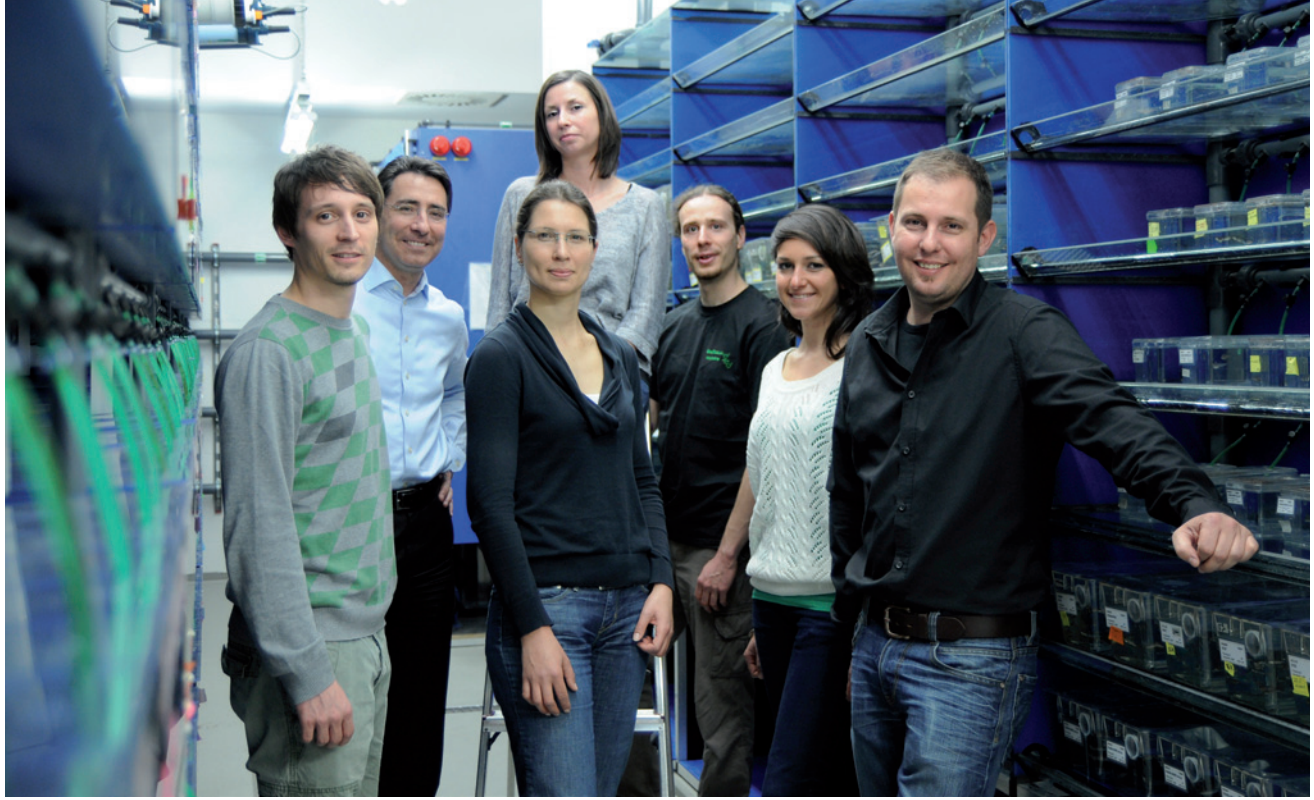


Department of Internal Medicine II

Dissecting the Molecular Pathology of Heart and Skeletal Muscle Disease

Head: Wolfgang Rottbauer

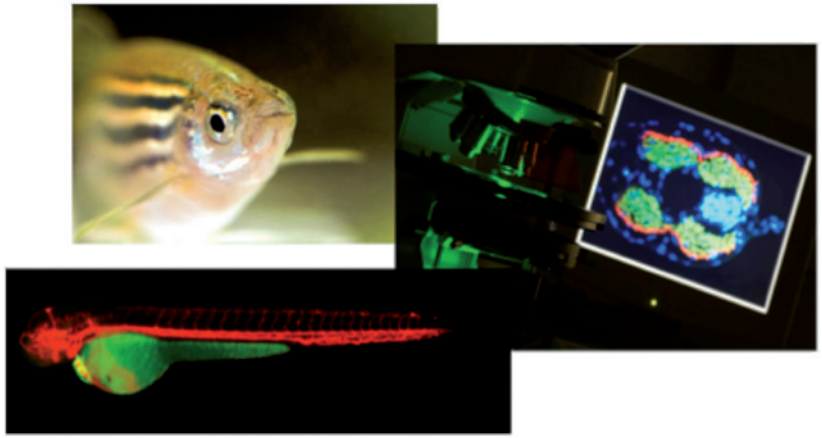
The Team:
Head of Department: W. Rottbauer
Group Leader: S. Just
Postdoc: I. Berger
PhD Students: J. Bührdel, S. Hirth, S. Rudeck, J. Segert
Study Programme Experimental Medicine Students: T. Zimmermann, M. Rattka
Additional Members of Thesis Advisory Committees: Ch. Buske (Ulm), F. Engel (Erlangen), D. Fürst (Bonn), M. Kühl (Ulm), F. Oswald (Ulm), U. Strähle (Karlsruhe), G. Weidinger (Ulm)

Molecular Cardiology

The main focus of the laboratory is to dissect novel genetic and molecular pathways of pathological cardiac and skeletal muscle development and growth using state-of-the-art forward and reverse functional genomics approaches in animal models (e.g. zebrafish, mouse). The long-term goal of our research is to identify novel therapeutic targets for cardiac and skeletal muscle diseases (in vivo high-throughput small compound screens). Currently, at the International Graduate School in Molecular Medicine Ulm, the following experimental PhD and MD projects are being pursued.
To develop targeted treatment strategies for human myofibrillar myopathies (MFM), the PhD project

of John Bührdel aims to elucidate the genetic basis and the precise molecular mechanisms that translate known MFM mutations into the myopathic phenotype using functional genomics in zebrafish. In a second PhD project, Steven Rudeck aims to dissect the molecular pathways leading to myofibril assembly and to identify new candidate genes such as SMYD1 and UNC-45 involved in human cardiac and skeletal muscle myopathies. Furthermore, in an attempt to develop novel molecular treatment strategies for heart failure, the PhD project of Sofia Hirth aims to further elucidate the role of ILK-signaling in cardiac stretch sensing and mechanotransduction. The main goal of the PhD project of Julia Segert is to unravel the precise genetic and molecular mechanisms that translate Nexilin mutations into the cardiomyopathic phenotype using in vivo and in vitro model systems.

The experimental MD research project of Tobias Zimmermann aims to decipher the molecular and cellular mechanisms that control cardiomyocyte proliferation and heart regeneration in zebrafish. To dissect the functional role of DCM-associated genes and disease modifying SNPs derived from GWA studies, the MD student Manuel Rattka uses state-of-the-art in vivo reverse genetics approaches.



The zebrafish is an excellent model to study cardiovascular and muscle development and function using forward and reverse functional genomics approaches.

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Selected Publications:

- *Just S, Berger IM, Meder B, Backs J, Keller A, Marquart S, Frese K, Patzel E, Rauch GJ, Katus HA, Rottbauer W (2011): Protein kinase d2 controls cardiac valve formation in zebrafish by regulating histone deacetylase 5 activity. Circulation. 124:324-334.*
- *Just S, Meder B, Berger IM, Etard C, Trano N, Patzel E, Hassel D, Marquart S, Dahme T, Vogel B, Fishman MC, Katus HA, Strahle U, Rottbauer W (2011): The myosin-interacting protein smyd1 is essential for sarcomere organization. J Cell Sci. 124:3127-3136.*
- *Meder B, Huttner IG, Sedaghat-Hamedani F, Just S, Dahme T, Frese KS, Vogel B, Kohler D, Kloos W, Rudloff J, Marquart S, Katus HA, Rottbauer W (2011): Pinch proteins regulate cardiac contractility by modulating integrin-linked kinase-protein kinase b signaling. Mol Cell Biol. 31:3424-3435.*
- *Meder B, Just S, Vogel B, Rudloff J, Gartner L, Dahme T, Huttner I, Zankl A, Katus HA, Rottbauer W (2010): Junb-cbfbeta signaling is essential to maintain sarcomeric z-disc structure and when defective leads to heart failure. J Cell Sci. 123:2613-2620.*
- *Hassel D, Dahme T, Erdmann J, Meder B, Huge A, Stoll M, Just S, Hess A, Ehlermann P, Weichenhan D, Grimmler M, Liptau H, Hetzer R, Regitz-Zagrosek V, Fischer C, Nurnberg P, Schunkert H, Katus HA, Rottbauer W (2009): Nexilin mutations destabilize cardiac z-disks and lead to dilated cardiomyopathy. Nat Med. 15:1281-1288.*
- *Hassel D, Scholz EP, Trano N, Friedrich O, Just S, Meder B, Weiss DL, Zitron E, Marquart S, Vogel B, Karle CA, Seemann G, Fishman MC, Katus HA, Rottbauer W (2008): Deficient zebrafish ether-a-go-go-related gene channel gating causes short-qt syndrome in zebrafish reggae mutants. Circulation. 117:866-875.*