

Original Article

Quercetin Enhances Tamoxifen-Induced Antitumor Activity Through Down-Regulation of Cyclin E2 Expression in Drug-Resistant Human Breast Cancer Cells

Shih-Hsin Tu^{1,2}, Kuo-Ching Yang³, Chi-Tang Ho⁴, Ching-Shui Huang^{1,2}, Ching-Shyang Chen⁵, Hui-Wen Chang⁶, Chien-Hsi Chang⁶, Chih-Hsiung Wu^{5,7,9*}, Yuan-Soon Ho^{6,8,9*}

¹Graduate Institute of Medical Sciences, Taipei Medical University, Taipei, Taiwan

²Department of Surgery, Cathay General Hospital, Taipei, Taiwan

³Department of Internal Medicine, Division of Gastroenterology, Shin Kong Wu Ho-Su Memory Hospital, Taipei, Taiwan

⁴Department of Food Science, Rutgers University, New Brunswick, NJ, USA

⁵Department of Surgery, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan

⁶Department of Laboratory Medicine, Taipei Medical University Hospital, Taipei, Taiwan

⁷Department of Surgery, Taipei Medical University-Shuang Ho Hospital, Taipei, Taiwan

⁸School of Medical Laboratory Science and Biotechnology, College of Medical Science and Technology, Taipei Medical University, Taipei, Taiwan

⁹Center of Excellence for Cancer Research, Taipei Medical University, Taipei, Taiwan

Abstract.

Quercetin is found in plant tissues known as flavonoids, and contains properties that act as a chemopreventive or chemosensitizer agent against human breast cancer. However, the oncogenic molecule inhibited by quercetin treatment has still not been identified in human breast cancer cells. The cyclin E2 (CCNE2) mRNA levels were demonstrated to be higher in tumor cells (3.55-fold, * $P = 0.005$) than in normal paired tissue samples, using real-time reverse-transcriptase polymerase chain reaction (RT-PCR) analysis ($n = 213$). We further demonstrated that relatively higher levels of CCNE2 protein expression were detected in the tamoxifen-resistant (TAM-R) MCF-7 cells. The results showed that CCNE2 protein expression levels were specifically inhibited in quercetin-treated (5 μM) TAM-R cells, either in the presence or absence of 4-OH-TAM (100 nM). Additionally, it was noted that combination treatment with 4-OH-TAM and quercetin significantly sensitized TAM-R cells to 4-OH-TAM. This study suggests that quercetin can be used as a chemosensitizer by targeting CCNE2 expression levels, which may be a novel strategy to overcome TAM resistance in breast cancer patients.

Keywords : quercetin, CCNE2, breast cancer, tamoxifen, cell cycle

原著論文

槲黃素透過細胞週期蛋白 Cyclin E2 的抑制作用增強對 Tamoxifen 抗藥性乳癌細胞之抗癌作用

杜世興^{1,2} 楊國卿³ 何其儻⁴ 黃清水^{1,2} 陳清祥⁵ 張慧文⁶ 張鑑熹⁶ 吳志雄^{5,7,9*} 何元順^{6,8,9*}