The biology of nuclear calcium: general principles of adaptations and strategies to develop a light-induced signaling enhancer (NUCLEAR CALCIUM)

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Title of project or programme

The biology of nuclear calcium: general principles of adaptations and strategies to develop a light-induced signaling enhancer (NUCLEAR CALCIUM)

Principal Investigators of project/programme grant

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Source of funding information

European Research Council

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2400000

Start date of award

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Total duration of award in months

60

The project/programme is most relevant to

- Neurodegenerative disease in general

Keywords

Research abstract in English

Adaptation is a characteristic of life. Changes in gene expression allow cells and organisms to transform signals from the environment into long-lasting adaptive responses that range from learning and memory, addiction and chronic pain, to immunity and plant-microbe symbiosis. The project is based on the idea that the rules and signals governing the rich repertoire of adaptations are simple and used nearly universally. The research program consequently follows the concept that persistent adaptations take place when calcium a widely used modulator of cell functions enters the cell nucleus to activate transcription. In the nervous system, nuclear calcium controls CREB-mediated transcription following synaptic activity and is required for memory and activity-dependent survival. Dysfunction of nuclear calcium signaling may lead to cognitive decline and neurodegeneration. We propose to develop methods for in vivo visualization of nuclear calcium signals in awake animals performing learning tasks and to establish, using key examples of adaptive responses, nuclear calcium a an evolutionary conserved regulator of adaptations. On the basis of common principles governing adaptive responses it becomes possible to develop general strategies to modulate adaptations irrespective of cell type or phylogenetic borders. At the heart of the proposal is the development of the proto-type of a nuclear calcium signaling enhancer. We exploit the optical properties of channel rhodopsin and aequorin to construct a light-induced signaling enhancer to boost physiological nuclear calcium responses and to restore them in disease or aging. The proposal has a focus on neuroscience and aims to provide proof-of-principle for unconventional treatments of neurodegeneration and age-related cognitive decline. In addition, the nuclear calcium concept is applied to immunology and plant biology to devise means of modulating immune responses and increasing plant growth by boosting symbiosis signaling.

Lay summary