Anticancer Drug Combinations, Studies for All Possibilities

Lu DY1*, Chen EH2, Lu TR3, Wu HY3 and Ding J2

1School of Life Sciences, Shanghai University, Shanghai 200444, PR China
2Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, PR China
3College of Science, Shanghai University, Shanghai 200444, PR China.

Abstract
Most cancer therapies are seldom effective by using single anticancer drug therapeutics based on multiple tumor genetic alterations and molecular abnormalities. Drug combinations are commonly practiced in clinics. Yet, anticancer drug combination utilities need to transform from empirical to science-guided enterprises. This editorial offers the background knowledge of drug combination therapies by mathematical enquiry.

Keywords: Drug combination; Mathematics; Cytotoxic anticancer drugs; Cancer stem cell; Personalized cancer therapy

Introduction
Cancer is a common disease that claims life about 7-10 million people annually in the world. As a result, cancer remains to be a great medical challenge worldwide [1,2]. Many efforts can impact on overall therapeutic outcomes in cancer patient treatments, especially in late-staged ones. One of these efforts is anticancer drug combinations. Long before, it was widely accepted that anticancer drug cocktail instead single drugs usually improved the therapeutic efficacies greatly [3-10]. Despite its great popularity and as a modern cliché, how to prescribe the single drugs usually improved the therapeutic efficacies greatly [3-10].

Since 178 anticancer drugs have been licensed worldwide [12], mathematically, huge numbers of drug combinations can be used. According to mathematical equation (calculation for 3 anticancer drug combinations):

\[ C= \frac{(178 \times 177 \times 176)}{(1 \times 2 \times 3)} = 924176 \]

It means there are 924176 possibilities must be studied in clinical situations. At present, we cannot compare all these combinational possibilities easily in lab and in clinics. Yet we can imagine that these different types of therapeutic efficacy comparison data will be finished according to the rapid progresses of automatic or computerized experimental investigations within 10 years. These types of experimental drug combination evaluations should be encouraged.

Two strategies can be speculated to solve this problem.

1. Assessments of drug combinational possibilities with equal attentions. This strategy is labor-intensity and needs a long period of time for large-scale experimenting and complex data analysis/statistics.

2. Discover good anticancer drug combinations and relationships step by step. For example, we may identify and verify drug combinational possibilities by using one in each drug category first. Then, gradually enlarge anticancer drug numbers and mechanisms of action on this field of anticancer drug combinational studies. Like anthrocycline, camptothecine and other series of anticancer drugs can be screened by one anticancer drug in each drug categories.

We suggest that these anticancer drug combinational studies must be focused on in vitro anti-proliferative studies for limiting on 1-3 tumors cell lines first. Higher levels of anticancer drug combinational paradigms can be assessed based on in vitro anticancer drug activity evaluations. If this is the case, we can achieve gradually and cost less.

Method
Different modular of anticancer drug combination strategies
Since no central dogma of anticancer drug combinations suitable for all cancer patients has been found, some propositions should be made first.

Previously, combination utilizations of cytotoxic anticancer chemicals with biotherapy or other therapeutic means are good strategies for cancer treatments [8-11]. Many similar examples are given later and will be discussed one by one. Several modular of anticancer drug combination systems are temporarily classified [10].

Mathematics of anticancer drug combinations
Since 178 anticancer drugs have been licensed worldwide [12], mathematically, huge numbers of drug combinations can be used.

To perfect anticancer drug combination study, many new ideas and techniques must be invented. For example, excellent automation techniques are the top priority. Growing joint-venture activities and projects might finally help to overcome cancer mortalities in future.

Mathematician and physical-majored talents
Owing to the huge numbers of drug sensitive or anti-proliferative activity testing data, mathematic or statistics analysis for these large data ought to be equally participated by mathematicians or physics-
majored students or scholars [13]. These types of research personnel may play unique roles on this field of anticancer drug combinational evaluation studies.

**Future Directions**

In future, we must pay more attentions on the breakthroughs of drug combinational rule discoveries and systemized and/or study each possibility of drug combinations in experimental or clinical studies. Only by these discoveries and systemizations, therapeutic efficacies for cancer treatments can be well improved. Since there is no central dogma available for clinical anticancer drug combinations of repeatable experimental protocols and hospital routines, we hope this article can serve as a bridge to embrace better therapeutic options.

**Conclusion**

Only after completions of all possible assessments of anticancer drug combinations, we can satisfy and enjoy the fruits and improvements of scientific developments and clinical therapeutic outcomes. This is an economic burden yet enormous feedback task. If we can implement it, many beneficial achievements may be expected. Let us kick off this project.

**References**