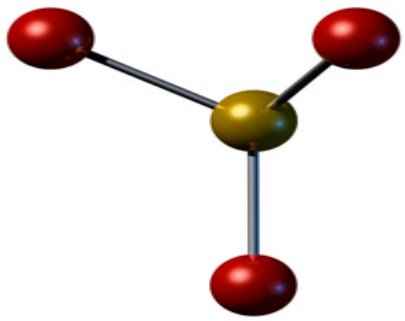
Quantifying signal transduction

Results in Brief

Real-time monitoring of cellular signalling events

Phosphorylation is one of the most important and ubiquitous cell regulatory events. EU-funded researchers assessed the dynamic events of intracellular phosphorylation in two model systems with important implications for targeted drug therapies for cancer and inflammatory responses.

HEALTH



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Understanding the cellular dynamics of phosphorylation, or the addition of a phosphate unit to a molecule and the associated signalling pathways has important and widespread application in developing drugs and therapies. For example, a certain tumour suppressor gene has more than 18 different phosphorylation sites, enabling quite complex control of activity.

European researchers initiated the ‘Quantifying signal transduction’ (QUASI) project in order to develop methods to dynamically monitor protein phosphorylation processes in individual living cells with a goal of targeting signalling pathways with existing drugs or the design of new ones as related to cancer and inflammatory disorders in particular.

Enzymes called kinases are responsible for phosphorylation. Specific enzymes act

on specific substrates, sort of like a lock and key. Phosphorylation of protein substrates can turn signal pathways on or off.

Mitogen-activated protein (MAP) kinases are a particularly ancient and well studied family of kinases that participate in numerous cellular-signalling events.

QUASI investigators chose the high osmolarity glycerol (HOG) MAP kinase pathway and the pheromone response pathway in yeast, among the best studied models of signalling pathways, as a means to develop tools enabling quantification in real-time of cell phosphorylation events.

Researchers adapted or developed approaches including isotope labelling, mass spectroscopy, bio-imaging with fluorescent markers, and chemical cross-linking to monitor kinases and key phosphorylation events.

Producing mutations and analogues of kinases and their targets enabled the team to identify specific enzyme substrate reactions and induce specific inhibitions of signalling. Conversely, mathematical models of the HOG and pheromone-signalling pathways based on experimental data represented how the pathways are activated.

Visualisation tools developed to animate the HOG and pheromone pathways should enhance understanding of intracellular signalling and prove useful in predicting drug effects.

The ambitious QUASI project contributed important techniques, data and tools for the study of ubiquitous but quite specific and complex phosphorylation-related cellular-signalling pathways, with important implications for targeted drug therapies.

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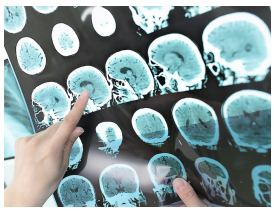

A better way of treating the effects of ischaemic stroke

Project Information

QUASI

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Project website

Project closed

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