



Dr. Ting-Chao Chou

Memorial Sloan-Kettering Cancer Center, USA

Drug combination strategies in viral therapy using the Combination-Index Theorem

Drug combination has been widely used for the treatment of cancer and AIDS. However, there are about 20 different definitions for synergism but none supported the others (Chou TC, Pharmacol. Rev. 58: 621-681, 2006; free web link: <http://pharmrev.aspetjournals.org/cgi/reprint/58/3/621>). The confusion on synergy definition have inflicted serious tolls in efforts, time and resources in biomedical research. The combination index (CI) theorem based on the median-effect principle of the mass-action law has been widely used for computerized drug combination studies. One article by Chou TC and Talalay P (Adv. Enz. Regul. 22: 27-55, 1984) alone, has been cited 2,351 times in 479 journals (www.researcherid.com/rid/B-4111-2009). However, not all researchers fully understand its theoretical basis and its flexible applications. This author has published 49 articles on drug combinations against HIV, HSV and CMV using the CI method. This paper will illustrate the experimental design, computerized simulation for quantitatively determining synergism ($CI < 1$), additive effect ($CI = 1$) and antagonism ($CI > 1$) using the F_a -CI plot (Chou-Talalay plot) or the isobolograms. The dose-reduction index (DRI) signifies how many folds of dose-reduction for each drug at a given effect are allowed in synergistic combination. DRI projects the reduced toxicity toward the host. In addition, how to efficiently pick the proper combination cocktails for maximal synergy will be demonstrated with Chou's "polygonogram". Two clinical trials, AZT + 3TC (366 patients, using statistical calculations) and AZT + IFN α (36 patients, using the CI method) are compared. It is demonstrated that in AZT + 3TC trials with $p < 0.001$, did not prove synergy, whereas in AZT + IFN α proved synergy ($CI < 1$). It is concluded that the median-effect principle and the CI theorem are efficient, quantitative and econo-green approach for the biomedical research, including the drug combination strategies in viral therapy.

Biography

Ting-Chao Chou received Ph.D. in Pharmacology from Yale University and postdoctoral fellowship from Johns Hopkins University. He became Member at Memorial Sloan-Kettering Cancer Center (MSKCC) and Professor of Pharmacology at Cornell University in 1988. He is Honorary Professor at Chinese Academy of Medical Sciences (1993-) and Visiting Professor at five universities. He is Director of Preclinical Pharmacology Core Laboratory at MSKCC.

Dr. Chou published 250 articles which have been cited 12,530 times with H-index 54. He coined the scientific terms: Combination Index (CI), Dose-Reduction Index (DRI), Normalized Isobologram, and Polygonogram. He is co-inventor of 30 U.S. Patents, some invented compounds are in clinical trials in cancer patients in the United States.