

ZSN Research Profile



Peter Claus

1993	Diploma in Biology, University of Göttingen, Germany
1996	Dr. rer. nat., University of Göttingen, Germany
1996-1997	Postdoctoral training at the Department of Developmental Biology, University of Göttingen, Germany
1997-1999	Postdoctoral Fellow at the Molecular Biology Institute, University of California Los Angeles (UCLA), USA
since 1999	Senior Scientist at the Department of Neuroanatomy, Hannover Medical School, Hannover, Germany
2005	Habilitation and Venia legendi for Anatomy, Hannover Medical School, Hannover, Germany
2009	Associate Professor, Hannover Medical School, Hannover, Germany

Current research

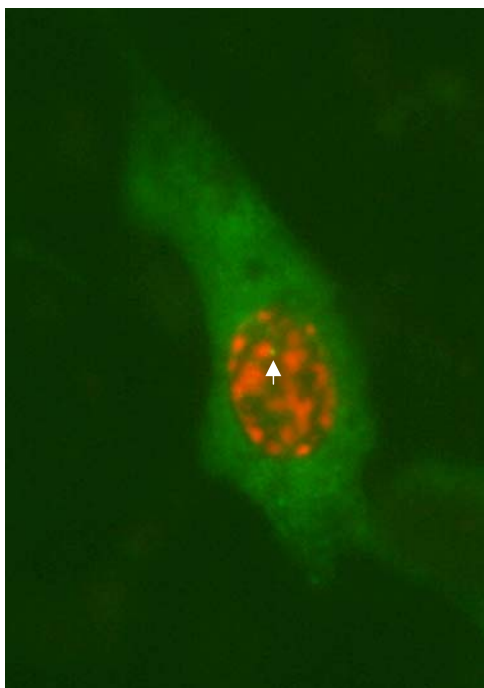
The molecular pathology of the neurodegenerative disease “Spinal Muscular Atrophy”

Spinal muscular atrophy (SMA) is a neurodegenerative disease in children accompanied by a massive loss of motoneurons causing death within the first two years of life. Mutations of the survival of motoneuron (SMN) gene are responsible for

this defect. SMN is an assembly protein for RNA-protein complexes in the nucleus and in axons of neurons. However, it is still unclear whether motoneuron cell death is due to nuclear or axonal functions of the SMN protein.

Although SMN is expressed ubiquitously, exclusively motoneurons degenerate in SMA. Initially, SMN has been characterized as a splicing assembly protein. Recently, it has been found that SMN is a general assembly protein for RNA-protein complexes critically involved in survival and maintenance of motoneurons with long axons, e.g. by transporting certain mRNA molecules along these structures. Defects in axonal functions seem to play an important role in the pathophysiology of SMA.

Our group has previously demonstrated that SMN is directly involved in the regulation of axonal growth. We have established a cell culture model for SMA which allows biochemical as well as morphometrical analyses of affected neurons. The lack of SMN results in significantly shorter neurites compared to normal conditions. This function is independent of SMN's well-defined role as a splicing complex assembly protein. Mechanistically, we recently defined a new function of the SMN protein in microfilament metabolism in axons.



The survival of motoneuron (SMN) protein in a living Schwann cell: SMN (green, SMN-EGFP) is distributed in the cytoplasm as well as in the nucleus. In the nucleus SMN localizes to nuclear bodies (white arrow), called Cajal bodies and nuclear gems. HMG1a-DsRed [formerly HMG-I] was used as a chromosomal marker (red signal).

Future Projects and Goals

To elucidate the molecular pathology of SMA it is required not only to investigate the nuclear functions of SMN with respect to splicing, but also to extend research to axonal functions of SMN. In our group, we analyze the molecular differences between axonal and nuclear SMN complexes with regard to structure of the complex as well as to functional parameters in neurons by: (1) Differential analyses of protein-protein interactions, (2) Identification of the mechanisms responsible for differential

axonal or nuclear localization, and (3) influence of SMN on the signalling cascades responsible for axon growth. The Claus group uses a wide spectrum of state-of-the-art molecular, biochemical and cell biology techniques, e.g. modern methodology of protein interaction research, RNAi and live cell imaging.

Selected publications:

Claus P., Döring F, Gringel S, Müller-Ostermeyer F, Fuhlrott J., Kraft T., Grothe C. (2003) Differential Intranuclear Localization of Fibroblast Growth Factor - 2 (FGF-2) Isoforms and Specific Interaction with the Survival of Motoneuron Protein. **J. Biol. Chem.**, 278:479-485.

Claus P., Bruns AF, Grothe C. (2004): Fibroblast growth factor-223 is binding directly to the survival of motoneuron protein and is associated with small nuclear RNAs. **Biochem J.** 384: 559-565.

Haastert K., Grosskreutz J., Jaeckel M., Laderer C., Bufler J., Grothe C., **Claus P.** (2005): Rat embryonic motoneurons in long-term co-culture with Schwann cells – a system to investigate motoneuron diseases on a cellular level in vitro. **J. Neurosci. Methods** 142: 275-284.

van Bergeijk J., Haastert K., Grothe C., **Claus P.** (2006): Valproic acid promotes neurite outgrowth in PC12 cells independent from regulation of the survival of motoneuron (SMN) protein. **Chem. Biol. Drug Design** 67: 244-247.

van Bergeijk J., Rydel-Könecke K., Grothe C. and **Claus P.** (2007): Functional domain mapping of the survival of motoneuron (SMN) protein: importance of the C-terminus for neurite outgrowth. **FASEB J.** 21: 1492-1502.

Bruns, A.F., van Bergeijk J., Lorbeer C., Nölle A., Jungnickel J., Grothe C., **Claus P.** (2009): The Growth Factor FGF-2 Regulates the Stability of Nuclear Bodies. **Proc. Natl. Acad. Sci. (PNAS)**, in press.

Group structure:

Group leader: Peter Claus
 Doctoral fellows: Anna Nölle, Jana O´mer, Sarah Al Rayes, Judith Deimel
 Technician: Hella Brinkmann

Contact:

Prof. Dr. Peter Claus
 Institute of Neuroanatomy, OE 4140,
 Building I3, Level 2, Room 1310
 Hannover Medical School
 Carl-Neuberg-Str.1
 30625 Hannover, Germany

Phone: +49-511-532-2932
 Fax: +49-511-532-2880
 E-mail: claus.peter@mh-hannover.de
 Web: <http://www.mh-hannover.de/neuroanatomie.html>