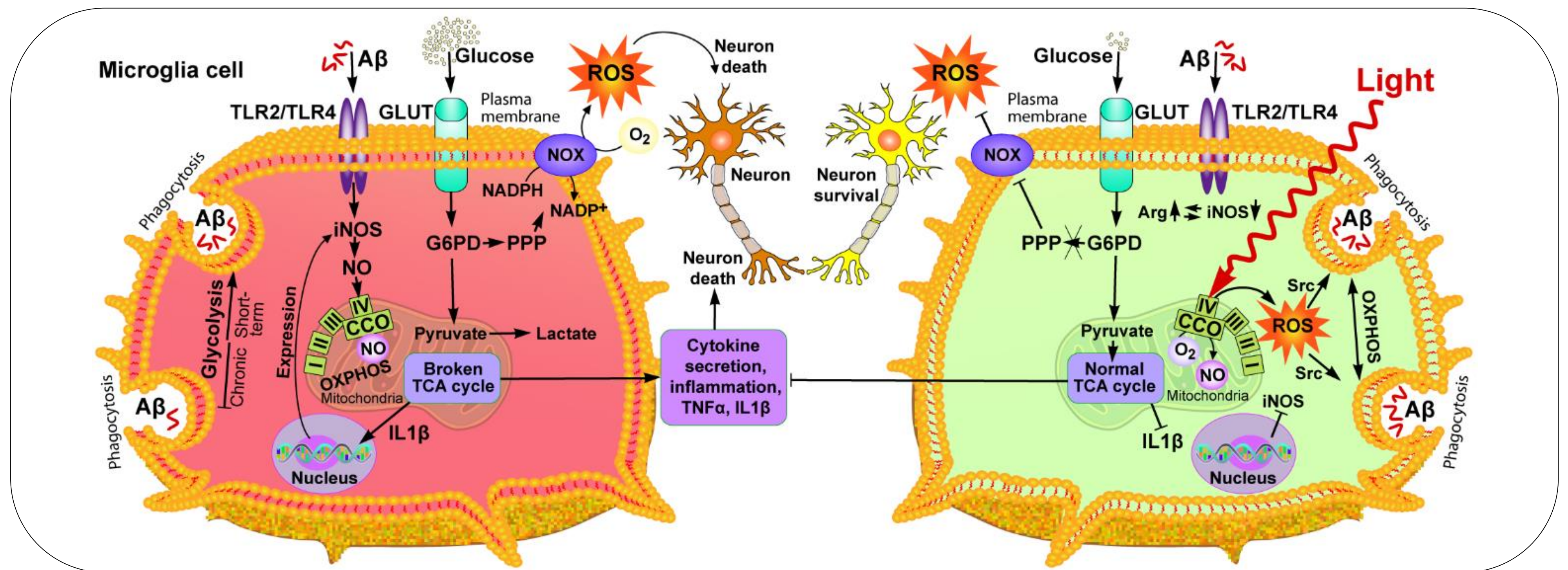


Fig. 7. The schematic diagram of the proposed mechanisms of NIR light and $A\beta$ actions on the metabolic regulators of microglia cells phenotype and functions.

CONCLUSIONS

$A\beta$ -treated microglia reveal metabolic changes and shift to the inflammatory phenotype. NIR light can reverse such $A\beta$ -induced changes and protect neurons from the associated damage. The NIR light induced regulation of activated microglia may provide a therapeutic strategy for controlling the progression of neuroinflammatory conditions in Alzheimer's disease. This study provides new insights into the role of NIR light in modulating oxidative stress and microglia metabolism.

REFERENCES 1. Tao et al. LSA (2021) 10:179. 2. Iaccarino et al, Nature (2016) 540(7632):230-235. 3. Purushothuman et al, Alzheimers Res. Ther. (2014) 6(1):2. 4. Duarte et al, J. Photoch. Photobio. B (2018) 189:55-65. 5. Gao et al. J. Biomed. Sci. (2009) 16(1):4. 6. Frank et al, J. Neurosci. (2006) 151(2):121-130. 7. Heo et al. Sci. Rep. (2019) 9:10114. 8. Hamblin et al. Mech. for LLT 6140 (2006) 614001.