COLLOQUIA IN CELLULAR SIGNALLING

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

Institute of Physiology, Schwarzspanierstraße 17, 1090 Vienna

"**Großer Hörsaal Physiologie**"

(Harald Sitte, Tel.: (01) 40160 31323, harald.sitte@meduniwien.ac.at,

Christoph Österreicher, Tel.: 40160 31376, christoph.oesterreicher@meduniwien.ac.at)

Friday, **12.10.2012 11:00 c.t.**

Christian Stockmann **(host: Chr. Österreicher)**

Juniorprofessor Dr. med.
Universitätsklinikum Essen
Institut für Physiologie
D-45122 Essen

"Myeloid cell-driven vascular remodeling: Tuning the microenvironment during tissue fibrosis and tumorigenesis"

Christian Stockmann (Christian.Stockmann@uni-due.de)

Abstract:
The process of vascular remodeling is a crucial mediator of tumor growth and Vascular Endothelial Growth Factor (VEGF) is considered to be the major angiogenic factor. However, high density of blood vessels does not necessarily promote tumor growth and it is increasingly recognized that the functionality of the vascular bed is the major determinant of tumor growth. Myeloid cells represent a major source of VEGF[1,2,3] and we have previously shown that a deletion of VEGF specifically in myeloid cells leads to improved functionality of intratumoral blood vessels, alleviated tumor hypoxia and increased susceptibility to cytotoxic agents[1]. Most of the preclinical models focus on the initial response of tumors to therapy and studies on avoidance of tumor relapse are rare. Therefore, we investigated whether the absence of myeloid cell-derived VEGF results in long-term tumor control after therapy. Our results indicate that the absence of myeloid cell-derived VEGF prevents tumor relapse by reshaping the tumor microenvironment with direct impact on the anti-tumor immune response after cytotoxic therapy. Furthermore, infiltration of inflammatory cells and vascular remodeling are both hallmarks of progressive organ fibrosis. However, the role of inflammation and angiogenesis generally and more specifically the significance of inflammatory cell-derived VEGF in this context is unclear. We were able to demonstrate in a model of pulmonary fibrosis that the process of angiogenesis, driven by myeloid cell-derived VEGF, can prevent rather than promote fibrotic organ damage[2] and our recent studies indicate that myeloid cell-derived VEGF is essential for the resolution of established tissue fibrosis.

1. Stockmann C, Doedens A, Weidemann A, Zhang N, Takeda N, Greenberg JI, Cheresh DA, Johnson RS. Deletion of vascular endothelial growth factor in myeloid cells accelerates tumorigenesis. **Nature** 2008;456:814-8.

2. Stockmann C, Kerdiles Y, Nomaksteinsky M, Weidemann A, Takeda N, Doedens A, Torres-Collado AX, Iruela-Arispe L, Nizet V, Johnson RS. Loss of myeloid cell-derived vascular endothelial growth factor accelerates fibrosis. **Proc Natl Acad Sci U S A** 2010;107:4329-34.