Abstract:
Urotensin-II (U-II) has been considered as one of the most potent vasoactive peptides, although its physiological and pathophysiological role is still not finally resolved. Recent evidence suggests that it promotes angiogenic responses in endothelial cells, although the underlying signalling mechanisms are unclear. Reactive oxygen species derived from NADPH oxidases are major signalling molecules in the vasculature. Because NOX2 is functional in endothelial cells, we investigated the role of the NOX2-containing NADPH oxidase in U-II-induced angiogenesis and elucidated a possible contribution of hypoxia-inducible factor-1 (HIF-1), the master regulator of hypoxic angiogenesis, in the response to U-II. We found that U-II increases angiogenesis in vitro and in vivo, and these responses were prevented by antioxidants, NOX2 knockdown and in Nox2(-/-) mice. In addition, U-II-induced angiogenesis was dependent on HIF-1. Interestingly, U-II increased NOX2 transcription involving HIF-1, and chromatin immunoprecipitation confirmed NOX2 as a target gene of HIF-1. In support, NOX2 levels were greatly diminished in U-II-stimulated isolated vessels derived from mice deficient in endothelial HIF-1. Conversely, reactive oxygen species derived from NOX2 were required for U-II activation of HIF and upregulation of HIF-1. In line with this, U-II-induced upregulation of HIF-1 was absent in Nox2(-/-) vessels. Collectively, these findings identified HIF-1 and NOX2 as...
partners acting in concert to promote angiogenesis in response to U-II. Because U-II has been found
to be elevated in cardiovascular disorders and in tumour tissues, this feed-forward mechanism could
be an interesting anti-angiogenic therapeutic option in these disorders.

Zeitschriftentitel / Abkürzung:
J Cell Sci

Jahr:
2012

Band:
125

Heft / Issue:
Pt 4

Seiten:
956-64

Sprache:
eng

Pubmed:

Print-ISSN:
0021-9533

TUM Einrichtung:
Kinderkardiologie und angeborene Herzfehler

Occurences:
- Einrichtungen > Fakultäten > Fakultät für Medizin > Kliniken und Institute > Lehr- und
  Forschungskooperationen mit den Kliniken und Instituten am Deutschen Herzzentrum > Klinik für
  Kinderkardiologie und angeborene Herzfehler (Prof. Hess) > 2012

entries: