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In vivo role of a redox protein against H_2O_2-induced cell death

Jin Ho Park*, Jong Cheol Kim, Jung Ro Lee, Ho Hee Jang, Jeong Chan Moon, Sun Young Kim, Sun Yong Lee, Chae Oh Lim, Kyun Oh Lee and Sang Yeol Lee

Environmental Biotechnology National Core Research Center, Division of Applied Life Science (BK21 program), Gyeongsang National University, Jinju, 660-701, Korea

Although biochemical properties of 2-Cys peroxiredoxins (Prxs)have been extensively studied, their real physiological functions in higher eukaryotic cellsremain obscure and certainly warrant further study. Here, we demonstrate that hPrxII,a cytosolic isotype of human 2-Cys Prx, has dual functions as a peroxidase and a molecular chaperone, and that these different functions are closely associated with its adoption of distinct protein structures. Upon exposure to oxidative stress, hPrxII assumes a high molecular weight (HMW) complex structure that hasa highly efficient chaperone function. However, the subsequent removal of stressors induces the dissociation of this protein structure into low MW proteins and triggers a chaperone-to-peroxidase functional switch. The formation of a HMW hPrxII complex depends on the hyperoxidation of its N-terminal peroxidatic Cys residue as well as on its C-terminal domain, which contains a 'YF-motif' that is exclusively found in eukaryotic 2-Cys Prxs. A C-terminally truncated hPrxIIexists as low and oligomeric protein species and doesnot respond to oxidative stress. Moreover, this C-terminal deletion of hPrxII converted it from anoxidation-sensitive to a hyperoxidation-resistant form of peroxidase. When functioning as achaperone, hPrxII protects HeLa cells from H_2O_2-induced cell death, as measured by a terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling assay and fluorescence-activated cell sorting analysis.