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Functional role of circulating APE1/Ref-1 in vascular inflammation

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Apurinic/apyrimidinic endonuclease 1/redox factor-1 (APE1/Ref-1) is a multifunctional protein that plays a central role in the cellular response to DNA damage and redox regulation against oxidative stress. In 2013, we first demonstrated the presence of the APE1/Ref-1 protein in the plasma of endotoxemic rats as a 37 kDa immunoreactive band that was then identified as rat APE1/Ref-1 by liquid chromatography/tandem mass spectrometry. APE1/Ref-1 levels in biological samples such as serum and urine have been reported in bladder cancers or ischemic heart diseases using a newly developed, sandwich enzyme-linked immunosorbent assay. Although the underlying mechanisms for secreted APE1/Ref-1 are yet to be fully delineated, a few reports have been able to provide some insight into its biological functions. During hyperacetylation in culture, a time-dependent increase in secreted APE1/Ref-1 was confirmed. Additionally, recombinant human APE1/Ref-1 with reducing activity induced a conformational change in cytokines receptor such as TNF-α receptor 1 by thiol-disulfide exchange. These results strongly indicate that circulating APE1/Ref-1 has anti-inflammatory activity against cytokine-induced vascular inflammations.