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The red blood cell: A novel mediator of cardiovascular disease and target for treatment

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It is well established that endothelial dysfunction is an early marker of cardiovascular disease and associated with poor outcome in coronary artery disease. Endothelial dysfunction is triggered by common cardiovascular risk factors such as type 2 diabetes and dyslipidemia. The molecular mechanisms underlying development of endothelial dysfunction include reduced bioavailability of nitric oxide (NO) and formation of reactive oxygen species (ROS) regulated by arginase. Arginase is upregulated in cardiovascular disease and diabetes, which contributes to cardiovascular dysfunction via reduced bioavailability of NO and increased oxidative stress. Recent data indicate that similar signaling events occur in the red blood cell (RBC). The RBC plays a role in the regulation of cardiovascular function via a mechanism involving RBC arginase and endothelial NO synthase. RBCs are able to export cardioprotective NO bioactivity under tight regulation of arginase. Inhibition of RBC arginase protects the myocardium from ischemia-reperfusion injury via a mechanism strictly dependent on endothelial NO synthase. Arginase is upregulated in patients with type 2 diabetes. This change promotes

increase in RBC ROS production via NO synthase uncoupling, increased myocardial ischemia-reperfusion injury and development of endothelial dysfunction. Inhibition of arginase and ROS formation in RBCs from patients with type 2 diabetes prevents the development of endothelial dysfunction and improves cardiac tolerance to ischemia. These data point towards a novel regulatory role of the RBC in cardiovascular disease, and targeting RBC dysfunction may be a beneficial therapeutic strategy.

SHORT BIOGRAPHY

Present position

2008 – Professor of Cardiology, Department of Medicine, Karolinska Institutet

2001 – Senior consultant Department of Cardiology
Karolinska University Hospital

2017 - Director Research and Education Cardiovascular Division,
Karolinska University Hospital

Previous employments and exams

Academic

2002 – 2008	Clinical Senior Research Position, Swedish Research Council, Medicine Clinical research position in Cardiovascular Medicine,
2001 – 2002	Research and Development Committe Karolinska Hospital
1998	Associate Professor of Cardiology
1992 – 1995	Post-doc clinical research position Swedish Research Council, Department of Medicine K2, Karolinska Institutet
1991	Associate Professor of Pharmacology
1988 PhD	Pharmacology Karolinska Institutet

Clinical

2001 -	Senior consultant in cardiology
2001 – 2002	Chief of Coronary Care Unit, Karolinska Hospital
1997 – 2001	Consultant in Cardiology, Karolinska University Hospital
1992 – 1997	Internship Cardiology and Internal Medicine; Karolinska University Hospital
1991	Licensed to medical degree
1997	Specialist competence in Cardiology achieved
1997	Specialist competence in Internal medicine achieved
1998	Specialist examination in cardiology issued by the Swedish Society of Cardiology

Other positions and assignments of trust

2006 -	Academic chair Cardiology Division, Dep of Medicine Karolinska Institutet
2015 -	Vice Chair Department of Medicine, Karolinska Institutet
2005 – 2011, 2016 -	Member of Scientific Board, Swedish Heart and Lung Foundation
2015 -	Member of the scientific evaluation panel Swedish Research Council
2013 – 2014	Member of scientific evaluation committee ALF grants Lund/Malmö

Supervision of PhD students

Main supervisor of 13 PhD students who have completed their doctoral thesis
Co-supervisor of 4 PhD student who have completed their doctoral thesis
Currently supervisor of 4 PhD students

Research grants

Currently holding research grants from as PI:
Swedish Research Council
Swedish Heart Lung Foundation
European association for the study of diabetes
Stockholm County Council/ALF
Diabetes Wellness Research Foundation
Karolinska Institutet Clinical Scientist Training Programme (CSTP)
Swedish Heart Lung Foundation Doctoral Funding

Original publications

Author of 202 original publications. **H-index 51**, citations *8 825* (Web of Sci).