β1-Integrin is up-regulated via Rac1-dependent reactive oxygen species as part of the hypertrophic cardiomyocyte response

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

ID 1195766
Author(s) Häuselmann, Stéphanie P; Rosc-Schlüter, Berit I; Lorenz, Vera; Plaisance, Isabelle; Brink, Marijke; Pfister, Otmar; Kuster, Gabriela M
Author(s) at UniBasel Pfister, Otmar ; Brink, Marijke ; Kuster Pfister, Gabriela ;
Year 2011
Title β1-Integrin is up-regulated via Rac1-dependent reactive oxygen species as part of the hypertrophic cardiomyocyte response
Journal Free radical biology & medicine
Volume 51
Number 3
Pages / **Article-Number** 609-18
Keywords beta(1)-Integrin, Rac1, Reactive oxygen species, Cardiomyocytes, Hypertrophy, Free radicals
beta(1)-Integrin mediates cardiomyocyte growth and survival and its proper regulation is essential for the structural and functional integrity of the heart. beta(1)-Integrin expression is enhanced in hypertrophy, but the mechanism and significance of its up-regulation are unknown. Because reactive oxygen species (ROS) are important mediators of myocardial remodeling we examined their role in regulated beta(1)-integrin expression. Hypertrophy was induced in neonatal cardiomyocytes by endothelin-1 (ET-1), which activated the regulatory NADPH oxidase subunit Rac1, evoked ROS, and enhanced fetal gene expression and cardiomyocyte size. ET-1 also enhanced cell adhesion and FAK phosphorylation and inhibited oxidative stress-induced cardiomyocyte apoptosis. Further, ET-1 increased beta(1)-integrin mRNA and protein expression via Rac1-ROS-dependent MEK/ERK and EGF receptor-PI3K/Akt activation as shown by adenoviral dominant-negative Rac1 or overexpression of copper/zinc-superoxide dismutase. The relevance of regulated beta(1)-integrin expression was examined in cardiomyocytes, in which targeting siRNA impeded the ET-1-induced beta(1)-integrin up-regulation. In these cells, ET-1-induced cell adhesion, FAK phosphorylation, and hypertrophic response were significantly blunted, whereas its antiapoptotic effect was predominantly unchanged, suggesting at least partial dissociation of prohypertrophic and prosurvival signaling elicited by ET-1. In conclusion, beta(1)-integrin up-regulation in response to ET-1 is mediated via Rac1-ROS-dependent activation of prohypertrophic pathways and is mandatory for ET-1-induced FAK activation, cell adhesion, and hypertrophic response.
Publisher Pergamon Press
ISSN/ISBN 0891-5849
URL http://www.ncbi.nlm.nih.gov/pubmed/21620958
edoc-URL http://edoc.unibas.ch/dok/A6338355
Full Text on edoc No;
Digital Object Identifier DOI 10.1016/j.freeradbiomed.2011.05.007
PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/21620958
ISI-Number WOS:000292856900004
Document type (ISI) Journal Article