Extra-nuclear estrogen signaling

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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

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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: 82

This document contains 3 pathways and 21 reactions (see Table of Contents)
In addition to its well-characterized role in estrogen-dependent transcription, estrogen (beta-estradiol, also known as E2) also plays a rapid, non-genomic role through interaction with receptors localized at the plasma membrane by virtue of dynamic palmitoylation. Estrogen receptor palmitoylation is a prerequisite for the E2-dependent activation of extra-nuclear signaling both in vitro and in animal models (Acconcia et al, 2004; Acconcia et al, 2005; Marino et al, 2006; Marino and Ascenzi, 2006). Non-genomic signaling through the estrogen receptor ESR1 also depends on receptor arginine methylation by PMRT1 (Pedram et al, 2007; Pedram et al, 2012; Le Romancer et al, 2008; reviewed in Arnal, 2017; Le Romancer et al, 2011).

E2-evoked extra-nuclear signaling is independent of the transcriptional activity of estrogen receptors and occurs within seconds to minutes following E2 administration to target cells. Extra-nuclear signaling consists of the activation of a plethora of signaling pathways including the RAF/MAP kinase cascade and the PI3K/AKT signaling cascade and governs processes such as apoptosis, cellular proliferation and metastasis (reviewed in Hammes et al, 2007; Handa et al, 2012; Lange et al, 2007; Losel et al, 2003; Arnal et al, 2017; Le Romancer et al, 2011). ESR-mediated signaling also cross-talks with receptor tyrosine kinase, NF-kappa beta and GPCR signaling pathways by modulating the post-translational modification of enzymes and other proteins and regulating second messengers (reviewed in Arnal et al, 2017; Schwartz et al, 2016; Boonyaratanakornkit, 2011; Biswas et al, 2005). In the nervous system, E2 affects neural functions such as cognition, behaviour, stress responses and reproduction in part by inducing such rapid extra-nuclear responses (Farach-Carson and Davis, 2003; Losel et al, 2003), while in endothelial cells, non-genomic ESR-dependent signaling also regulates vasodilation through the eNOS pathway (reviewed in Levin, 2011).

Extra-nuclear signaling additionally cross-talks with nuclear estrogen receptor signaling and is required to control ER protein stability (La Rosa et al, 2012)

Recent data have demonstrated that the membrane ESR1 can interact with various endocytic proteins to traffic and signal within the cytoplasm. This receptor intracellular trafficking appears to be dependent on the physical interaction of ESR1 with specific trans-membrane receptors such as IGR-1R and beta 1-integrin (Sampayo et al, 2018)
**Literature references**


**Editions**

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PRMT1 methylates ESRs

Location: Extra-nuclear estrogen signaling

Stable identifier: R-HSA-9632182

Type: transition

Compartments: cytosol