COLLOQUIA IN PHYSIOLOGY AND VASCULAR BIOLOGY

Venue: Medical University Vienna, Center for Physiology and Pharmacology,

Institute of Pharmacology, Waehringerstrasse 13a, 1090 Vienna,

"**Leseraum**".

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(host: Johannes Schmid)

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"Cross talk of the NF-κB/IKK and AR signalling pathways in prostate carcinoma"

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Abstract.

Prostate cancer (PCa) is a most common neoplasm and the second cause of cancer related death in elderly men. While treatment of organ confined PCa involves radical prostatectomy or radiation therapy, current treatment for advanced prostate cancer is mainly based on androgen ablation therapies like chemical or surgical castration and/or the application of antiandrogens. Although the majority of PCa respond to androgen ablation, many tumors recur in an androgen insensitive manner. The majority of these so-called castration-resistant prostate cancers (CRPCa) continue to depend on AR-signalling, but bypass their requirements for physiological levels of androgens. NF-κB signalling is another survival and growth conferring mechanism which seems to be essential for another (AR-deficient) subset of PCa. However, NF-κB/IKK-signalling and AR signalling show also an extensive cross talk. We recently demonstrated that the AR is a target of the IkappaB kinases (IKKs) and the activity as well as the nuclear localization of the AR is modulated by IKK1. The important role of IKK1 for AR positive PCa cell lines is further supported by our finding that IKK1, and not IKK2, is the major regulator of the canonical NF-κB signalling pathway in these cells. By contrast, NKX3.1, a prostate specific tumor suppressor and AR target gene is down regulated upon stimulation of PCa cells with the NF-κB agonists TNFα or PMA+Ionomycin, underlining the complexity of the NF-κB:AR cross talk in PCa cells.