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Effects of intra- and extracellular factors on anti-aging *klotho* gene expression

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ABSTRACT. Inactivation of the *klotho* gene in mice causes serious systemic disorders, resembling human aging. However, at the molecular level, its action mechanisms are not well understood. The stimulatory or inhibitory effects of cis- and trans-regulatory factors on the *klotho* gene expression are also still unclear. We studied the effects of intra- and extracellular factors on human *klotho* gene expression. For this purpose, pHKP-Luc and pHKP-GFP reporter vectors were constructed with the 2.1-kbp upstream region of human *klotho*, covering its promoter region, using luciferase and GFP genes as the reporter. A series of vectors that have deletions in the upstream region of the *klotho* gene were constructed to assay cis-acting factors. Deletion of some parts of the *klotho* gene upstream region significantly affected reporter gene expression in HEK293 cells. p16 and p53 proteins inhibited reporter luciferase expression under the control of human *klotho* promoter in a dose-dependent manner. Calcium and phosphate ions stimulated *klotho* expression.

p21, PTH, IGF-1, and angiotensin-II had no significant effect on *klotho* expression in HEK293 cells.

Key words: *klotho* gene; Anti-aging; Apoptosis; PTH; IGF-1; Angiotensin-II

