



Department of Internal Medicine I

Development and Maintenance of Malignant and Inflammatory Phenotypes in Gastrointestinal Diseases

Head: Thomas Seufferlein

At the Department of Internal Medicine I, the focus of our research addresses primarily key signaling pathways and principles of cell biology that initiate and maintain malignant transformation in gastrointestinal cancer. These signaling events are closely linked to embryonic development and stem cell biology. Our second focus is autoimmunity and immune responses in the gut, pancreas and the liver. We aim to identify and delineate molecular pathways responsible for early events in cancer development, the tumor host interaction as well as metastasis and disease progression. In this context, we use genetically engineered animal models and state-of-the-art techniques in cell biology and biochemistry in order to identify the contribution of subcellular compartmentalization as a regulatory principle in tumor biology. Projects in our department address angiogenesis, growth control, secretion, transcriptional regulation and epigenetics in cancer, migration and metastasis as well as the identification and targeting of tumor stem cells. We further develop vaccination strategies for the specific control of chronic Hepatitis-B virus (HBV) infection and autoimmune type 1 diabetes.

The Team:

Head of Department: T. Seufferlein

Professors/Group Leaders: M. Dollinger, A. Kleger, A. Lechel, F. Oswald, R. Schirmbeck, M. Wagner, G. von Wichert

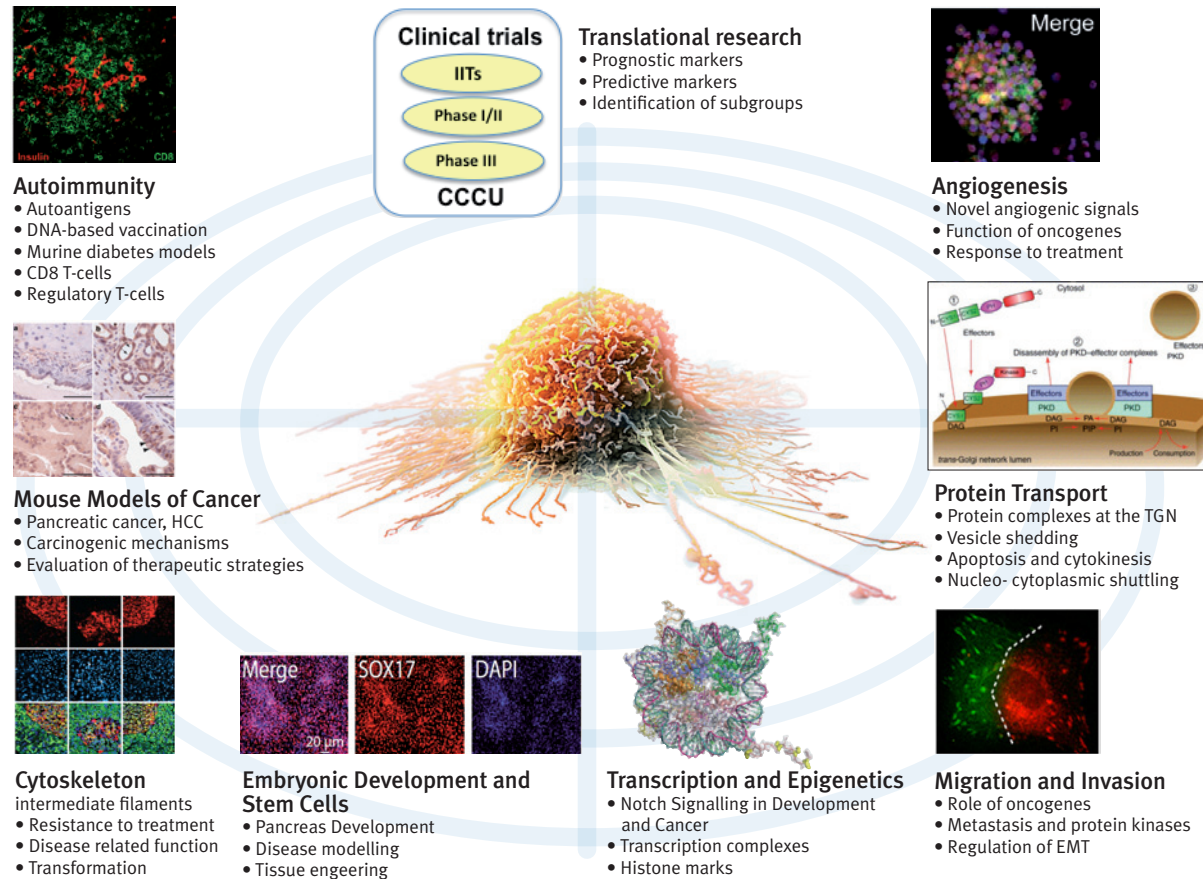
Postdocs: M. Armacki, N. Azoitei, T. Eiseler, S.-F. Katz, P. Riedl, G. Román Sosa, A. Illing

PhD Students: A. Becher, M. Hohwieler, P. Klöble, H. Müller, C. Münzberg, R. Qin, M. Raiwa, V. Rossini, R. Russel, J. Schroer, R. Sroka, A. Staab, K. Stifter, V. Thiel, C. Weidgang, C. Wille

Additional Members of Thesis Advisory Committees:

Dr. Arnold (Freiburg), Prof. Borggrefe (Gießen), Prof. Ellenrieder (Marburg), Prof. Ignatius (Ulm), Dr. Kaether (Jena), Prof. Seckl (London), Prof. de Vos (Sheffield)

The findings of our research projects will be useful for elucidating the patho-mechanisms of gastrointestinal cancer, liver diseases and diabetes, and will be used to identify novel therapeutic strategies for these diseases. Besides these efforts in basic research, the Department of Internal Medicine I is the coordinating institution for many clinical multicenter studies addressing the prevention and treatment of gastrointestinal cancers.



The research groups at our department use a broad spectrum of animal models and state-of-the-art techniques. We aim to address key signaling pathways and molecular mechanisms that initiate and maintain malignant transformation in gastrointestinal cancer as well as autoimmunity and immune responses in the gut, pancreas and the liver.

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Selected Publications:

- Wacker SA, Alvarado C, von Wichert G, Knippschild U, Wiedenmann J, Clauß K, Nienhaus GU, Hameister H, Baumann B, Borggreffe T, Oswald F (2011): RITA, a novel modulator of Notch signalling, acts via nuclear export of RBP-J. *EMBO J*.
- Krdjija D, Münzberg C, Maass U, Hafner M, Adler G, Kestler HA, Seufferlein T, Oswald F, von Wichert G (2012): The phosphatase of regenerating liver 3 (PRL-3) promotes cell migration through Arf-activity-dependent stimulation of integrin alpha 5 recycling. *J Cell Sci*.
- Eiseler T, Koehler C, Nimmagadda SC, Jamali A, Funk N, Joodi G, Storz P, Seufferlein T (2012): Protein Kinase D1 mediates anchorage-dependent and independent growth of tumor cells via the zinc-finger transcription factor Snail1. *J Biol Chem*.
- Busch T, Armacki M, Eiseler T, Joodi G, Temme C, Jansen J, von Wichert G, Omary MB, Spatz J, Seufferlein T (2012): Keratin 8 phosphorylation regulates keratin reorganization and migration of epithelial tumor cells. *J Cell Sci*.
- Pusapati GV, Eiseler T, Rykx A, Vandoninck S, Derua R, Waelkens E, Van Lint J, von Wichert G, Seufferlein T (2012): Protein kinase D regulates RhoA activity via rhotekin phosphorylation. *J Biol Chem*.
- Armacki M, Joodi G, Nimmagadda SC, de Kimpe L, Pusapati GV, Vandoninck S, Van Lint J, Illing A, Seufferlein T (2013): A novel splice variant of calcium and integrin-binding protein 1 mediates protein kinase D2-stimulated tumour growth by regulating angiogenesis. *Oncogene*.