

COLLOQUIA IN CELLULAR SIGNALLING

Venue: Medical University Vienna, Center for Physiology and Pharmacology,
Institute of Pharmacology, Waehringerstrasse 13a, 1090 Vienna, "**Leseraum**".

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Friday **05.12.2014 12:00 s.t.** **Christoph Höller** (host: J. Zezula)
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"MAP-Kinase Signaling – from Bench to Bedside and back in Melanoma"

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Abstract:

The MAP-Kinase pathway has for a long time been a well-known driver of cell growth in tumor cells. Despite this knowledge successful blockade of the MAP-Kinase pathway, most often through attempts to block upstream molecules, like RAS, did not show any pre-clinical or clinical success. This changed with the discovery of a predominant mutation in the B-RAF kinase, more specifically the V600 mutation, which can be detected in up to 50% of melanomas, a tumor which in its metastatic stage was until recently incurable. Through the design of kinase inhibitors which bind specifically to the mutated B-RAF protein, these tumors can be selectively targeted and a fast onset of clinical response, a high response rate and an overall survival benefit compared to previous standards of chemotherapy are characteristics of these new drugs. On the other hand, new side effects, specifically linked to the mode of action of the B-RAF inhibitors, as well as specific mechanisms of resistance to these drugs have been identified by linking back information from clinical trials to the research bench and have significantly increased our understanding of the signaling pathway itself, as well as the general plasticity of a tumor cells signaling networks.

This lecture will give an overview about the clinical development, side effects of- and mechanisms of resistance to B-RAF inhibitors. It will furthermore provide an outlook on current and future developments that will help us to overcome the obstacles associated with these early steps of clinical intervention in a major signaling pathway.