

T-type voltage gated calcium channels and vascular function



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T-type channels play an important role in renal hemodynamics, contractility of resistance vessels and pacemaker activity in the heart. At least two types of T-type channels, $Ca_v3.1$ and $Ca_v3.2$, are expressed in blood vessels, the kidney and the heart. They contribute to both vasoconstriction and vasodilatation. T-type ($Ca_v3.1$) channels are involved in an endothelial cell-dependent dilatation and $Ca_v3.1$ T-type channels in endothelial cells co-localize with endothelial nitric oxide synthase (eNOS). In particular, during depolarization of mesenteric resistance arteries of young mice, the opening of $Ca_v3.1$ T-type channels modulates the influx of calcium ions which in turn stimulate eNOS, and increase production of nitric oxide (NO) and thereby affect the NO-dependent dilatation. Clinical studies suggest that T-type calcium channel blockers improve endothelial dysfunction and it was hypothesized that T-type channels contribute to the endothelial dysfunction during ageing. The NO-dependent relaxations of aortae and mesenteric arteries were significantly diminished in arteries of one year old Wt but not old $Ca_v3.1^{-/-}$ mice. Furthermore, DAF fluorescent imaging showed significantly lower NO levels in mesenteric arteries of old Wt compared to old $Ca_v3.1^{-/-}$ mice.

In conclusion, T-type channels contribute to contraction of human and mouse blood vessels. Furthermore, $Ca_v3.1$ and $Ca_v3.2$ T-type calcium channels contribute to vasodilatation through different mechanisms. Since T-type channel deficient mice are protected against age-dependent endothelial dysfunction, T-type blockers might protect against such dysfunction.

Curriculum Vitae

Date of birth: 17.05.1971

Academic qualifications and professional experience:

- 2013- Professor with special responsibilities. Cardiovascular and Renal Research, University of Southern Denmark (SDU)
- 2011-2012 Research Management Master Class, Copenhagen Business School
- 2011 Maternity Leave, 6 month
- 2010-2011 SDU, Management course
- 2010- Deputy Head of Research, Cardiovascular and Renal Research, SDU
- 2009-2010 Research Management Course, Copenhagen Business School.
- 2007-2013 Associate Professor, Physiology and Pharmacology, SDU
- 2006 Maternity Leave, 6 month
- 2004-2007 Assistant Professor, Physiology and Pharmacology, SDU
- 2001-2004 Post. Doc, National Institutes of Health, National Institute of Diabetes, Digestive and Kidney Diseases, Bethesda, USA
- 2001 Ph.D., Physiology. Contraction mechanisms in renal resistance vessels illustrated by *in vitro* techniques. SDU
- 1998-2001 Ph.D. Student, Dept. of Physiology and Pharmacology, SDU
- 1998 M.Sc. (Master of Science) Biology and Chemistry, Odense University

Honors and awards:

Danish Hypertension Society and Novartis Research Award (2010). LeoPharma's Hypertension award, Danish Hypertension Society (2005). Renal Research Recognition Award, American Physiological Society (APS) (2005). Fellows award for Research Excellence (2004), National Institutes of Health (NIH), USA. First Place Awardee, Aventis Pharma Awards for Excellence in Renal Research, APS (2003).

Research duties and management: Danish representative in the Management Committee of the EU COST network "ADMIRE". Board member of the Scandinavian Physiological Society.

Head of a research group including 10 people and deputy dept. head.

Opponent at 12 ph.d defences and reviewer on 9 associate professor and 2 professorships. Section editor Current opinion, Pharmacology (2015). Associate Editor, Acta Physiologica, symposium issue (2010 and 2015). Member of the editorial board Am. J. Physiol. , Frontiers Vascular, Frontiers Hypertension. On reviewing committee for Faculty of 1000 medicine. Chair of two international meetings, on scientific committee for several international meetings.

Research focus:

My main research interests are vascular function both in normal physiological settings and in cardiovascular and renal diseases. My research group uses techniques from the molecular level, to *in vitro* techniques to the integrated *in vivo* level. I focus on resistance vessels and their involvement in regulation of blood flow and blood pressure.

Funding:

Research grants from Danish Medical Research Council, Lundbeck Foundation, Carlsberg Foundation, Novo-Nordic Foundation, Danish Heart Foundation, Danielsen Foundation, AP Møller Foundation, Danish Kidney Foundation.

Supervision: Supervisor for 15 bachelor students, 8 graduate students and 7 Ph.D students.

Publications: 66 publications in for example JCI, PNAS, Circ Res.