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Doxorubicin-induced drug resistant mechanism was inhibited by combination treatment of H12

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Doxorubicin (DOX), which is known as Adriamycin, is one of the most effective anticancer drugs and has been widely used in various chemotherapeutic regimens to treat patients with cancer. H12, aminothiazole derivative, is known as strong anti-proliferative effects chemical with nanomolar concentration range. The combination therapy is common approach to improve the cancer treatment. In this study, we confirmed the anti-cancer effect of combination drug and validated molecular mechanisms with DOX and H12. The cytotoxicity of each single drug and combination treatment were analyzed by MTT assay and the combination index (CI) value were calculated by Compusyn software for the evaluated combination effect in MDA-MB 231 breast cancer cells. Combination treatment group showed synergistic effect more than 40 times concentration compared to DOX single treatment (CI>1). After analysis of gene expression profiling analysis, we selected different expressed genes(DEGs) between single and combination treatment groups. 1,624 probes were significantly changed expression patterns in treatment groups. Especially, 347 probes were showed combination groups specific DEGs, which were composed of 142 up- and, 205 down-regulated. After gene ontology analysis, 347 DEGs were contained Inositol Pyrophophates Biosynthesis, 1D-myo-inositol Hexakisphophate Biosythesis V, Dermatan Sulfate Biosythesis, Notch Siganling, and Dermatan Sulfate Biosynthesis related pathway. The combination treatment of DOX and H12 showed synergistic anticancer activities toward MDA-MB 231 breast cancer cells.

Biography

Park has studied oncology and molecular biology for 10+ years, during which time he has authored several reports. He has worked on the Research Fellowship in the Chung-Ang University.

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