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非類脂醇抗炎性藥物之訊息傳導探討 -II

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計畫主持人：周明勇

計畫參與人員：楊世煌

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Abstract

Background It is well known that heat shock proteins (HSPs) act as chaperones which can bind to several kinds of proteins to assist proteins maintain or recover their functional conformation, however, the underling mechanism remains controversial. The aim of this study is to investigate the role of HSP70 in heat-induced p53 signaling in OC2 cells, a human oral cancer cell line.

Materials and methods OC2 cells or cell lysates were incubated at different temperatures (37, 39, 41 and 43℃) for 3 hours. The Western blot was employed to quantify differences in master regulative molecule of cell cycle. Immunoprecipitation was used to detect the relationship among proteins. Patterns of changes in expression were scanned and analyzed using the NIH image 1.56 software. All the data were analyzed by ANOVA.

Results Heat shock induced the accumulation of p53, phosphorylation of p53 at serine 15 and increased the expression of its downstream target genes, p21 and Bax/Bcl-2. ERK 1/2 played a negative role in p53 regulation. HSP70 existed in monomeric form and oligomerized after heat shock. In the meanwhile, the expression of p53-MDM2 and HSP70-proteins complex such as p53, p21, Bax, MDM2 and phosphor-ERKs were all induced by heat shock.

Conclusion Activation of p53 signaling involved in apoptosis induced by heat shock. HSP70 acts as a chaperone regardless of the proteins denatured or not. We suggest that the role of HSP70 played in p53 signaling may assist the stablization of p53 to avoid heat shock-induced conformational changes.

Keywords oral cancer, hyperthermia, heat shock protein, tumor suppressor gene p53, apoptosis