Institute of Biochemistry and Molecular Biology

Tissue Homeostasis: Development, Aging and Regeneration

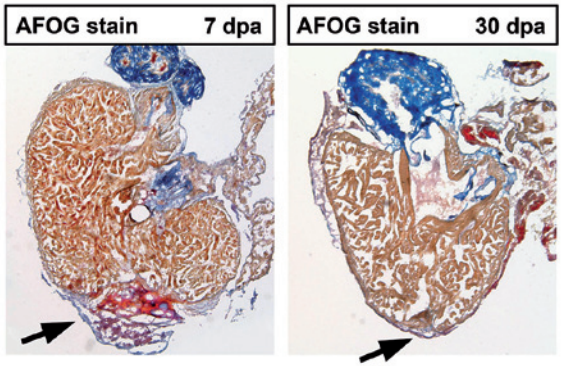
Head: Michael Kühl

We at the Institute of Biochemistry and Molecular Biology investigate the molecular basis of tissue and organ development during embryogenesis. We also wish to learn more about how different tissues and organs are maintained during aging and how they regenerate after injury. To tackle these questions, we use different model organisms such as *Mus musculus, Xenopus laevis, Danio rerio, Drosophila melanogaster* as well as murine embryonic stem cells.

The Team:
Head of Institute: M. Kühl
Professor: G. Weidinger
Group Leaders/Postdocs: K. Bundschu, M. Cederlund, S. Kühl, B. Mühl, P. Pandur, A. Pfister, M. Philipp
PhD Students: M. Burczyk, W. Cizelsky, M. Dalvoy, A. Hempel, Y. Guo, Z. Mirzojan, M. Radenz, H. Tauc, T.C. Tena, K. Werner, D. Wehner, C.C. Wu
Additional Members of Thesis Advisory Committees:
H. Aberle (Düsseldorf) T. Böckers (Ulm), F. Conlon (Chapel Hill), S. Hoppler (Aberdeen), H. Geiger (Ulm), P. Gierschik (Ulm), H. Jasper (Novato), S. Just (Ulm), T. Kielmann (Oulu), B. Möpps (Ulm), W. Rottbauer (Ulm), S. Vainio (Oulu)

Different groups of the institute study heart development (Kühl, Pandur and Philipp Labs). The heart is the first functional organ during vertebrate development. Defects during cardiac development result in congenital heart diseases occurring in approximately 1% of all newborns and are estimated to be the cause of 10% of stillbirths and spontaneous abortions. Defects in regulatory molecules that function in early heart development have been linked to congenital cardiovascular malformation. Detailed analyses of normal heart development at the molecular level will help us to understand the pathological changes that occur in congenital heart diseases. Moreover, the recent identification of adult cardiac stem cells that can differentiate into functional cardiomyocytes opens up a new perspective in the long-term therapy of heart diseases and reinforces the need to understand the process of normal cardiac development. For similar reasons, we study pronephros development in *Xenopus* (Kühl lab). The pronephros represents the functional embryonic kidney in this species.

Another focus of the institute is to uncover cellular and molecular mechanisms underlying the elevated regenerative capacity of lower vertebrates. In contrast to mammals, fish and amphibians can completely restore many internal organs and their appendages after injury. A detailed understanding of the mechanisms regulating this naturally occurring regeneration will aid the development of regenerative

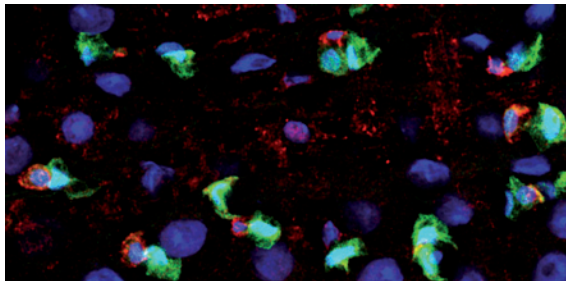


Zebrafish can fully regenerate their hearts after injury. Histological staining of heart sections at seven days post amputation of the apex of the ventricle shows fibrin-rich wound tissue in red, and resolution of the wound and absence of a collagen-rich scar which stains blue, at 30 days post amputation.

Ulm University
Institute of Biochemistry and Molecular Biology
Prof. Dr. Michael Kühl
Albert-Einstein-Allee 11
89081 Ulm, Germany
Tel. +49 (0)731 500 23281
Fax +49 (0)731 500 23277
michael.kuehl@uni-ulm.de
www.uni-ulm.de/med/med-biomolbio.html

therapies in humans. The Weidinger Lab studies heart and appendage regeneration in the zebrafish model. We focus on the role of extracellular signaling pathways and use systems biology approaches to uncover regulatory networks controlling regeneration, and study the mechanisms inducing cellular plasticity during regeneration.

We also study molecular changes underlying the aging process using intestinal stem cells in *Drosophila* (Pandur lab) and hematopoetic stem cells in the mouse (Kühl lab, in cooperation with the group of K.L. Rudolph, Jena) as model systems. Finally, the molecular design and the regulation of the Wnt signaling network are analyzed by the Kühl and Weidinger labs. We use a combination of signaling assays in fish and frog embryos and cultured cells, biochemical approaches and mathematical modeling to uncover novel molecular regulators of this important signaling network. This modeling is performed in collaboration with H. Kestler (Ulm). For this purpose, we use quantitative models based on ordinary differential equations and qualitative models. For both models, hypotheses will be generated by computer-based simulations that can either be verified or falsified by experimental means in cell-based assays.



The image shows cells of the *Drosophila* midgut. Intestinal stem cells are positive for the GFP-reporter and the Notch ligand Delta (red).

Selected Publications:

- *Herrmann F, Groß A, Zhou D, Kestler HA, Kühl M (2012): A boolean model of the cardiac regulatory network determining first and second heart field identity. PLOS One, 7, e46798.*
- *Tauc HM, Mann T, Werner K, Pandur P (2012): A role for Drosophila Wnt-4 in heart development. Genesis, 50, 466-481.*
- *Bugner V, Tecza A, Gessert S, Kühl M (2011): Peter Pan functions independent of its role in ribosome biogenesis during early eye and craniofacial cartilage development in Xenopus laevis. Development, 138, 2369-78.*
- *Kagermeier-Schenk B, Wehner D, Ozhan-Kizil G, Yamamoto H, Li J, Kirchner K, Hoffmann C, Stern P, Kikuchi A, Schambony A, Weidinger G (2011): Waif1/5T4 inhibits Wnt/beta-catenin signaling and activates noncanonical Wnt pathways by modifying LRP6 subcellular localization. Dev. Cell. 21, 1129-1143.*
- *Knopf F, Hammond C, Chekuru A, Kurth T, Hans S, Weber CW, Mahatma G, Fisher S, Brand M, Schulte-Merker S, Weidinger G (2011): Bone regenerates via dedifferentiation of osteoblasts in the zebrafish fin. Dev. Cell. 20, 713-724.*
- *Knopf F, Schnabel K, Haase C, Pfeifer K, Anastassiadis K, Weidinger G (2010): Dually inducible TetON systems for tissue-specific conditional gene expression in zebrafish. PNAS. 107, 19933-19938.*