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Regulation of poly ADP-ribosylation of VEGF by an interplay between PARP-16 and TNKS-2

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Abstract

The biological activity of vascular endothelial growth factor (VEGF), the major cytokine regulating the process of angiogenesis is tightly controlled at multiple levels including processes involving post-translational modification such as ADP-ribosylation and glycosylation. ADP-ribosylation is a reversible NAD^+-dependent modification, catalyzed by poly ADP-ribose polymerase (PARP) or ADP-ribosyl transferase (ADPRTs) and has been reported by us and others as a modification that reduces the biological activity of VEGF. The factors responsible for any such modification should occur in the secretory pathway, i.e., in the endoplasmic reticulum and Golgi. Our investigation carried out in this direction revealed that ADP-ribosylation of VEGF requires the interplay between members of poly ADP-ribose polymerase (PARP) family in the secretory pathway, viz., ER associated PARP-16 and Golgi associated Tankyrase-2 (TNKS-2). The data presented in this manuscript suggest that PARP-16 catalysis the priming mono ADP-ribosylation of VEGF which is a prerequisite for poly ADP-ribosylation of VEGF by TNKS-2.

Keywords: ADP-ribosylation; Angiogenesis; PARP-16; TNKS-2; VEGF.

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