Chapter 7
Systems Biology Methodologies for the Understanding of Common Oncogenetic Mechanisms in Childhood Leukemic and Rhabdomyosarcoma Cells

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ABSTRACT

Human neoplasias are considered lethal in the majority of cases. Cancer does not discriminate between age, gender, or race. Besides the detrimental health effect caused by the disease, it also has a great impact on the quality of life of those affected by it. One of the main characteristics of cancer is that it deprives the patient from their human dignity, at least compared to other diseases. For example, more people die every year from coronary disease than from cancer, but the latter is considered more severe due to the slow, painful, and deteriorating effect it has on the human body. However, in the case of childhood hematologic neoplasias, progress in the field of treatment has taken immense steps forward, and five-year survival reaches 80%. At the same time, several new therapeutic agents, such as glucose analogs or telomerase inhibitors, are currently being tested in clinical trials, and several others, such as kinase or proteasome inhibitors, are already in the market. Yet the most effective therapies are the ones performed with classical chemotherapeutics, which are non-specific and more aggressive.

DOI: 10.4018/978-1-61350-120-7.ch007

One of the main concerns of modern life is the level and quality of health services, and at the same time, there is a great debate on the nature of health services provision, i.e. public or private. One of the main burdens of health services is drug administration. Especially in the case of cancer treatment, drug administration is extremely expensive, both for the patient and the health provider. If we think in terms of the Western world, then this is really a matter of finance, and the majority of the population can afford, either by private or state health insurance, the cost of a cancer treatment. However, if we see things in terms of developing countries or under-developed countries, where finances and health insurance are limited, then cancer treatment can not even be considered as an option for the majority of the population. The etiology for the high cost of cancer treatments comes from the process of drug development, as the latter takes almost 10 years of research and about 800 million dollars for a drug to reach the market. Most of the efforts in drug discovery are based mainly on the method of trial and error. This, in turn, is mainly due to the lack knowledge on the mechanisms underlying the disease.

Therefore, let us imagine a best case scenario where oncogenesis is understood, at least in part, and drug design, effectiveness, and side effects could be resolved by simply modeling the system. This would dramatically reduce drug costs, with positive consequences not only for treatment, but also on the social level. Drugs would become much more affordable, hence curing and improving the lives of more people. This hypothetical, best-case scenario should point scientists to move towards the direction of attempting to make scientific endeavors for the social benefit. Systems biology is a discipline that does indeed move towards that direction. Of course, as most things in life, the use of systems biology could be used in a dual manner, that is, for social benefit or profit.

INTRODUCTION

The Definition and Necessity of Systems Biology in Biological Phenomena

Systems biology can be considered a relatively young discipline. It was in the advent of the 21st century that the first coordinated attempts became reality. However, the term had been previously mentioned both as a necessity and as a discipline. We couldn't phrase it in better words than *Mihajlo Mesarović* in 1968:

…in spite of the considerable interest and efforts, the application of systems theory in biology has not quite lived up to expectations…one of the main reasons for the existing lag is that systems theory has not been directly concerned with some of the problems of vital importance in biology… The real advance in the application of systems theory to biology will come about only when the biologists start asking questions which are based on the system-theoretic concepts rather than using these concepts to represent in still another way the phenomena which are already explained in terms of biophysical or biochemical principles. …then we will not have the application of engineering principles to biological problems but rather a field of systems biology with its own identity and in its own right… (Mesarovic, 1968) (adopted from the book Systems Biology-Dynamic Pathway Modeling by Olaf Wolkenhauer (Wolkenhauer, 2010)).

But in order to further define the field of systems biology we should refer to an older reference from *Henri Poincaré*:

…life is a relationship among molecules and not a property of any molecule…Science is built up of facts, as a house is with stones. But a collection of facts is no more a science than a heap of stones is a house… (Wolkenhauer, 2010).