Updated Understanding of Cancer

Subjects: Biochemistry & Molecular Biology | Physiology | Immunology

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Cancer is a tumorigenesis process that forms a mass of cells that we call a tumor. During tumorigenesis, the cells that compose the tumor can be benign or malignant. When the cells in the tumor are normal but old, the tumor is termed benign. When the cells in the tumor are abnormal and can grow uncontrollably, the tumor is malignant. Sometimes a benign tumor can transform into a malign one if the normal old cells begin to develop abnormalities, such as DNA mutations, and grow rapidly. - by Cristian Muresanu

DNA damage | cancer | DNA mutations | telomere | genetic | immune checkpoint therapy | fasting | mitochondrial metabolic reprogramming

1. Short Presentation,

During my search for understanding cancer, I observed several problems that have not been clearly explained. The first one is that cancer never evolves from normal healthy cells, with the exceptions mentioned in the paper.

When dealing with the majority of cancers, which are very slowly progressing, the normal cells start to undergo the so called cell damages, such as minor DNA lesions, a minor reduction of ATP production in the mitochondria and other minor damages. In a healthy individual, these kind of damages are very often produced and instantly corrected with the body’s natural cell damages corrections mechanism, and this the the first line the defence.

However, when environmental factors are becoming more disruptive, then, too many cells in the body, (or in a certain organ or tissue), are undergoing a lot of cell damages, and they accumulate with the passage of time, and then they became irreparable. From minor changes, the cells are experiencing complex changes, on multiple levels, such as telomeres shorten, major reduction of ATP production (without mtDNA mutations), and the cell enters the senescent stage. If the cell is having a very slow replicating rate, that might have an advantage, compare to fast replicating cells, because more errors are accumulating at each replication. The first outcome of these kind of problems is inflammation which trigger oxidative stress.

Obviously, our body start to use the second line of defence, which is the apoptosis. However, even if the ability of DNA repair enzymes to trigger apoptosis was known to prevent cancer, other cells may become apoptosis-resistant and survive. The reduction of the DNA repair mechanism is known as DNA repair-deficiency disorder — a medical condition that can lead to accelerated age related diseases, or an increased risk of cancer.

But in order to attain that goal of a long term survival, the cancer cells are creating special conditions, and this is very bad because of the fact that cancer cells need a lot of ATP (for maintaining a high rate of cancer metabolism). Therefore, the mitochondrial reactive oxygen species (ROS) are known to trigger hypoxia-induced transcription factors which promote extracellular ATP production, followed up shortly by ATP internalization inside the cancer cells. So, it doesn't matter anymore that the internal ATP is no longer produced, because they now have even larger amount of ATP from the outside. Normal cells cannot do that.

At this stage, the mitochondria is already having mtDNA mutations. The patient is always starting to go for treatment when he got scared enough, and at that moment in time, his cancer is already in stage 2 cancer promotion, or even stage 3.

There is not enough evidence to tell you if the complex personalized treatment plan, (proposed in this review article), might have a significant effect on a stage 3 cancer progression, therefore I mentioned, that it is best to be used, during stage 2 cancer promotion, which already include all of the complex problems presented on Figure 1.

Why using all proposed therapies in conjuction with each other ? Because, if you look at the abstract figure, there are several processes taken place in the body simultaneously. That means, some of the affected cells are only having DNA damage and telomere shortening and reduced ATP production, but other cells are having DNA mutations and much longer telomeres, and major extracellular ATP production followed by immediate ATP internalisation.

If we only address a therapy which act upon one single problem, for example inhibiting aberrant telomerase activity in the cancer cells, this may affect the senescent cells which could be also targeted and they die, although senescent cells are still capable to function but at a lower capacity and performances.

If we only address a therapy which act upon directly the mitochondria, to stop ATP internalisation, then the mitochondria itself may become capable to start ATP production again, but still, cancer cell may survive and continue to multiply, maybe at a lower speed, because cancer cells still have longer telomeres.

There are two major promising therapies which are currently under development and they are: the immune checkpoint therapy which can be used for precise targeted damaged cells which have DNA damages and the other one is called mitochondrial metabolic reprogramming which may restore the ATP production, therefore stopping the release of hipoxia-induced transcription.

But if the tumor is pressing vital organs, even if it is only a small one, then the classical known therapies, such as surgery, radio-, chemo- must be addressed, but only at the level which makes the other two therapies successful, for example, instead of using, let’s say, 7 chemo sessions, we may use only one, (and surgery, if necessary), and then continue with the immune checkpoint therapy and mitochondrial metabolic reprogramming. And there are also other problems.

2. Thinking about the future

If any of the treatments are too agressively applied to a certain type of cancer, it is possible that the cancer cells themselves may become chemoresistant and after few sessions they adapt to chemo. Another bad news is that in specific environmental conditions, senescent cells may transmit false signals to healthy cells in order to become senescent [1].

This is similar “crying out loud help!, help!” in a biochemical way, and the other healthy cells are starting to “use” these signals in order to “help” their “sisters”, but this is only an irrational response to some environmental factors.

Even so, due to the complexity of cancer and its ability to avoid all natural defence systems, including the third line of defence known as phagocytosis of the cancer cells by the immune white blood cells, if none of them are functionable, then all we can do for the patient is to give him enough time in order to change whatever is possible in his lifestyle, emotional stress, diet, apply many sessions of psychotherapy, fasting before and after medical treatments, and during this longer period of time, his immune system may become capable to identify the cancer cells and phagocytise them all. The phagocytosis checkpoints could be the new targets for cancer, but more research is needed.

However, there is no miracle cure for cancer, and if the patient is not participating with great interest and sincerity at these therapies, then the results might not be good enough. But will all these offering him much longer time than any of them applied only as single ? We believe so, yes, and it would be logic to make this assumption, because it could be in the benefit of the patient, because even if the progression of cancer stopped at a certain stage but does not progress more than that, the patient may survive many years, maybe without relapse, if he sticked to the dietary guidelines, psychotherapy sessions and lower the emotional stress. But that means the patients need to be educated in this regard.

What's next ? that remained to be verified especially if these protocols might be applied (in the near future or not too distant future) at affordable costs for the average people (cancer’s patients).

References

1. M. DeMaria; Cellular Senescence and Tumor Promotion. *Geriatric Oncology* **2017**, *1*, 55-69, 10.1007/978-3-319-44870-1_79-1.