

pH in the cells of the vascular wall: Regulation and importance for vascular function



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It is well known that changes in acid-base homeostasis have important effects on vascular function, i.e. extracellular acidosis leads to vasorelaxation. Surprisingly little is known about the pathways which are important for these vascular effects of altered acid-base status. In fact it is not even known whether extracellular or intracellular pH is important and to what extent bicarbonate and CO₂ are also important for the vascular effects of deranged pH homeostasis

In this lecture I will focus on the regulation of intracellular pH in the smooth muscle cells and endothelial cells of the vascular wall and how changes in pH of these cells impacts on vascular function.

I will show how, sodium coupled transport of both bicarbonate and protons over the cell membrane is crucial for regulation of pH in endothelial cells and smooth muscle cells.

I will further discuss how changes in these transport pathways affect endothelial NO production and gap junction communication between endothelial and smooth muscle cells with consequences for endothelial derived hyperpolarization, which again has important consequences for endothelial mediated regulation of vascular tone. I will also discuss how changes of pH in the smooth muscle cells affect the Rho-kinase enzymatic activity and consequently vascular tone. I will show data that strongly indicates that these effects are important for the blood pressure control in mice and provide a suggested mechanism for the finding that variations in the gene coding for the sodium coupled bicarbonate transporter expressed in the smooth muscle cells and the endothelial cells has importance for blood pressure control in humans.

Selected publications

Boedtkjer E, Kim S, Aalkjaer C. Endothelial alkalinisation inhibits gap junction communication and endothelium-derived hyperpolarisations in mouse mesenteric arteries. **Journal of Physiology.** 2013;591:1447-1461

Boedtkjer E, Damkier H, Aalkjaer C NHE1 knockout reduces blood pressure and arterial media/lumen ratio with no effect on resting pHi in the vascular wall. **Journal of Physiology** 2012; 590:1895-1906

Boedtkjer E, Praetorius J, Matchkov V, Stankevicius E, Mogensen S, Füchtbauer A, Simonsen U, Füchtbauer E-M, Aalkjaer C. Disruption of Na⁺,HCO₃⁻-cotransporter NBCn1 (slc4a7) inhibits NO-mediated vasorelaxation, smooth muscle Ca²⁺-sensitivity and hypertension development in mice. **Circulation** 2011;124:1819-1829

Boedtkjer E, Aalkjaer C. Insulin inhibits Na⁺/H⁺-exchange in vascular smooth muscle and endothelial cells in situ: involvement of H₂O₂ and tyrosine phosphatase SHP-2. **American Journal of Physiology** 2009;296:H247-H255

Boedtkjer E, Praetorius J, Füchtbauer EM, Aalkjaer C. Antibody-independent localization of the electroneutral Na⁺-HCO₃⁻ cotransporter NBCn1 (slc4a7) in mice. **American Journal of Physiology** 2008;294:C591-C603.

Boedtkjer E, Praetorius J, Aalkjaer C. NBCn1 (slc4a7) mediates the Na⁺-dependent bicarbonate transport important for regulation of intracellular pH in mouse vascular smooth muscle cells. **Circulation Research.** 2006, 98:515-523.

Curriculum Vitae

Personal data

Born: August 9 1954, Horsens, Denmark
Present occupation: Professor of physiology

Education and employments

2014- Professor, Institute of Biomedicine Copenhagen University
1998- Professor, Institute of Biomedicine, Aarhus University
1988-1997 Associate professor, Institute of Pharmacology, Aarhus University
1981-1988 Assistant professor, Institute of Biophysics Aarhus University
1981 Final University Examination in Medicine, Aarhus University

Doctoral thesis

1989 Some aspects of sodium metabolism in arterial resistance vessels

Sabaticals

1986; 6 months Dept. Medicine, Leicester, UK
1992; 6 months Dept. Clin Pharmacol, St. Mary's Hospital, London, UK
1997; 3 months Inst Mol Cell Physiology, Yale University, New Haven, US

Selected honors

1984 3 years stipend from K Abildgaard, Løvens Kemiske Fabriks forskningsfond.
1988 Demuth Award, The International Society of Hypertension
1989 ICI Award, Danish Hypertension Society.
1998 Novo Nordisk Prize joint with professor dr. med. MJ Mulvany.
2002 Teacher of the year, Medical Faculty, Aarhus University
2008 Teacher of the year, Medical Faculty, Aarhus University

Positions of trust

Scientific Journals

Editorial Board of Hypertension, Clinical Science, American Journal of Physiology, Journal of Vascular Research, Vascular Pharmacology. Reviewer for multiple journals on physiology.

Evaluator:

Welcome Foundation, UK; INSERM Département de l'évaluation Scientifique, France, Chairman evaluation panel Dept. Preclinical Experimental Medicine, Lunds University, Sweden. Evaluation of 20 Ph.D. theses in Denmark, Sweden and Holland.

1990-93 and 2006- Member of the Danish Heart Foundation Research Committee

1990-1997 Member of the board of the Danish Hypertension Society

2000-2006, 2012- Member of the board of European College of Cardiovascular Research.

2007- Member of the Scientific Advisory Board of the Foundation for Circulation Health, Imperial College, London, UK

2009 - Member of the International Advisory Panel of the British Heart Foundation Studentship Programme

Scientific Publications

A total of 178 peer-reviewed papers, 2 editorials, 30 review articles and 146 original research papers. H-index 41, total citations 7260