

Novel pharmacological approaches to treatment of pulmonary hypertension

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Pulmonary hypertension is characterized by a pulmonary arterial pressure above 25 mmHg which results in right ventricular hypertrophy, failure and death. The disease is classified in pulmonary arterial hypertension, pulmonary hypertension owing to left heart disease, pulmonary hypertension owing to chronic lung disease, chronic thromboembolic pulmonary hypertension, and pulmonary hypertension with unclear multifactorial mechanism. Pharmacological treatments for pulmonary hypertension are based on the concept of restoring endothelial vasodilator-dependent function and include apart from L-type calcium channel blockers, prostacyclin mimetics, endothelin receptor antagonists, and phosphodiesterase type 5 inhibitors. These treatments have markedly improved the prognosis in pulmonary arterial hypertension, but largely fail to reduce the pressure load on the pulmonary circulation and right ventricle. Moreover, there is unmet needs for both diagnosis and treatment of the much more prevalent forms of pulmonary hypertension e.g. pulmonary hypertension due to chronic lung disease and left heart disease. In chronic hypoxic pulmonary hypertension in rats we investigated three different pathways: (1) the apelin pathway, (2) modulation of the bioavailability of superoxide, and (3) whether modulation of calcium-activated K channels could be a potential target for treatment. The inhibition of vasoconstriction induced by apelin was impaired in chronic hypoxic rats, while treatment with tempol and apocynin was able to prevent, but they did not reverse pulmonary hypertension. Calcium-activated K channels (KCa2.3 and KCa3.1) channels are expressed in the rat and human pulmonary circulation, and KCa3.1 were downregulated and associated with endothelial dysfunction, while KCa2.3 channels were markedly upregulated in chronic hypoxic rats. KCa2.3 channels may serve as a potential target for treatment of pulmonary hypertension.

CURRICULUM VITAE

Ulf Simonsen

Civil status

Date of birth February 17, 1963. Married to Susie Mogensen, Diploma of Engineering, B.Sc. and we have five children.

Education

2007 Management course related to the employment as head of department.

1998-2000 Followed the obligatory courses related to the speciality in Clinical Pharmacology

1997 B-authorisation (Danish authorisation to practice as a medical doctor without supervision).

1994 Doctor in Medicine, Faculty of Medicine, Universidad Complutense de Madrid, Spain. The thesis was based on 4 original publications and one review on the role of endothelial function and autonomic nerves for regulation of the coronary circulation.

1991 Medical doctor, University of Aarhus.

Employments

2011- Professor, Department of Biomedicine, Aarhus University.

2006-2011 Head of Department of Pharmacology

2005-2011 Professor, Department of Biomedicine, Aarhus University

1998 Associate professor, Department of Pharmacology, Faculty of Health Sciences, University of Aarhus, Denmark

1997 Worked as trainee in general practice, Vorup, Randers, Denmark.

1996 Assistant professor, Department of Pharmacology, Faculty of Health Science, Aarhus University

1995 Department of Orthopaedic Surgery, Silkeborg County Hospital and Department of Haematology, Århus County Hospital.

1991-1994 Ph.D. student, Faculty of Medicine, Universidad Complutense de Madrid, Spain. Finished December 1994 with "Apto cum Laude".

1988-1990 Research student, Department of Pharmacology, Aarhus University.

Scientific work

The research group aims to develop novel pharmacological approaches to improve endothelial function in cardiovascular disease. Endothelial cell function and signal transduction is investigated under normal and pathophysiological conditions both in collaboration with basic science as well as clinical departments. Endothelial dysfunction is also linking cardiovascular disease to erectile dysfunction, and plays an important role in the development of pulmonary hypertension. Heading a research group in pulmonary and cardiovascular pharmacology with assistant prof. Thomas Dalsgaard (10 people, 4 PhD students, 2 medical students, 4 science students, 2 technicians). Author or co-author on > 110 peer reviewed papers in international journals and several book chapters. Co-inventor of amine-transport inhibitor for treatment of erectile dysfunction.

Academic work

Editorial work. Associate editor at Basic and Clinical Pharmacology (~100 manuscripts/year), Pharmacological Reviews (impact-20), Journal of Vascular Research, Journal of Sexual Medicine, and invited review editor British Journal of Pharmacology (2009), and in editorial board of Frontiers in Pharmacology.

Ad hoc reviewer for > 20 journals, and regular reviewer for funding organisations including: Wellcome Foundation (UK), National Research Council in Israel and Georgia.

Reviewer on PhD theses in DK, Sweden, Belgium, and Spain. Reviewer on master and bachelor theses.

Invited talks, seminars, and ordinary oral presentations in Western Europe, Asia, and United States.

Member of committee on pathophysiology in relation to consultations on erectile dysfunction hosted by World Health Organisation 1999, 2003, and 2009.

Honors

2007 Entrance as external member of the Royal Spanish Pharmaceutical Academy.

Administration

Member of evaluation committees in Denmark and Sweden in connection with employment of scientific staff (assistant prof., lecturers, professors).

Chairman of the Danish Society for Pharmacology and Toxicology from 2007-2011.

Chairman of the Danish Society of Pharmacology 2011-

Member of the council controlling the Danish Hypertension Society 2003-2007.

Member of the steering committee of European Council for Cardiovascular Research (ECCR) from 2008.

Head of Department of Pharmacology, Aarhus University 2006-2011.

Teaching and supervision

Teacher in physiology for veterinarian students 1991-1995, Complutense University, Spain and in pharmacology for medical and science students since 1996, Aarhus University. Teacher since 1991 at pre- and postgraduate courses on cardiovascular physiology and pharmacology. Organizer of postgraduate courses on nitric oxide measurements (2004-2007), Aarhus University, and teacher at PhD courses in Denmark and Spain. Censor in pharmacology for medical students from 1999-2010, for pharmaceutical students (2000-). Supervisor for more than 20 PhD students/diploma students from the Health and Science and technology, Aarhus University. Currently main supervisor for four PhD students. Supervisor for several visiting students and PhD students from foreign collaborating laboratories.