Cellular responses to stimuli

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Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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Literature references


Reactome database release: 81

This document contains 3 pathways (see Table of Contents)

https://reactome.org
Individual cells detect and respond to diverse external molecular and physical signals. Appropriate responses to these signals are essential for normal development, maintenance of homeostasis in mature tissues, and effective defensive responses to potentially noxious agents (Kültz 2005). It is convenient, if somewhat arbitrary, to distinguish responses to signals involved in development and homeostasis from ones involved in stress responses, and that classification is followed here, with macroautophagy and responses to metal ions classified as responses to normal external stimuli, while responses to hypoxia, reactive oxygen species, and heat, and the process of cellular senescence are classified as stress responses. Signaling cascades are integral components of all of these response mechanisms but because of their number and diversity, they are grouped in a separate signal transduction superpathway in Reactome.

**Literature references**

Response to metal ions

Location: Cellular responses to stimuli

Stable identifier: R-HSA-5660526

Though metals such as zinc, copper, and iron are required as cofactors for cellular enzymes they can also catalyze damaging metal substitution or unspecific redox reactions if they are not sequestered. The transcription factor MTF1 directs the major cellular response to zinc, cadmium, and copper. MTF1 activates gene expression to up-regulate genes encoding proteins, such as metallothioneins and glutamate-cysteine ligase (GCLC), involved in sequestering metals. MTF1 represses gene expression to down-regulate genes encoding transporters that import the metals into the cell (reviewed in Laity and Andrews 2007, Jackson et al. 2008, Günther et al. 2012, Dong et al. 2015). During activation MTF1 in the cytosol binds zinc ions and is translocated into the nucleus, where it binds metal response elements in the promoters of target genes. Activation of MTF1 by cadmium and copper appears to be indirect as these metals displace zinc from metallothioneins and the displaced zinc then binds MTF1.

Metallothioneins bind metals and participate in detoxifying heavy metals, storing and transporting zinc, and redox biochemistry.

Literature references


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Cells are subject to external molecular and physical stresses such as foreign molecules that perturb metabolic or signaling processes, and changes in temperature or pH. Cells are also subject to internal molecular stresses such as production of reactive metabolic byproducts. The ability of cells and tissues to modulate molecular processes in response to such stresses is essential to the maintenance of tissue homeostasis (Kultz 2005). Specific stress-related processes annotated here are cellular response to hypoxia, cellular response to heat stress, cellular senescence, HSP90 chaperone cycle for steroid hormone receptors (SHR) in the presence of ligand, response of EIF2AK1 (HRI) to heme deficiency, heme signaling, cellular response to chemical stress, cellular response to starvation, and unfolded protein response.

**Literature references**


**Editions**

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