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General dynamic theory quantitates "synergism" of two drugs in animals or in clinical trials with only ten data points by computer simulation

The Combination Index (CI) theorem¹ with its CombuSyn software², based on the Median-Effect Equation (MEE) of the mass-action law (MAL), has been cited by 5,336 papers in 1,086 biomedical journals, where CI=1, <1, and >1 indicates additive, synergism, and antagonism, respectively3. Despite of worldwide popularity of the CI methods, >98% of the combo studies were carried out *in vitro*. Most *in vivo* combo studies in animals, especially in clinical trials, are with experimental design or protocol design improperly done that are impossible to determine synergism of antagonism4. For any drug combination studies, multiple doses of each are absolutely required in order to obtain the median potency (Dm) and shape/dynamic (*m*) of the MEE-parameters for the CI calculation. Based of MAL, all dose and effect curves can be linearized by the ME-Plot, so the theoretical minimum requires only two data points for computer to generated dose-effect curve, with the 3rd point being dose zero and the 4th point being the median-dose point (Dm) which is the universal reference-point for single and multiple entities and the common-link for the 1st –order and high-order dynamics5. In this Keynote Presentation, (I) Two anti-Cancer agents, Taxotere + T-67 synergy against colon carcinoma xenograft using a total of 70 nude mice (with only 10 data points) using diagonal design and CI method will be illustrated with computer simulation; and (II) Two anti-HIV clinical trials are compares: (a) AZT+3-TC, using 366 patients, but AZT had used only one dose which made it impossible to determine synergy. By contrast, (b) AZT+IFN used only 36 patients, 3 doses design with CI method/simulation which econo-greenly quantitated synergism.

Biography

Ting-Chao Chou born in Taiwan, received Ph.D. in Pharmacology from Yale University and Post-Doctoral Fellowship from Johns Hopkins University School of Medicine. He joined Memorial Sloan-Kettering Cancer Center (MSKCC) and became a member, and Professor of Pharmacology at Cornell University Graduate School of Medical Sciences in 1988. He is Honorary Professor of Chinese Academy of Medical Sciences. He retired from MSKCC in June 2013. Dr. Chou published 403 papers with 27,138 citations (Google Scholar) with h-index of 69. He introduced The Median-Effect Theory of the Mass-Action Law (1976) and co-developed The Combination Index Theorem, CalcuSyn and CompuSyn software. His theoretical paper introducing the CI method and software (Chou TC & Talalay P. Adv. Enzyme Regul. 22:27-55, 1984) for quantitative determination of synergism (CI<1), additive effect (CI=1) and antagonism (CI>1) has been cited 5,336 times in over 1,086 bio-medical journals. Dr. Chou is inventor/co-inventor of 40 US Patents. He is the Founder & President of PD Science, LLC (USA).

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