Institute of General Zoology and Endocrinology

Regulation of Androgen Receptor Corepressors

Prostate cancer (PCa) is the most common cancer diagnosed in elderly men in western countries. The development and progression of PCa is initially androgen-dependent but hormone refractory tumours frequently occur after hormone ablation therapy. This may result from the dysregulation of androgen receptor cofactors interacting with the receptor that regulates its transcriptional activity.

The Team:

Head of the Institute: K.-D. Spindler
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Upregulation of NCoR-protein by androgen treatment (DHT) in LNCaP prostate cancer cells. PSA = prostate

NCoR localization is not influenced by androgen treatment. Immunostaining of NCoR in DHT-treated (right) and untreated (left) LNCaP prostate cancer cells.
The interaction between nuclear receptors and cofactors effects posttranslational modifications most commonly by phosphorylation. Protein kinase CK2 is a serine/threonine kinase which is elevated in various tumours and is a prognostic marker for prostate carcinoma. The nuclear receptor corepressor (NCoR), which inhibits the transcriptional activity of the AR, contains several CK2 phosphorylation sites. We are interested in the phosphorylation of NCoR, its influence on the regulation of NCoR-and androgen receptor-function, and its relevance for prostate cancer progression.

Regulation of Nuclear Receptor Activity by Modulation of the Receptor Concentration

Cooperation project with the Institute of Physiological Chemistry

Transcriptional activity of nuclear receptors is mainly determined by: receptor concentration; intracellular localization; interaction with ligand; proteins; and hormone response element. Our work will focus on posttranscriptional modifications of the human androgen receptor and the Drosophila ecdysteroid receptor (phosphorylation, ubiquitinylation, sumoylation) and their influence on receptor activity, stability and localization.

Selected Publications: