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ACCEPTED MANUSCRIPT

Redox Regulation of the Tumor Suppressor PTEN by the Thioredoxin

System and Cumene Hydroperoxide

Seong-Jeong Han^{a,b1}, Ying Zhang^{a1}, Inyoung Kim^{a1}, Kee-Oh Chay^a, Hyun Joong Yoon^a, Dong

Il Jang^b, Jiyoung Park^c, Hyun Ae Woo^c, Iha Park^a[‡], Seung-Rock Lee^a[‡]

^aDepartment of Biochemistry, Department of Biomedical Science, Research Center for Aging and Geriatrics, Research Institute of Medical Sciences, Chonnam National University Medical School, Gwangju 501-190, Republic of Korea

^bCOTDE Inc. 19-3, Ugakgol-gil, Susin-myeon, Cheonan-si, Chungcheongnam-do, 330-882, Republic of Korea

^cCollege of Pharmacy, Graduate School of Pharmaceutical Sciences, Ewha Womans University, Seoul 120-750, Republic of Korea

ip071@jnu.ac.kr

leesr@jnu.ac.kr

*Corresponding author. Tel.:+82 61 379 2779; fax.:+82 61 379 2782.

*Corresponding author. Tel.:+82 61 379 2775; Fax.:+82 61 379 2782

ABSTRACT

Intracellular redox status influences the oxidation and enzyme activity of the tumor suppressor phosphatase and tensin homolog on chromosome 10 (PTEN). Cumene hydroperoxide (CuHP), an organic hydroperoxide, is a known tumor promoter. However, molecular targets and action mechanism of CuHP in tumor promotion have not been well characterized. In this study, we investigated the effect of CuHP on the redox state of PTEN in HeLa cells. In addition, the intracellular reducing system of oxidized PTEN was analyzed by using a biochemical approach and the effect of CuHP on this reducing system was also analyzed. While PTEN oxidized by hydrogen peroxide is progressively converted to its

¹ These authors contributed equally to this work.

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