

Harness the power of light

Biomedical applications based on optogenetics

Liting Duan

July 9, 2018



Magical light?



Harness the power of light

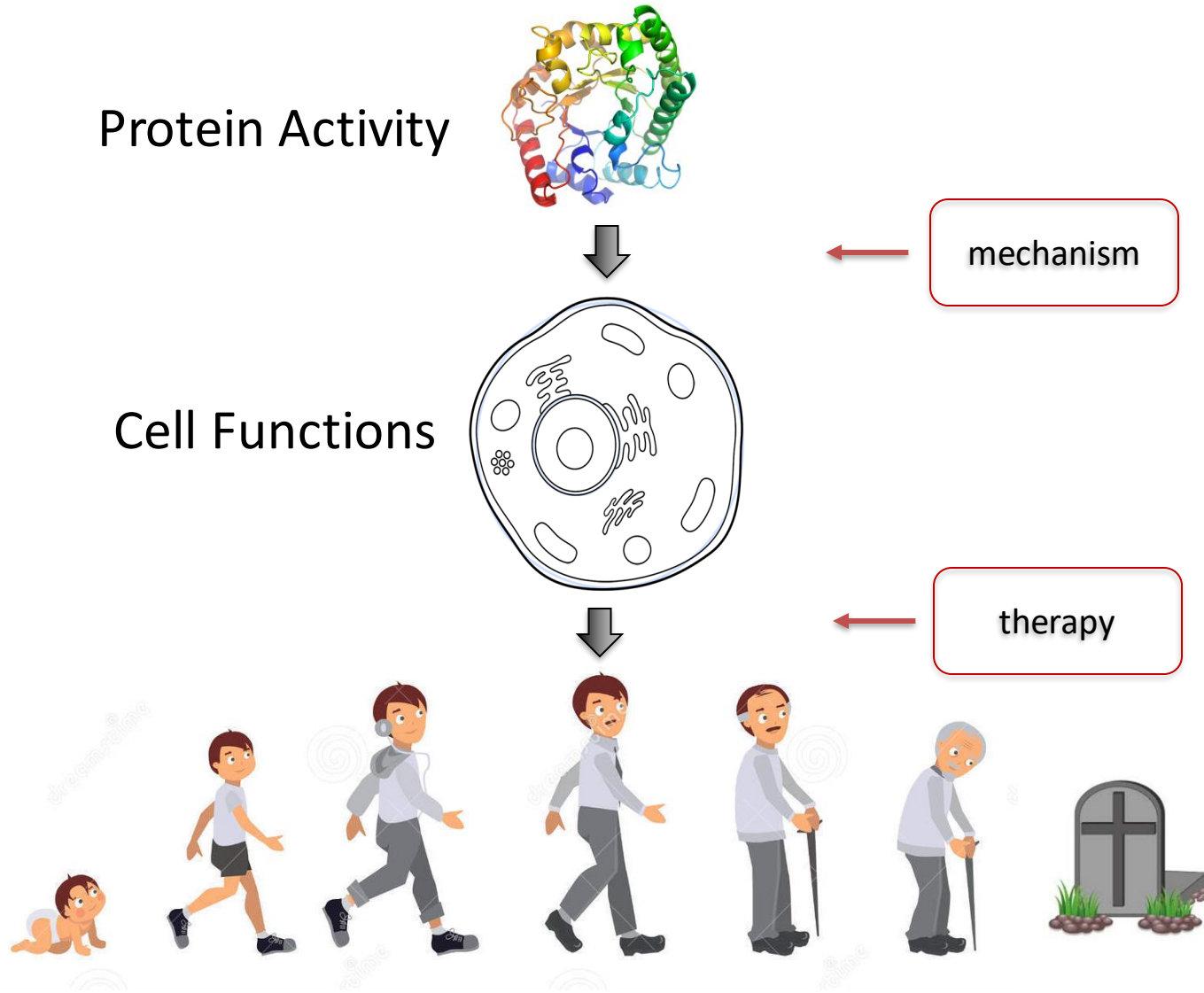
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Control Protein Activity: reveal mechanism and develop therapeutics



The Importance of **Temporal** and **Spatial** Coordination

White blood cell chasing bacteria



bacteria



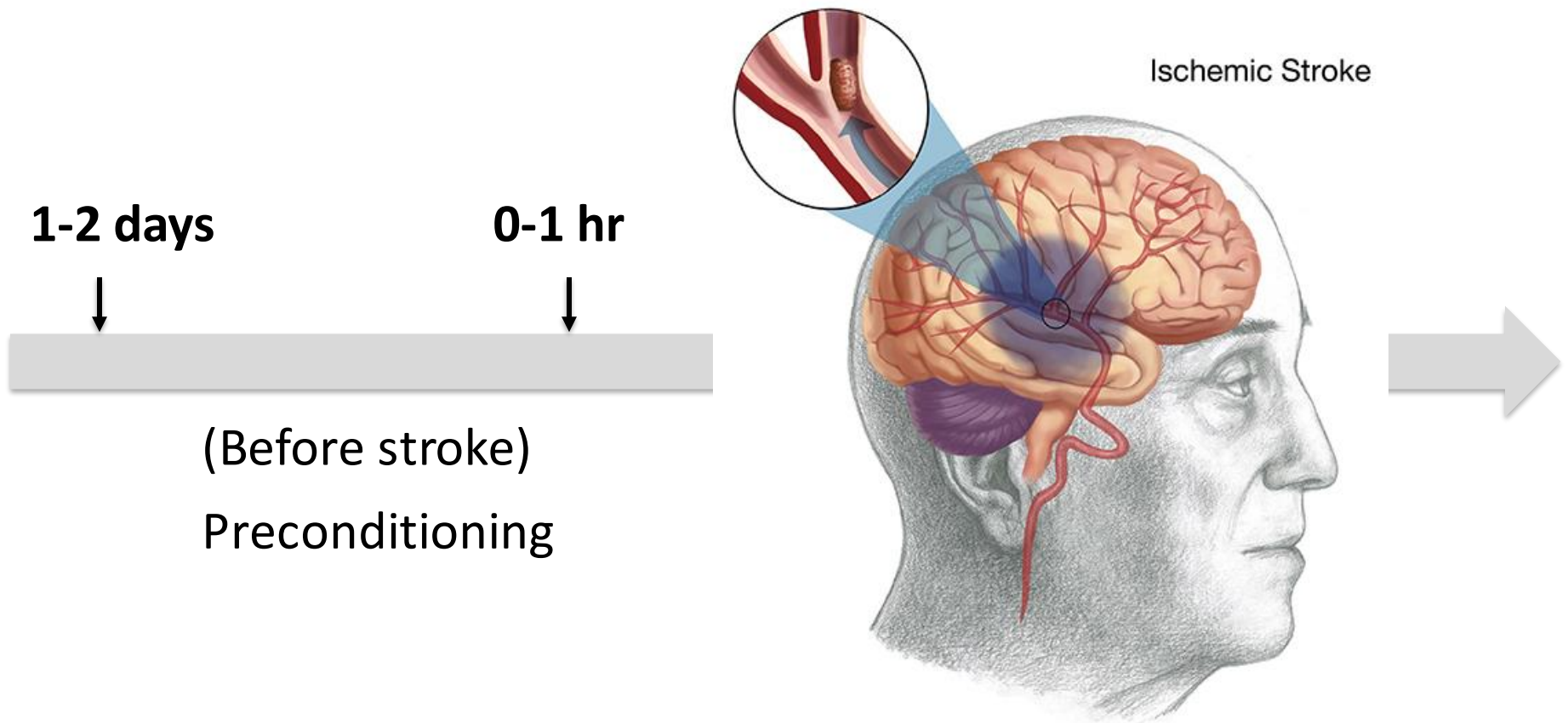
White blood cell



Movie by David Rogers, Vanderbilt University, in the 1950s

Precise regulation of protein activities

Correct **timing** of pretreatment protects ischemic stroke patients



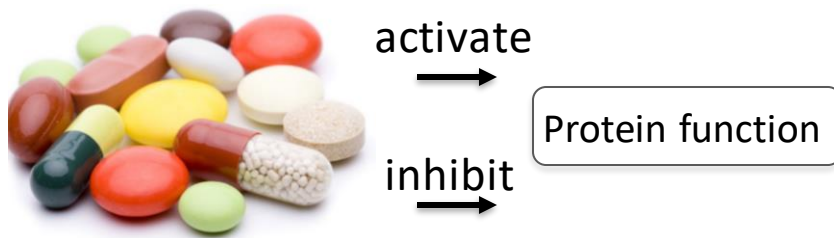
Ischemic Stroke

(Before stroke)
Preconditioning

Conventional methods to regulate protein activities

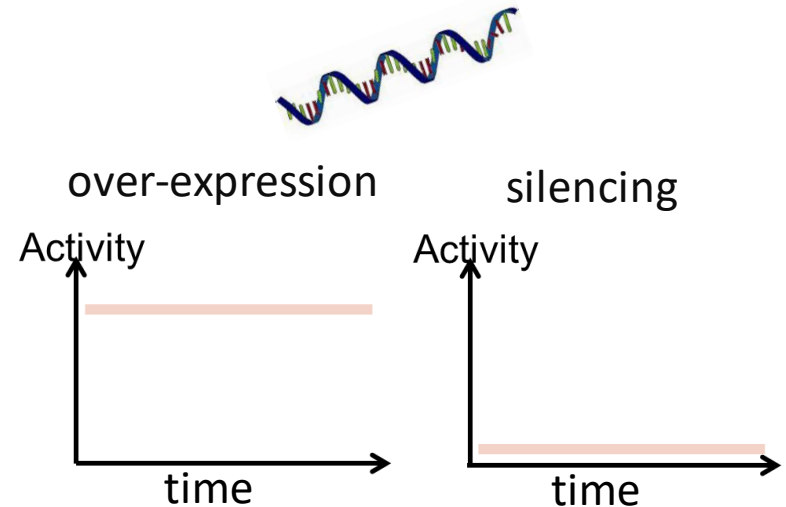
No spatiotemporal control !

Pharmacological perturbation



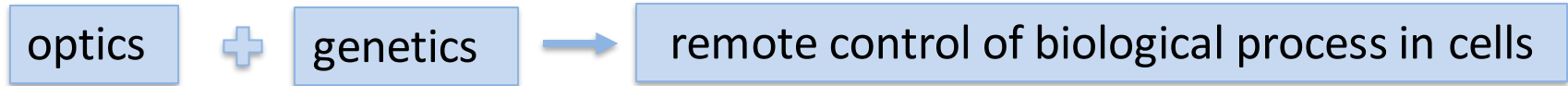
- Side effects / non-specific
- No spatial control
- very limited time control

Genetic Perturbation



- No spatial control
- No temporal control

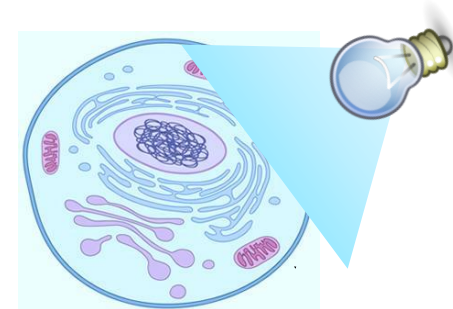
Optogenetics



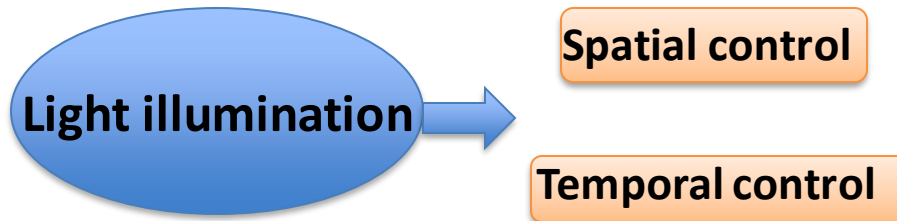
Encoding Light-sensitive protein



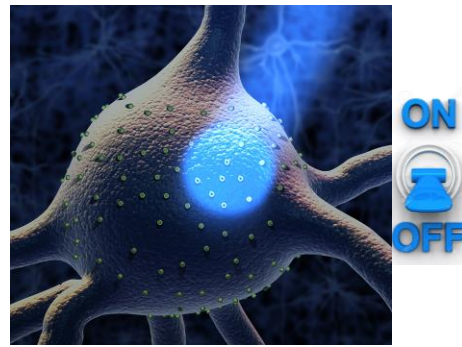
Expressing Light-sensitive protein



Controlling cell behavior



Optogenetics Application



Light controls the movement of mouse

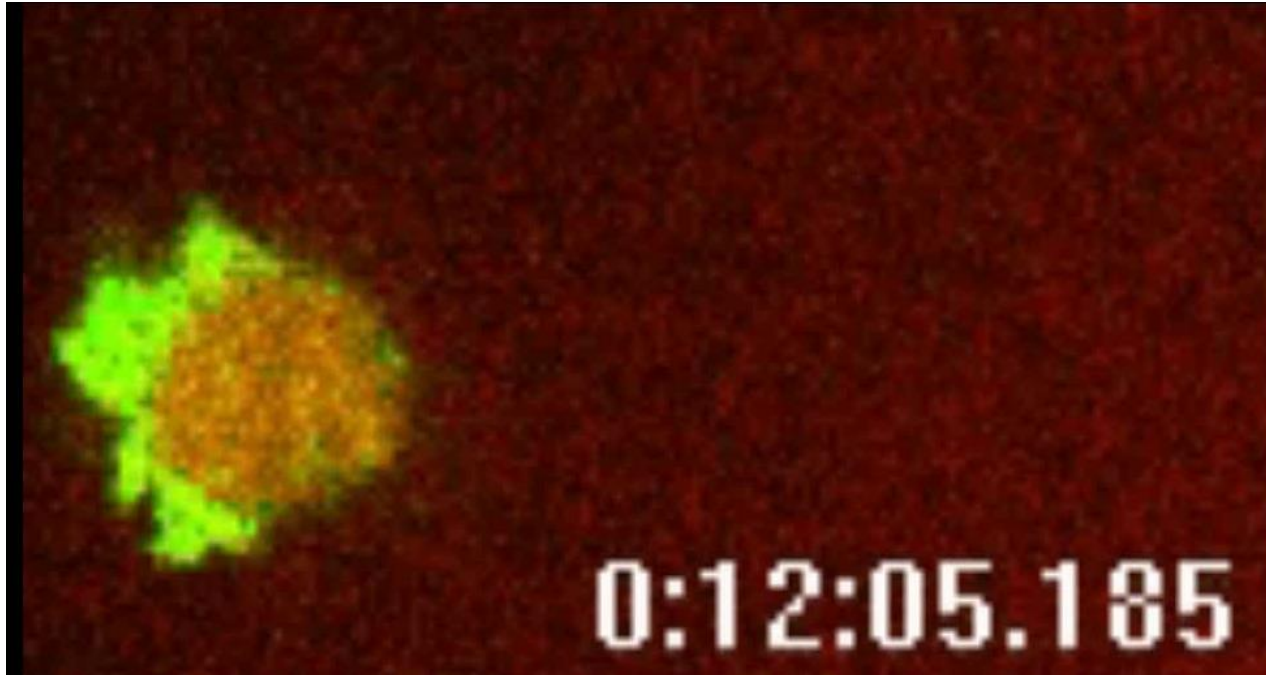


Light controls the drinking behavior



Optogenetics Application

Light Controls Individual Cell Migration

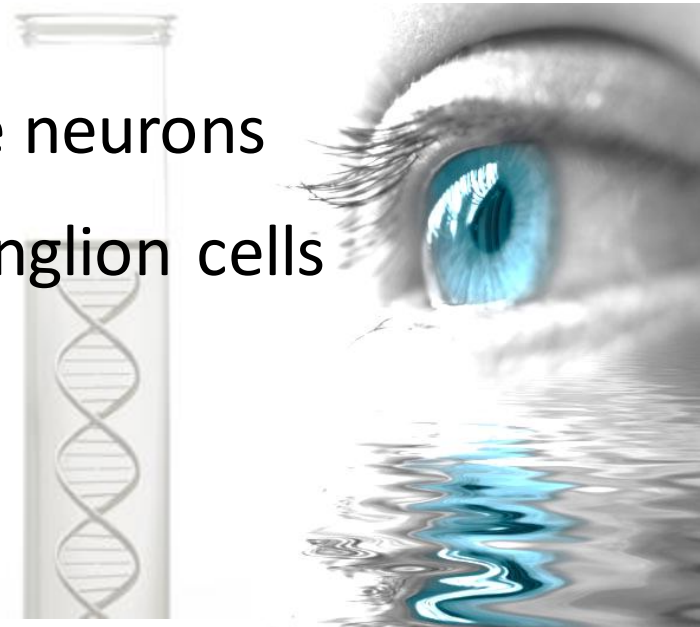


Optogenetics: gene therapy



RetroSense Therapeutics

- Gene therapy against *blindness*
 - conferring light sensitivity to eye neurons
 - delivering the ChR2 to retinal ganglion cells
- First clinical trial in human in 2016



Outline

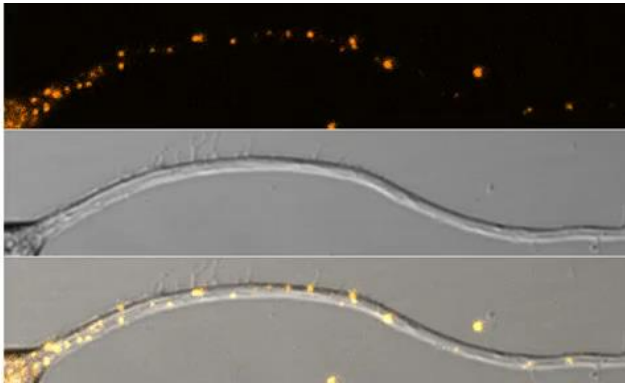
1

Developing optical control of **organelle transport**

2

Developing optical control of **signaling pathways**

organelle transport in cells

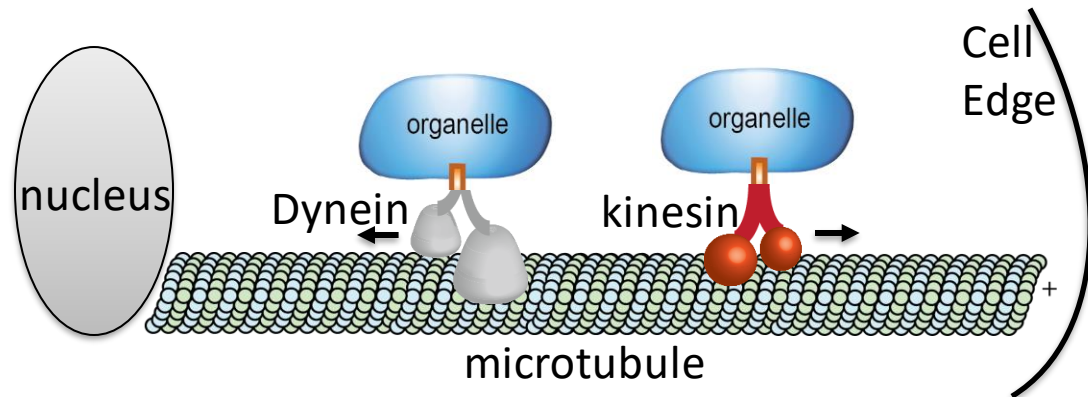
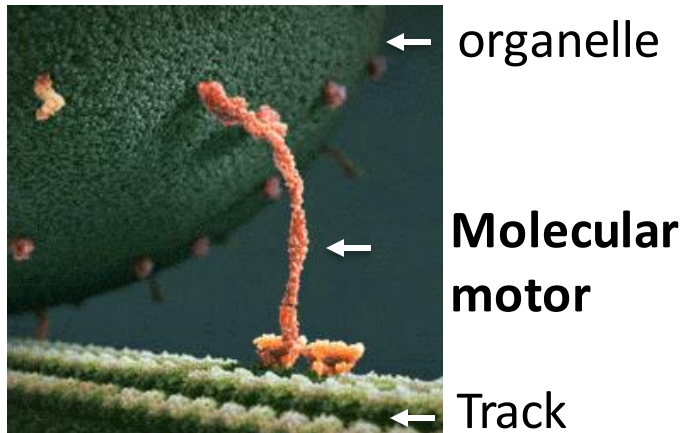


Organelle in a chick neuron

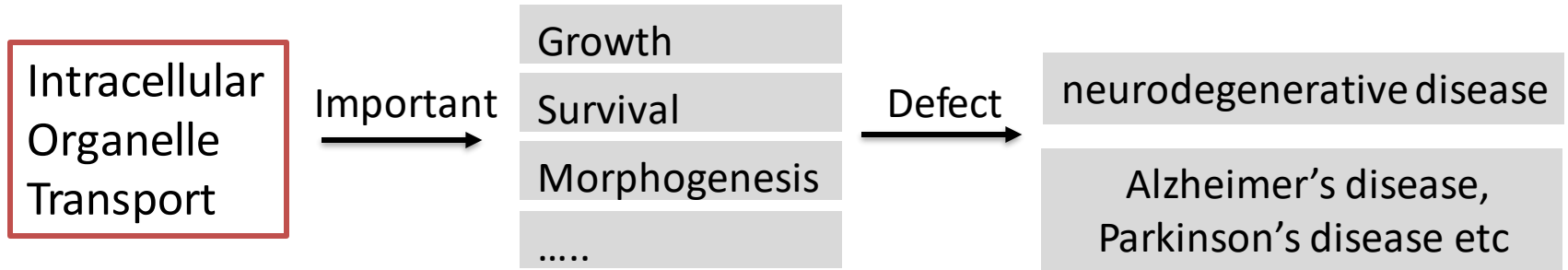
Goshima et al, J Pharmacol Sci, 114: 168-79 (2010).



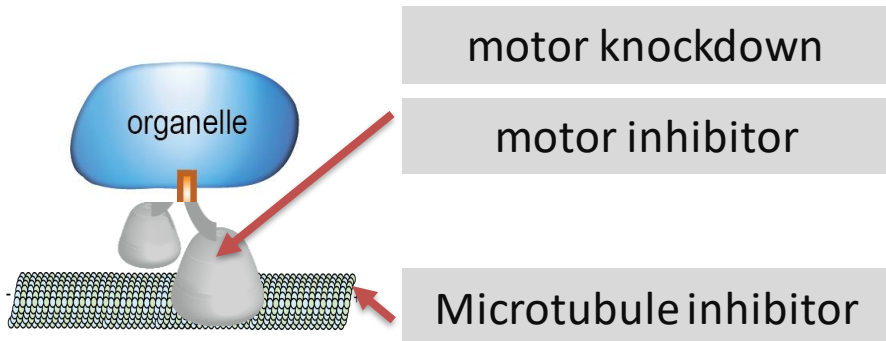
Highway traffic



organelle transport in cells



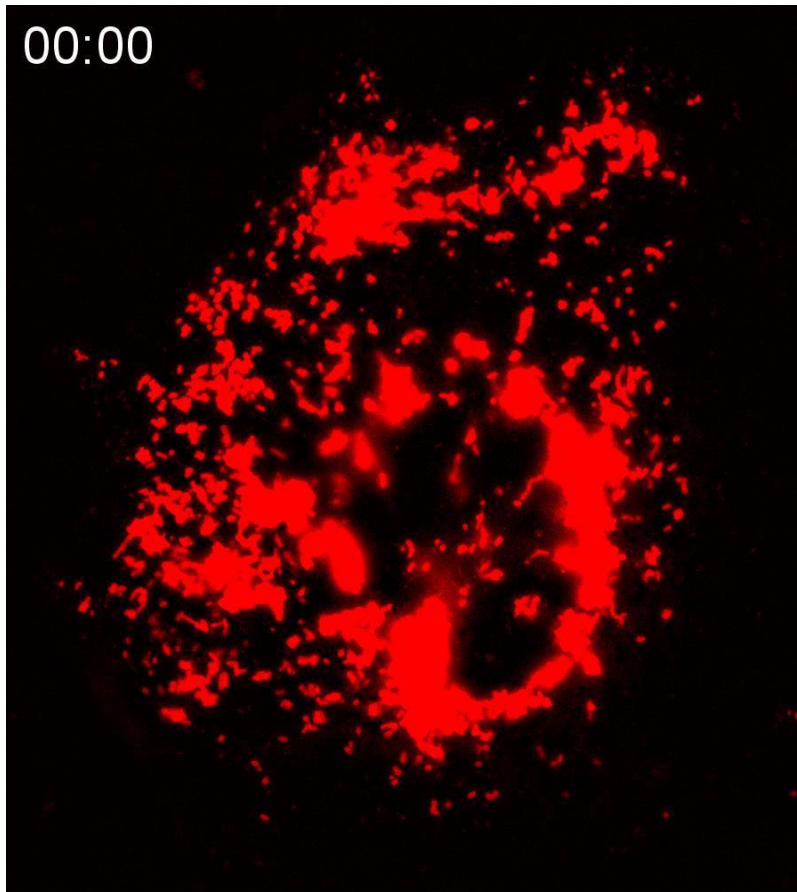
Current method



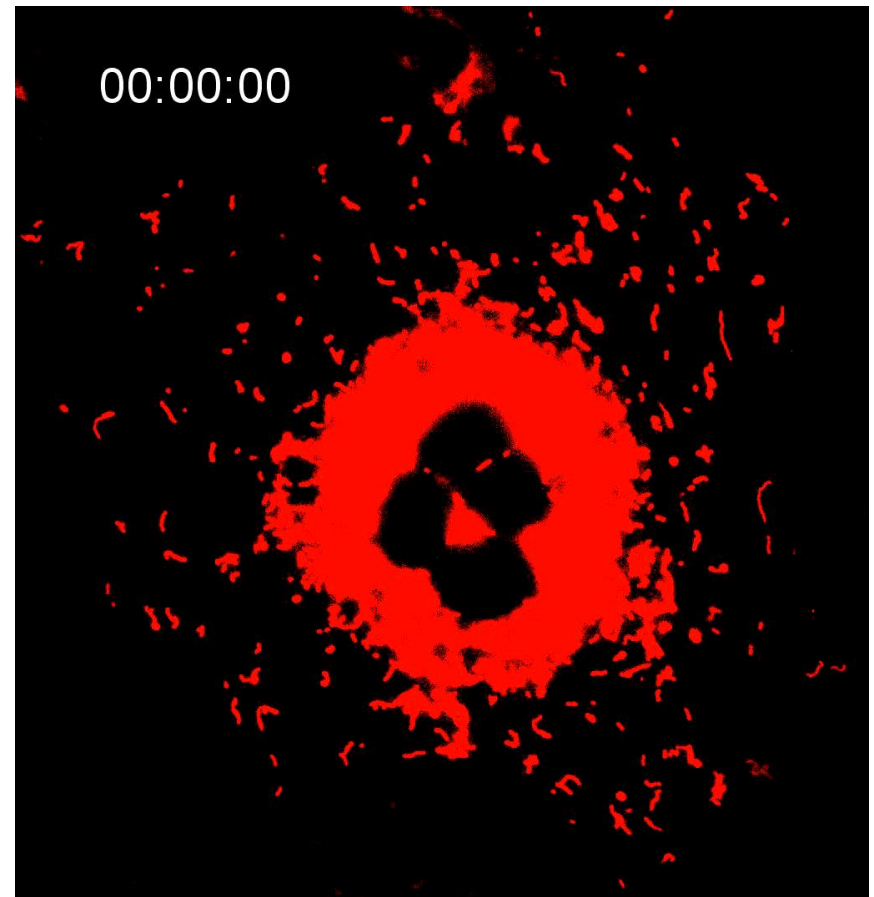
- Irreversible
- Non-specific
- No spatial/temporal control

Light-induced movement by different motors

Light-induced mitochondria movement **towards cell edge**



Light-induced mitochondria movement **towards cell nucleus**

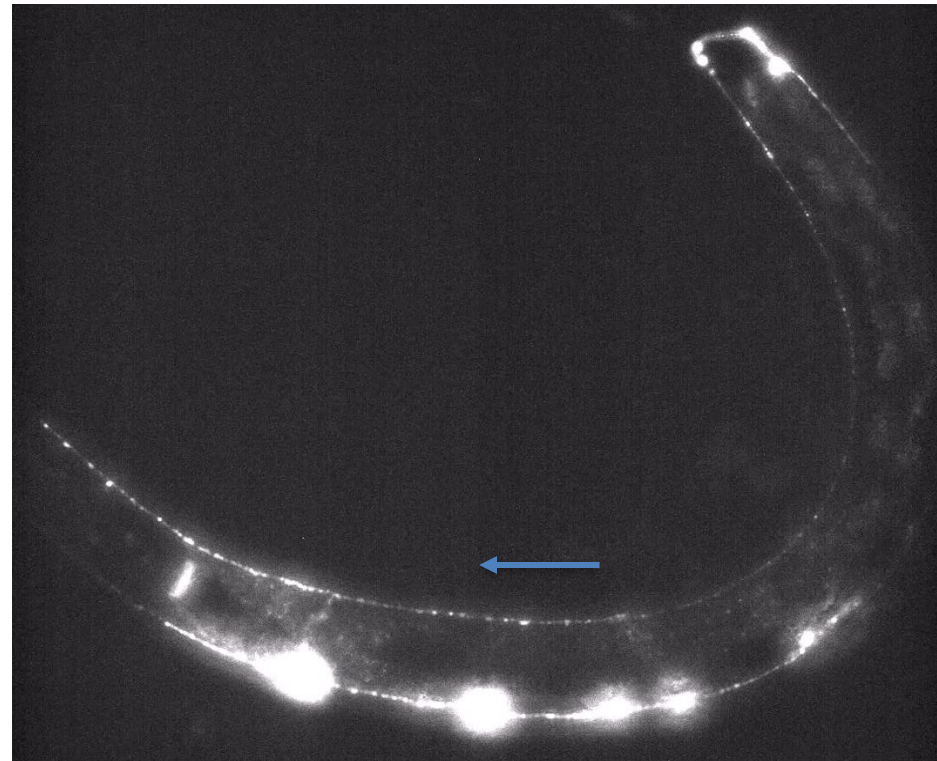
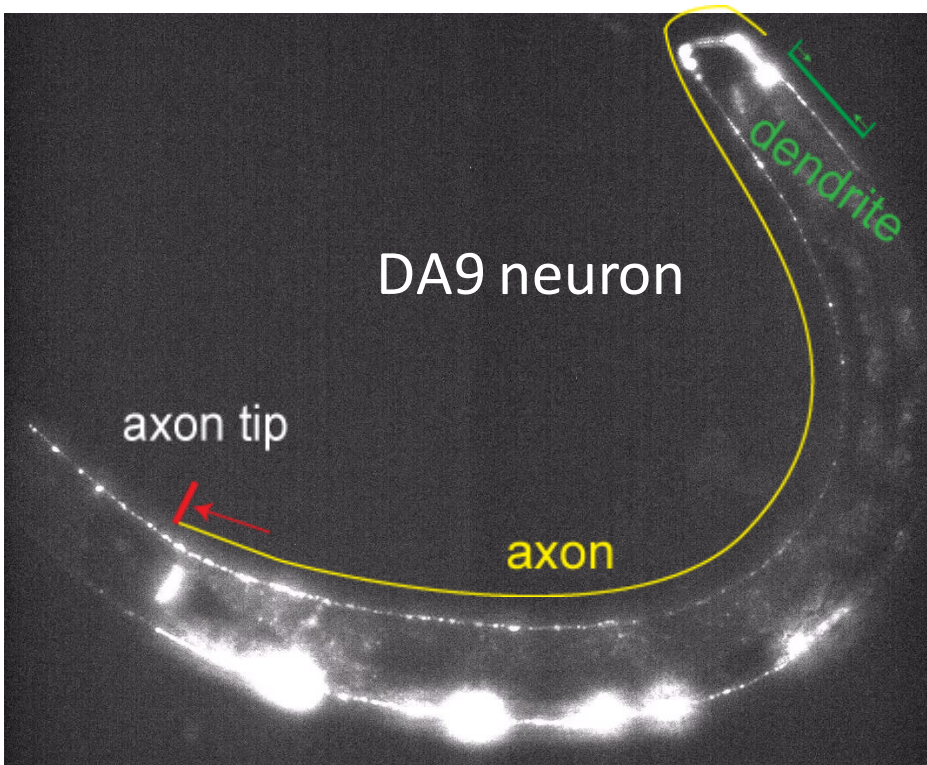


1

In Vivo application:light-induced transport of synaptic vesicles in *c. elegans*

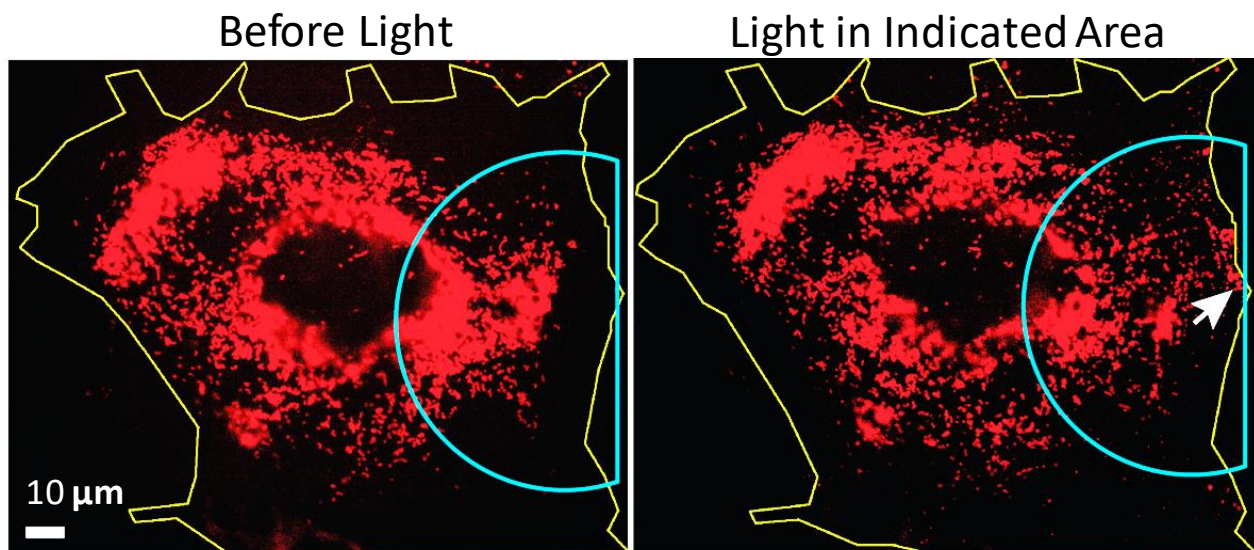
- light

+ light

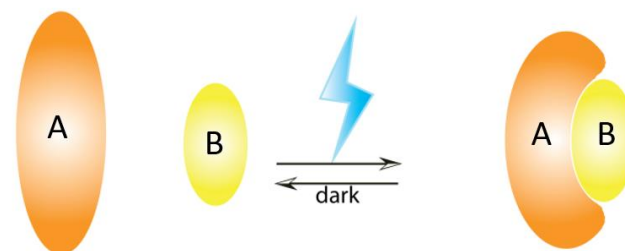


Spatial and temporal Control Of Light-induced Organelle Redistribution

Spatial
Control



Temporal
Control



Outline

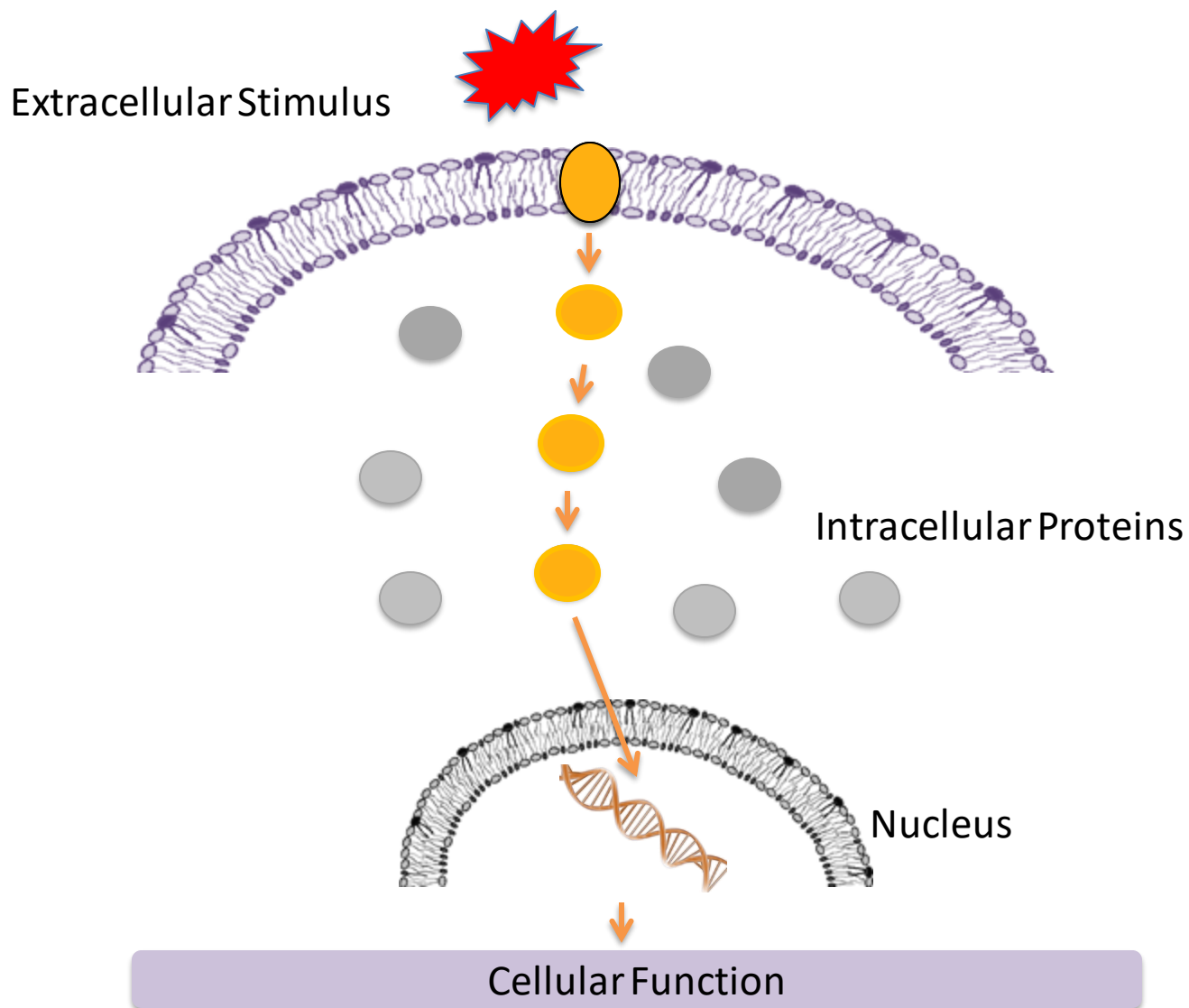
1

Developing optical control of **organelle transport**

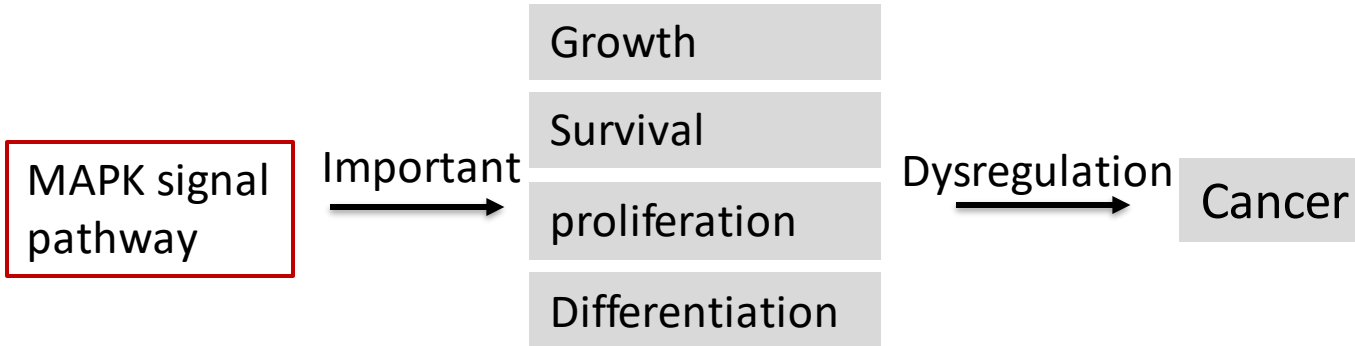
2

Developing optical control of **signaling pathways**

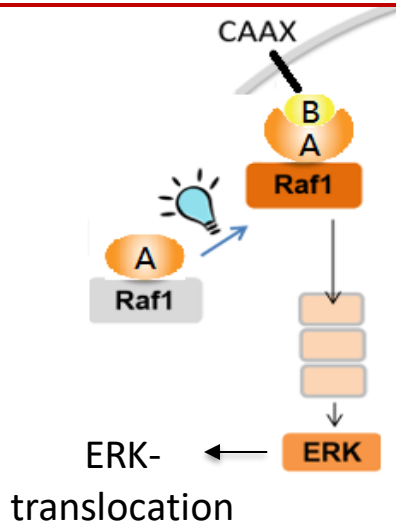
Intracellular Signaling Pathway



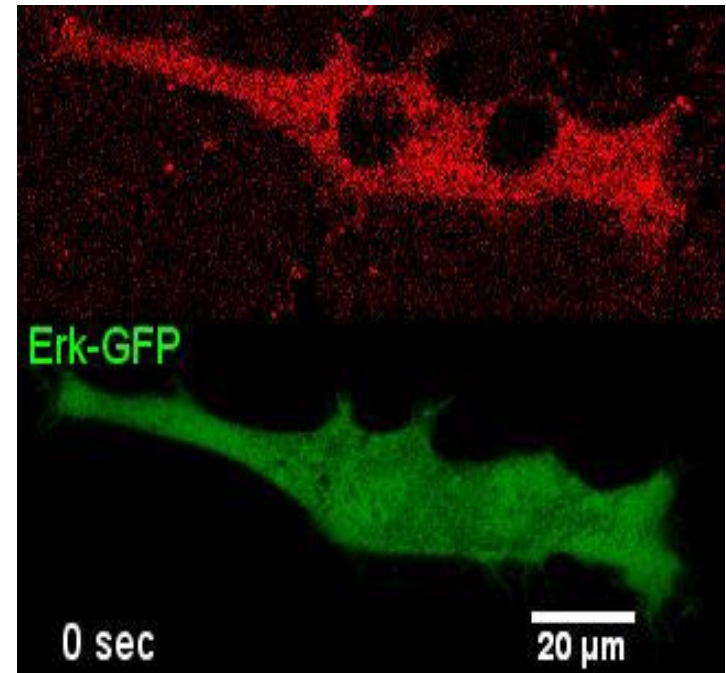
Light Control of MAPK Activation: temporal pattern of activation matters



Design of Light-induced MAPK Activation

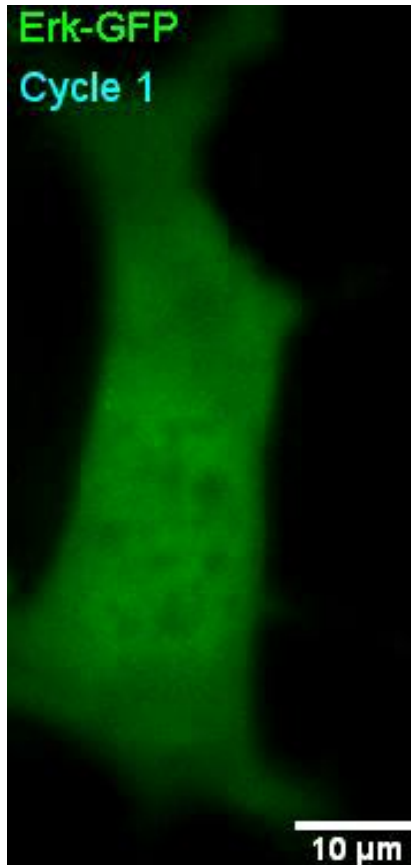


Raf activation
assayed by ERK-GFP
translocation

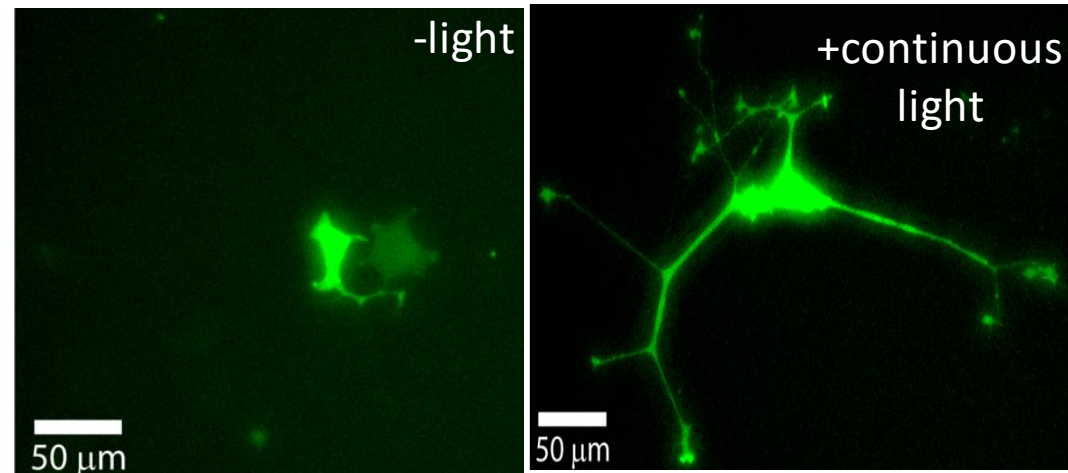


Temporal Control of MAPK signalling

Repeated Light illumination →
reversible activation



Continuous Light Activation → PC12 neurite growth



Take-Home Note



Optogenetic strategies can be developed to control various intracellular activities

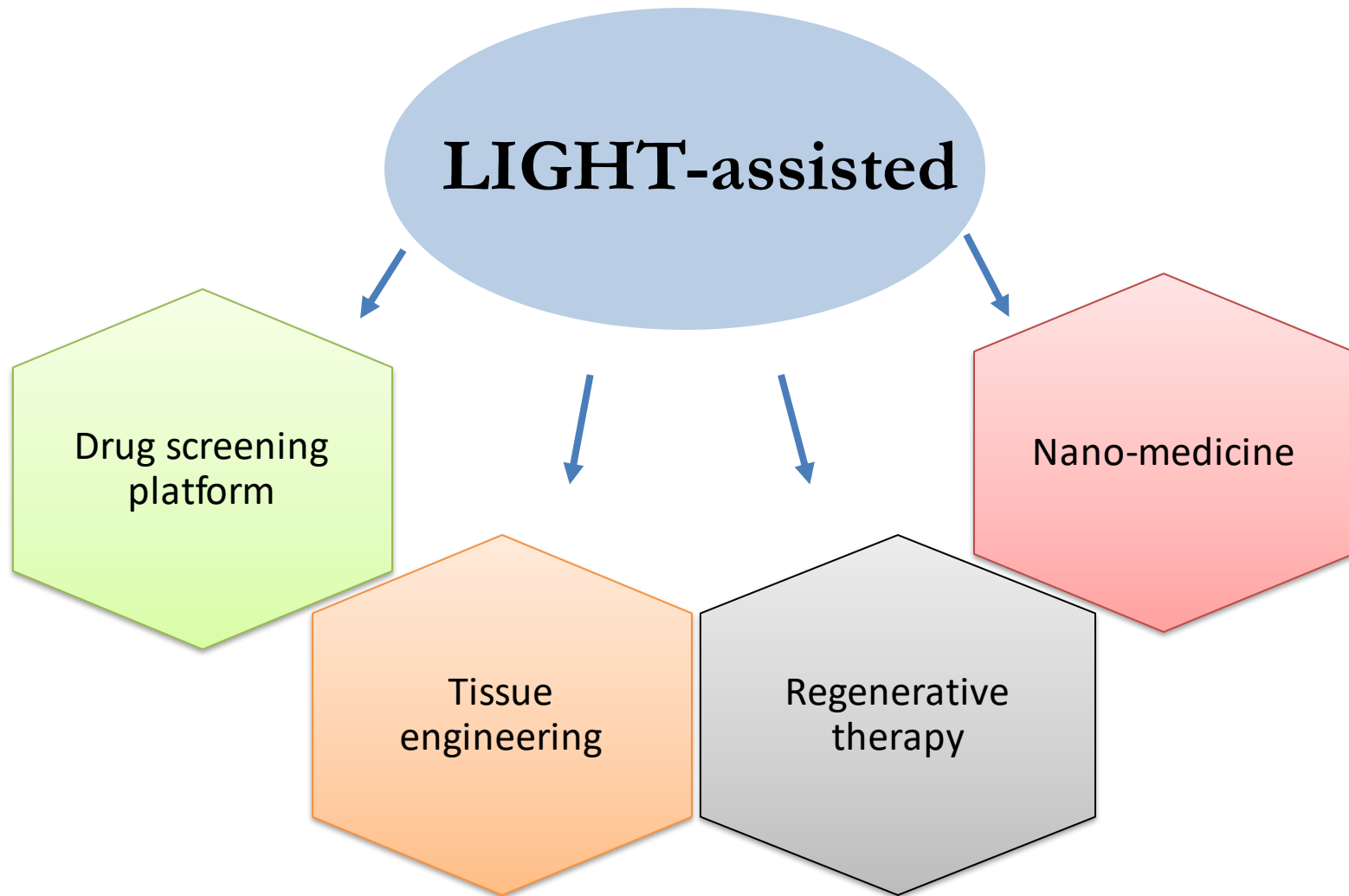


Optogenetic control can achieve high specificity, spatial and temporal precision



Optogenetic tools can be further optimized to meet the great demand of optogenetic applications

Future Research



END

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Room 410

Welcome any further question !

