

Research Assistant: Cardiovascular and cerebrovascular diseases

Fall 2020

Credits: 6

Location: Copenhagen

Prerequisites: Dependent on the 6-credit Research Opportunity - listed on the [DIS Course Website](#)

Research Area

Lars Jørn Jensen's group (Cerebrovascular Physiology) study arteriolar function in health and disease. We investigate fundamental mechanisms in regulation of arteriolar tone involved in the control of blood pressure and organ perfusion (with emphasis on the brain). We specialize in myogenic tone, flow-mediated vasodilatation, and structural remodeling, which are key determinants of vascular function in vivo. We strive to describe new molecular mechanisms, and to apply this research using animal models of hypertension, aging and obesity/diabetes. In collaboration with the LifePharm In Vivo Pharmacology Centre (UCPH), we assist in development of porcine models of obesity and diabetes through our expertise in microvascular function.

Project title: Basic characterization of the proteome expressed in small resistance arteries of the pig brain.

We are interested in mapping the following family of proteins: Multi-drug resistance proteins (PGP; MRP; BCRP); Claudins; Occludin; ZO-1; ROCK1/2; Rho-GEFs; G α 12; CaV3.X channels (T-type); CaV2.1 channels (P/Q-type); TRPA1; TRPC6; TRPV4; SKCa/IKCa channels; Kir2.x channels; KATP channels; Insulin-R; IGF1-R; TGFBR1-2; MCR1-4 Receptors. We want to map the expression and localization of these targets using standard molecular biological tools coupled with Mass Spectrometry in order to use the pig brain as a translational model to study human cerebrovascular function and disease. The experiments will be focused on immunofluorescence microscopy using specific antibodies recognizing epitopes of the expressed proteins mentioned above, and will clarify the cellular localization and the relative expression levels compared to a positive control sample. As such an exhaustive characterization has not previously been performed in the pig brain the results are likely to be published eventually (although not necessarily right after the course).

Recent publications:

1. **Hansted AK, Bhatt DK, Olesen J, Jensen LJ, and Jansen-Olesen I.** Effect of TRPA1 activator allyl isothiocyanate (AITC) on rat dural and pial arteries. *Pharmacol. Rep.* 71, 565-572 (2019) (IF 2.787).
2. **Björling K,* Joseph PD,* Egebjerg K,* Salomonsson M, Hansen JL, Ludvigsen TP, and Jensen LJ (Corr.)**. Role of age, Rho-kinase 2 expression, and G protein-mediated signaling in the myogenic response in mouse small mesenteric arteries. *Physiol. Rep.* 6(17), e13863: DOI: 10.14814/phy2.13863 (2018). * Shared first-authorship.
3. **Klein A, Joseph PD, Christensen VG, Jensen LJ, and Jacobsen JCB.** Lack of Tone in Mouse Small Mesenteric Arteries Leads to Outward Remodeling, which can be Prevented by Prolonged Agonist-Induced Vasoconstriction. *Am. J. Physiol. (Heart Circ. Physiol.)*: 315(3):H644-H657, 2018. doi: 10.1152/ajpheart.00111 (IF 3.569).
4. **Gradel AKJ, Salomonsson M, Sørensen CM, Holstein-Rathlou N-H, and Jensen LJ (Corr.)**. Long-term diet-induced hypertension in rats is associated with reduced expression and function of small artery SK_{Ca}, IK_{Ca}, and Kir2.1 channels. *Clinical Science* 132, 461–474, 2018 (IF 4.936)
5. **Jensen LJ, Nielsen MS, Salomonsson M and Sorensen CM.** T-type channels and autoregulation of local blood flow. *Channels (Austin)* 11 (3), 183–195, 2017. (IF 2.008)

6. **Mikkelsen MF, Björling K and Jensen LJ (Corr.)**. Age-dependent impact of Cav3.2 T-type calcium channel deletion on myogenic tone and flow-mediated vasodilatation in small arteries. *J. Physiol.* 594.20:5881–5898, 2016. (IF 4.731 – BFI level 2)
7. **Frandsen RH, Salomonsson M, Hansen PBL, Jensen LJ, Braunstein TH, Holstein-Rathlou N-H, Sorensen CM**. No apparent role for T-type Ca²⁺ channels in renal autoregulation. *Pflügers Arch - Eur J Physiol.* 468:541–550, 2016. (IF 3.654)
8. **Løhr M, Folkmann JK, Sheykhzade M, Jensen LJ, Kermanizadeh A, Loft S and Møller P**. Hepatic oxidative stress, genotoxicity and vascular dysfunction in lean or obese Zucker rats. *PlosOne* 10(3):e0118773. doi: 10.1371/journal.pone.0118773, March 4th, 2015 (IF 4.411)
9. **Boonen HCM, Moesgaard SG, Birck MM, Christoffersen BØ, Cirera S, Heegaard PMH, Højboøge TR, Jensen LJ, Mortensen A, Olsen LH, Sheykhzade M, Tang J and Lykkesfeldt J**. Functional network analysis of obese and lean Göttingen minipigs elucidates changes in oxidative and inflammatory networks in obese pigs. *Pflugers Arch - Eur J Physiol.* 466:2167–2176, 2014 (IF 3.654)
10. **Ngo AT, Riemann M, Holstein-Rathlou N-H, Torp-Pedersen C and Jensen LJ (Corr.)**. Significance of K_{ATP} channels, L-type Ca²⁺ Channels and CYP450-4A enzyme in oxygen sensing in mouse cremaster arterioles *in vivo*. *BMC Physiol.* 13:8, 2013. (IF 2.0)
11. **Jensen LJ (Corr.) and Holstein-Rathlou N-H**. The vascular conducted response in cerebral blood flow regulation. *J. Cereb. Blood Flow Metab.* 33: 649-656, 2013. (IF 4.929)
12. **Björling K, Morita H, Olsen MF, Prodan A, Hansen PB, Lory P, Holstein-Rathlou N-H and Jensen LJ (Corr.)**. Myogenic tone is impaired at low arterial pressure in mice deficient in the low voltage-activated Cav3.1 T-type Ca²⁺ channel. *Acta Physiol. (Oxford)* 207, 709–720, 2013. (IF 4.066)

What is the 6-Credit Research Assistant course?

The 6-Credit Research Assistant semester course is an experiential learning opportunity that allows students to develop research skills in a professional research setting. As a research assistant, you perform research under the supervision of a mentor (a lead scientist in the external research group). The mentor is able to offer both academic and professional advice. In addition to acquiring research experience, the goal is to develop a student/mentor relationship that benefits both the DIS student and Copenhagen-based research institutions.

Learning Objectives

Through this course, DIS students will learn techniques and skills in their field of interest and as applicable to the research focus. Students will be part of an active research team and experience the dynamics of a European research institution. Throughout the semester, students will keep a research journal recording their daily involvement in the research project. At the end of the semester, all students involved in this course will participate in a Research Symposium to present their semester work to peers and invited professionals.

Expected Learning Outcomes

- Obtain hands-on research experience in cutting-edge laboratories
- Learn the ability to plan, conduct and critically evaluate experimental laboratory data
- Obtain the ability to perform self-directed and self-motivated experimental research
- Learn how to review scientific research papers and evaluate and criticize the experimental data
- Be able to actively participate in scientific discussions with professionals of the research area with a critical approach to the research
- Learn how to write a scientific research paper with your experimental data and present it in a professional way

Structure of Project Work

The student's research project will be a part of a larger, ongoing research project at the research institution. The student must be able to enhance the research being performed and investigate phenomena of interest to them, their mentor, and the research team. The project should be self-directed and self-motivated under the

mentor's guidance and supervision. A gradual transition toward independence is encouraged as a student gains confidence and is able to self-direct their work.

It is not expected that the student pursues a project where s/he is able to obtain definitive publishable results. The project chosen and agreed upon between the student and mentor should be focused and designed to produce results within the DIS semester calendar. While it is not necessary for the results to be significant (in that the results find a solution to the problem or hypothesis proposed), arguably any results to the proposed question are significant to the next phase of a research project.

Approach to teaching

The course requires an average of 20 hours a week of laboratory and/or clinical-based research in external research groups at local hospitals, universities, or other research institutions. The students will experience a very hands-on class, where some of the hours will be in a laboratory setting and some of the hours will be theoretical hours, where students read, write and prepare their research. Students will be provided with the basic scientific knowledge of the field and be introduced to the methods needed to conduct the experiments. Regarding teaching style, especially in the laboratory setting, the approach is "learn by doing". For the theoretical parts, students are expected to immerse themselves in the topic and take responsibility so they achieve the highest learning outcome by actively participating in our discussions and in their presentations.

Expectations of the students

The 6-credit Research Assistant semester course is designed for highly motivated students with a strong interest in developing their research skills. During the theoretical part students are expected to actively participate in discussions and critically evaluate the research and ethical components within the field. During the practical part students are expected to actively engage by planning and performing their own experiments and carefully monitor the conducted experiments and analyzing the collected data. Moreover, students are encouraged to critically evaluate possible issues if experiments do not go the way they should, and suggest modifications to experiments or reflect on potential mistakes. Overall the most important part is being enthusiastic about the science and active participation in the form of questions, discussions and critical thinking.

DIS Contact

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Jeanette Erbo Wern, PhD, DIS Copenhagen faculty and Copenhagen Coordinator: jwe@dis.dk

Course Location

This DIS course will be located at an external institution. Students will need to arrange a schedule with their mentor which will allow them to complete an average of **20 hours work per week** (total hours may vary according to research opportunity and expectation of mentor). Often this means that students are expected to group their other DIS courses into two days, so that they have two full days free for lab work.

Assignments

Throughout the semester, students are expected to complete various assignments to verify their involvement and learning; these will be of benefit to both the student and mentor. The students will be expected to compose the following:

A **literature summary review** will give the student the opportunity to seek out existing peer-reviewed articles and, therefore, enhance their scientific knowledge regarding the specific research field. In addition, it is essential that the student has knowledge of previously produced research by the research institution with which they are working.

An **outline of the research project** will provide the student with a foundational structure to help guide the project's completion. By creating an outline, the student will be able to better comprehend the objective of her/his efforts. The mentor will also be able to use the outline to assess areas in which the student's current knowledge and understanding may be lacking.

A **research abstract** explaining the importance and overall objective of the research the student has done. The abstract provides the student an outlet to think about their research concisely, thereby gleaming the most essential points from the project completion.

In conjunction with the submission of the research abstract there will be a **research symposium** where

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students will present the research they have carried out throughout the semester. Students will create a poster that supports their abstract and outlines the main aspects of their work; the poster is created with the guidance and approval of the research mentor. The poster session is part of a research symposium organized by DIS to showcase end-of-semester work across the curriculum.

The **research paper** is the final product of the 6-credit research assistantship. The paper will explain the student's work throughout the semester and will include the overall process, the project's significance, and the contribution to the field of research in which the student engaged. Please note: this research paper is not produced with the intent of publishing. The final research paper will include the following:

- Abstract
- Introduction
- Background
- Method(s)
- Results
- Discussion
- Conclusions

Evaluation

Literature Summary Review (5%)

Outline of Research Project (5%)

Abstract (5%)

Research Paper (10-15 pages) (60%)

Poster Presentation at Research Symposium (20%)

Participation (5%)

Research Assistants are required to participate in two (2) workshops during the semester. The content of the workshops is subject to change and may include overviews/introductions of skills your mentor will expect you to execute, as well as discussions on the goals of research and the ways in which research questions are culturally and historically-contingent. Workshop examples include, but are not limited to:

- Literature Search and Citation Skills
- Research Ethics
- Interpreting and Analyzing Data and the Significance of Results
- Communicating Research Findings (including poster production)
- Structure of Abstracts and Research Paper

Required Readings

Relevant scientific papers will be sent out before the start of the course.

Research Mentor:



Lars Jørn Jensen, Associate Professor, Ph.D.

Ph.D. in Physiology at the August Krogh Institute, University of Copenhagen (UCPH) in March 1999. He has 2.5 years working experience from the pharmaceutical industry (Lundbeck; development of anti-depressants). University researcher and teacher of cardiovascular physiology at UCPH from 2002 to present (first employed as postdoctoral fellow, then assistant professor, then associate professor). He has international research experience from Massachusetts General Hospital/Harvard Medical School, Boston, MA (1997-98) and Kyushu University, Fukuoka, Japan (2004-2006). He has attracted a number of external grants and supervised several Master level students and Ph.D.'s.

Copenhagen Research Coordinator



Jeanette Erbo Wern

Ph.D. Immunology 2001-2005 (Inst. Of International Health, Immunology and Microbiology, University of Copenhagen, Denmark). Post doc 2006-2009 (Inst. of International Health, Immunology and Microbiology, University of Copenhagen, Denmark). M.Sc. 2001 (Inst. Of International Health, Immunology and Microbiology, University of Copenhagen, Denmark). Senior Scientist 2010-2013 (Immune Targeting Group, Bioneer, Cph, Denmark). Senior Scientist 2013-2016 (Dept. of Infectious Disease Immunology, Statens Serum Institute, Cph, Denmark). With DIS since fall 2016

Academic Regulations

Please make sure to read the [Academic Regulations](#) on the DIS website. There you will find regulations on:

- [Course Enrollment and Grading](#)
- [Attendance](#)
- [Coursework, Exams, and Final Grade Reports](#)

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