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Review

Biliverdin reductase: new features of an old enzyme and its potential therapeutic significance

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Abstract:
Biliverdin reductase (BVR) was known for a long time solely as an enzyme converting biliverdin to bilirubin, the major physiological antioxidant. Recent years revealed unique features of this protein which are not related to its reductase activity. The most intriguing and surprising finding is its dual-specificity kinase character. As such serine/threonine/tyrosine kinase BVR is involved in regulation of glucose metabolism or in control of cell growth and apoptosis. In consequence, it may play a role in pathogenesis of many diseases, such as diabetes or cancers. Moreover, in the nucleus BVR, being a leucine zipper-like DNA binding protein, can act as a transcription factor for activator protein 1 (AP-1)-regulated genes. It has been shown that BVR modulates ATF-2 and HO-1 expression, what suggests its potential role in control of AP-1 and cAMP-regulated genes. In conclusion, BVR together with its substrate, biliverdin, and product, bilirubin, are revealed to be important players in cellular signal transduction pathways, gene expression and oxidative response. These features make BVR unusually interesting and unique among all enzymes characterized to date.

Key words:
heme oxygenase 1, biliverdin reductase, antioxidant, dual-specificity kinase