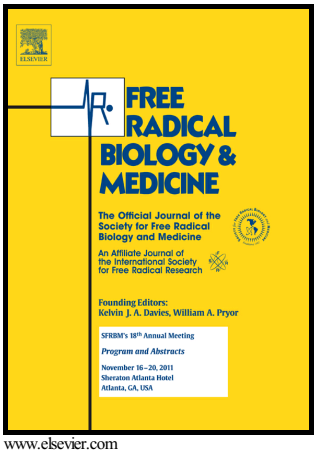
Vascular remodeling: a redox-modulated mechanism of vessel caliber regulation

Leonardo Y. Tanaka, Francisco R.M. Laurindo



www.elsevier.com

PII: S0891-5849(17)30034-5
DOI: http://dx.doi.org/10.1016/j.freeradbiomed.2017.01.025
Reference: FRB13181

To appear in: *Free Radical Biology and Medicine*

Received date: 18 December 2016
Revised date: 13 January 2017
Accepted date: 15 January 2017

Cite this article as: Leonardo Y. Tanaka and Francisco R.M. Laurindo, Vascular remodeling: a redox-modulated mechanism of vessel caliber regulation, *Free Radical Biology and Medicine* http://dx.doi.org/10.1016/j.freeradbiomed.2017.01.025

Vascular remodeling: a redox-modulated mechanism of vessel caliber regulation

Leonardo Y. Tanaka, Francisco R. M. Laurindo

From the Vascular Biology Laboratory, Heart Institute (InCor), University of São Paulo School of Medicine, São Paulo, Brazil

*Corresponding author. Francisco R M Laurindo, MD PhD. Vascular Biology Laboratory, Heart Institute (InCor), University of São Paulo School of Medicine, Av. Enéas Carvalho Aguiar, 44, Annex II, 9th Floor, São Paulo, Brazil. CEP 05403-000, Tel.: +55 11 26615185, FAX: +55 11 2661 5920. E-mail: francisco.laurindo@incor.usp.br

Abstract

Vascular remodeling, i.e. whole-vessel structural reshaping, determines lumen caliber in (patho)physiology. Here we review mechanisms underlying vessel remodeling, with emphasis in redox regulation. First, we discuss confusing terminology and focus on *strictu sensu* remodeling. Second, we propose a mechanobiological remodeling paradigm based on the concept of tensional homeostasis as a setpoint regulator. We first focus on shear-mediated models as prototypes of remodeling closely dominated by highly redox-sensitive endothelial function. More detailed discussions focus on mechanosensors, integrins, extracellular matrix, cytoskeleton and inflammatory pathways as potential of mechanisms potentially coupling tensional homeostasis to redox regulation. Further discussion of remodeling associated with atherosclerosis and injury repair highlights important aspects of redox vascular responses. While neointima formation has not shown consistent responsiveness to antioxidants, vessel remodeling has been more clearly responsive, indicating that despite the multilevel redox signaling pathways, there is a coordinated response of the whole vessel. Among mechanisms that may orchestrate redox pathways, we discuss roles of superoxide dismutase activity and extracellular protein disulfide isomerase. We then discuss redox modulation of aneurysms, a special case of expansive remodeling. We propose that the redox modulation of vascular remodeling may reflect (1) remodeling pathophysiology is dominated by a particularly redox-sensitive cell type, e.g., endothelial cells (2) redox pathways are temporospatially coordinated at an organ level across distinct cellular and acellular structures or (3) the tensional homeostasis setpoint is closely connected to redox signaling. The mechanobiological / redox model discussed here can be a basis for improved understanding of remodeling and helps clarifying mechanisms underlying prevalent hard-to-treat diseases.