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Editorial

Tumor evolution: The road map to future cancer therapeutics

Kambiz Afrasiabi, M.D.[1,*]

[1]Associate Project Scientist, Brain Tumor Research Lab, University of California, Irvine, CA 92617, USA

*Author for correspondence:
Email: kambiz@hs.uci.edu

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Abstract

The last eighty or so years of history of cancer therapeutics has witnessed the development of more sophisticated agents, aiming at destruction of cancer cells. We are armed with a diverse group of chemo, immuno, and targeted therapeutic agents, as well as tumor vaccines, CAR-T, and BiTE [1].

The common denominator among all is ignoring the most fundamental pillar on which the forward move of tumor mass is based, namely tumor evolution along the thermodynamics arrow of time. Tumor evolution in certain ways is akin to evolution of life on this planet, which has acquired higher levels of sophistication and diversity. Neoplastic transformation and its evolutionary path could be divided into three main phases: initiation, promotion, and progression. Our future cancer therapeutics is expected to intercept with this evolutionary path. This necessitates a deep understanding of the dynamics of this path, and the necessary means including AI, and Nano–delivery to execute this task [2].

Main Text

Deep understanding of normal evolution of living organisms is a prerequisite to understanding of aberrancies that arise in it. As such, neoplastic transformation is the prototype example of such an aberrancy. Initiation of normal mitosis following fertilization is an attempt at minimizing cellular network entropy and materialization of paternal genomic imprinting. This guides embryogenesis and formation of normal state. Neoplastic transformation in essence is a move in the opposite direction i.e.: Paternalization of maternal genomic imprinting, and significant increase in cellular network entropy, over a short period of time [3].

There is a massive amount of built-in genetic and molecular machinery to counteract this path, and secure forward move. This task is achieved through sensors and executors that we can see at every corner of cellular and sub-cellular compartment [4].

This ranges from P53 and BCL2 Family all the way to Telomeres. Consequently, it is not surprising that it would take between twenty and thirty years for the first malignant cell in solid tumors to come into existence. Promotion and progression phases of neoplastic transformation take much less time. That amount of time is spent in securing significantly higher amount of cancer cell network entropy of future generations, and massive increase in cancer cell diversity inside the tumor mass, the so-called intra-tumor heterogeneity. Chromosomal instability is secured through progressive increase in cancer cell network entropy [5].

Tumor mass also generates innumerable intra-tumoral cross talk and plasticity as well as interchangeability mechanisms to achieve its survival and forward evolutionary move. Additionally, tumor mass employs microenvironment to achieve this goal. This could be seen very well in the case of aggressive solid tumors. As one example, Glioblastoma multiforme has evolved into TMC (Tumor mass cell) and its sub compartments, as well as STIC (Stem cell like initiating cancer cells) Zones. The latter at the rim, and the first one, inside the tumor mass. Single cell sequencing technology has led to the birth of spatial genomics [6].

The hope is that single cell master regulator complex network entropy calculations, would lead to the birth of spatial entropyomics. Above technologies would bring the evolutionary path of different malignancies to light in a customized fashion. From this point on, our focus would be on the design of mechanisms to intercept with the forward move of tumor mass. Along this line, Nano machines, Nano delivery, and artificial intelligence could be put to work to achieve this goal [7].

It is expected that Nano-machines would deliver the missing micro-RNA or execute gene editing through CRISPR Technology [8] and modify epigenome of the driver zone. Artificial intelligence is expected to identify multiple generations of driver zone, along the thermodynamics arrow of time, ranging from past to present and future. This data would be used by Nano-Technology and delivery team for appropriate design of tumor evolution forward move interception mechanisms. This kind of achievement would lead to significant prolongation of a patient's life, and even if cure would not be feasible, cancer could potentially become one of the many chronic diseases.

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