Acta Scientific Pharmaceutical Sciences (ISSN: 2581-5423)

Volume 4 Issue 9 September 2020

Opinion

# Cancer Energy Metabolism

**Daniel Gandia***

*IQVIA and Department of Cancer Medicine, Buenos Aires, Argentina*

***Corresponding Author:** Daniel Gandia, IQVIA and Department of Cancer Medicine, Buenos Aires, Argentina.

**Received:** July 27, 2020

**Published:** August 19, 2020



Cancer is a disease with dominant genetic traits that continuously evolves during the whole tumor lifecycle. This evolution is present at the different biological organization levels meaning molecular-cell and tissue-related ones.

The process comports one of the highest medical challenges and disease complexities, metastases, that if not correctly treated, the patient presents a clinical deterioration that can lead to a clinical starvation condition.

Nowadays, we are really in good shape with all the treatments present in the clinical setting, rendering with the combination of them, satisfactory cancer-cure rates and long-term survivals in our patients.

Pharmacologically speaking, we can target many cell areas, going from the "old DNA-related one" with Chemotherapy, to the nearly recent known cytosolic molecular pathways with protein mutations, that comport directed-therapies with novel molecular entities. These new drugs also and not only Chemo, have off - target toxicities, for the cellular pathways "touched" are common on tumoral and in normal cells (for e.g. protein kinases).

At a glance it seems that to "treat the altered protein function" is easier than to block the cancer mutated genes that origin them. But no, we can do both things for we have more gene drivers than transcription protein factors. These last ones are a few selected ones so difficult to target that they have become a high priority of research interest. Currently new compounds that act directly on them are on early clinical development phases.

The driver genes, KRAS for e.g., have also a new duty, that is the control of the expression and regulation of the neoplastic cell respiratory system. This is metabolism and one of the Cancer hallmarks as Weinberg named it. It has transcriptional-translational regulations necessarily involved.

We remember that at our University days, to have listened in biochemistry about Warburg and Crabtree effects in Cancer cells. They really were the eye-openers in the development of tumor metabolism as another tumor's vulnerability cell site. Warburg effect refers to aerobic glycolysis, "the old cell fermentation pathway" as a more suitable spot of energy for the cell, even in the presence of aerobic cellular oxygen conditions. And the second one, the Crabtree effect, works by repressing respiratory flux by the glycolytic cytoplasmatic pathway (it seems that some enzymes of it, compete with the mitochondria for the free cytosolic ADP in order to build ATP).

Related to the before-mentioned, the Cancer cell loves fast cytosolic glycolysis even when much less of ATP moles are achieved as compared to the aerobic mitochondrial respiration. This is related to the cell's growth and doubling volume for the programmed next cell division, needing so, an easy and fast delivery of energy for this process. This physiologically occurs in embryonic cells, where rapid cell division for e.g. after gastrulation are needed in order to begin posteriorly with cell differentiation and tissue-organ construction.

So, two "phenotypic respiratory Cancer cell populations" are commonly present in a tumor, the first the glycolytic aerobic one and the other, which is related to mitochondria respiration. This adds to Cancer an enormous inner complexity: the tumor comports the driver genes and transcription factors, both also controlling the 2-cell energy-respiratory systems, impacting this, on cell differentiation and tumor heterogeneity.

We can imagine that we need a clock on the cell to know when metabolism regulation is addict to new drugs. At the mitochondria, the experiments of blocking the respiratory chain with some drugs, resulted in a poised cell and death. We can´t be so specific for the cancer cells with that type of inhibitory metabolic therapy. We have a lot of work to do for this Cancer hallmark as Robert Weinberg named it.

The task to how reprogrammed tumor cell metabolism is a research must, with important physiological implications: to be selective and specific with drugs that target "the Cancer glycolysis and the tumoral mitochondria" seems dangerous and unreal at present. They aren´t undruggable targets, but yes fragile ones, when chemically touched.

In the eighties, Lonidamine, a drug that works at the mitochondria, making it change from the creased to a condensed state, was introduced in the clinical arena, but it wasn´t at all a game-changer drug.

The upstream regulation of metabolism at the gene drivers and transcription factors levels that control metabolism, is an easier arena for research and development.

Like this, the inhibitors of the modulators of the transcription factor gene expression and protein-protein interactions inhibitors, are a reality in early Phase 1 Trials.

The forthcoming years will tell us the positive clinical results with this kind of drugs or show us that the regulation metabolism pathway is still an elusive cancer druggable target.