NR3C2 ligands bind NR3C2 (in the HSP90 chaperone complex)

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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

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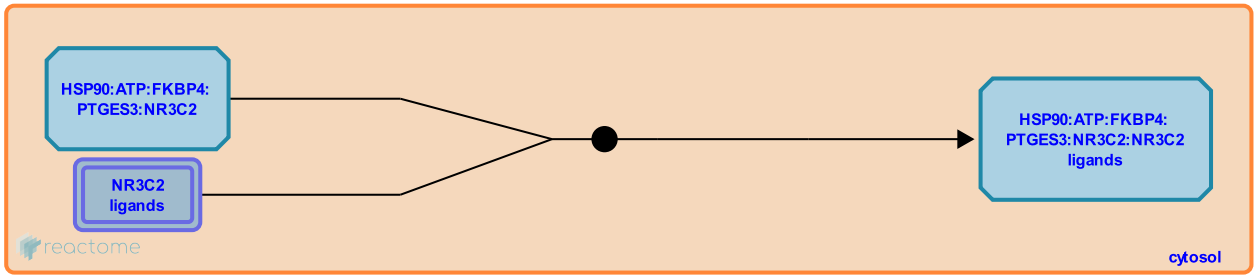
Stable identifier: R-HSA-5618099

Type: binding

Compartments: cytosol



Steroid hormones receptors (SHRs) are intracellular transcription factors that can be activated by binding specific ligands (i.e., steroid hormones (SH)) to the ligand-binding domain (LBD) (Ray DW et AL. 1999; Pike AC et al. 1999; Bledsoe RK et al. 2002; Li Y et al. 2005; Kumar R and McEwan IJ 2012; Kumar R et al. 2011; Williams SP & Sigler PB 1998; Tanenbaum DM et al. 1998; Lusher SJ et al. 2012). LBD (E-region) resides in the C-terminal half of the receptor and in addition to ligand binding function contains a transcriptional activation function (AF2), sequences for dimerization, heat shock protein association, intermolecular silencing and intramolecular repression (Kumar R and McEwan IJ 2012). The binding of hormone acts as an allosteric switch to regulate SHR-DNA and SHR-protein interactions, including interdomain interactions and/or dimerization (Kumar R and McEwan IJ 2012).

SHs are synthesized from cholesterol in the adrenal cortex (glucocorticoids, mineralocorticoids, and adrenal androgens), the testes (testicular androgens, estrogen), and the ovary and placenta (estrogen and progestogen or progestins) (Payne AH & Hales DB 2004; Hu J et al. 2010;). SHs reach their target cells via the blood, where they are bound to specific carrier proteins (Grishkovskaya I et al. 2000; Hammond GL 2016). SHs detach from the carrier proteins and because of their lipophilic nature readily diffuse through the plasma membrane of cells (Oren I et al. 2004). Within the target cells SHs bind to steroid hormone receptors (SHRs) which are present in a heterocomplex with heat shock protein HSP90 and co-chaperones (e.g., immunophilins p23) (Echeverria PC & Picard D 2010). The ATP-bound form of HSP90 and chaperone-mediated conformational changes are required to keep SHRs in a ligand binding-competent state (McLaughlin SH et al. 2002; Pratt WB et al. 2008; Krukenberg KA et al. 2011).

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Editions

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