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Mathematical models of RNA expression profiles: Potential applications to drug discovery research and personalized medicine

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uring the past five years, we have identified two mathematical equations that quantitatively fit the genome-wide RNA level data measured from (i) budding yeast undergoing nutritional stressand (ii) the breast cancer tissues of 20 patients before and after treating with anticancer drug, doxorubicin. The Poisson distribution formula was found to fit the probability of observing either the beneficial or the harmful RNA expression patterns exhibited by 988 genes in a given number of breast cancer patients, from which a quantitative measure of the efficacy of doxorubicin, referred to as the "micro-therapeutic index (mTI)", could be calculated, i.e., mTI= 2.5. The beneficial RNA expression patterns are defined as those tumor-induced RNA level changes that are reversed by doxorubicin. Conversely, if the tumor-induced RNA level changes are enhanced or augmented, we have harmful RNA expression patterns. The same RNA level data set was found to fit another mathematical equation called BRE (blackbody radiation-like equation) that was derived from the blackbody radiation formula discovered by M. Planck in 1900 which introduced the concept of energy quantization of electrons inside the atom, suggesting that the energy levels of RNA inside the living cell may be similarly quantized. BRE is a generalized form of the Planck radiation formula, generated by replacing the Universal constants and temperature with a and b and rescaling the x- and y-axis with A and B: y =(a/(Ax + B)5)/(e(b/(Ax + B))-1), where y=the probability of observing RNA levels within a given range, x=the ranges of RNA levels. Using the Solver program in Excel, we were able to determine the numerical values of the four parameters that best fit BRE to the RNA level data. These parameter values were found to different between the RNA level data measured before (BE) and after (AF) the drug treatment: a= 1.65x1013 BE and 6.7x1012 AF; b = 40.31 BE and 34.2 AF; A=4.199 BE and 3.34 AF; and B=0.259 BE and 0.444 AF. This finding, if confirmed by further research, would support the notion that BRE can be used as a quantitative method to characterize the effects of drugs (as well as toxicants) on genome-wide RNA metabolism in both normal and diseased cells, thus providing a novel strategy for drug discovery.

Biography

Sungchul Ji received a PhD degree in Physical Organic Chemistry in 1970 from the State University of New York at Albany and carried out Postdoctoral researches in enzymology, biophysics, systems physiology, and toxicology at the University of Wisconsin (Madison), University of Pennsylvania School of Medicine, Max Planck Institute of Systems Physiology at Dortmund (Germany), and the University of North Carolina School of Medicine, before joining Rutgers University School of Pharmacy in 1982 as an Associate Professor. His decades-long research has resulted in a book entitled Molecular Theory of the Living Cell: Concepts, Molecular Mechanisms, and Biomedical Applications, published in 2012.

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