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Short Communication

Tackle an Oncogene without Forgetting to Activate a Tumor Suppressor One

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Opinion

Cancer cells have many ways to evade homeostatic body mechanisms.

Some of these are essentials for the "milieu interior" of Claude Bernard, for rheologic pathways are severely altered in tumors: coagulation serving for, and platelets helping in the metastatic cascade, and disseminated intravascular coagulation as a paraneoplastic phenomenon. So here we have examples of the opposite "rule" of Claude Bernard: there is no homeostasis of the hemostasis.

The first step for Cancer is to "evade" the interstitial tissue pressure within the primary tumor. Second, the shedding of Cancer cells from it, third, the intravasation, fourth the circulation of tumors cells in the bloodstream, fifth the extravasation into the interstitial connective tissue, today called tumor microenvironment and sixth the metastases forming and growth in the "correct organ -tissue- soil".

If we leave the before-mentioned physiopathology processes and get into the tissue-cells itself, more organizational complexity is observed here. Primary tumor Cancer cells are continuously cell cycling, so dividing, comporting different genotypic and phenotypic cell populations with different cell kinetics dynamics and different fates.

Accordingly, to recent data, it seems that the subcellular molecular process is not a random one, but a programmed one. As previously was thought that DNA-Cancer-sick lesions weren't uniform, were random, no, nowadays it seems they are really organized and structured!

Damaged DNA - introns and exons "know" where to go and get a place in order to perform the "best oncoprotein". In immune oncology, do the "best neoantigen", leading to the more mutations, the more neoantigens, the more tumor mutational burden and finally and happily due to this last, the best possibility of immune tumor response.

DNA-repair mechanisms are an essential in biologic-Cancer-prevention-tumors-forming, and perhaps more important that the activation of oncogenes. We study a tumor biopsy carefully, examined both, and for e.g., both are mutated, P53, the mother of

DNA-repair with tumor suppressor activities and an oncogene such as KRAS is amplified and mutated.

At this time-picture, both are present, both are maintaining the cancer disease process evolution and destiny, but in this ying-yang who was first mistaken? Are we authorized to say that one is more important than the other?

Evolutionary speaking, KRAS is one, or the one more ancient oncogene [1]. It was named until recently "the undruggable target". Recently, awesome advances have been produced with this oncogene at the Cancer Medicine level.

A peculiar chemical pocket (G12C) was discovered which is plausible of blockade by novel small molecules such as Sotorasib and Adagrasib, leading they use nowadays in the clinical setting to excellent results in NSCLC(Non-Small-Cell-Lung-Cancer) and colorectal cancers. They are really "game changers drugs".

P53 (TP53), a tumor suppressor gene with more than 800 million years in evolution, is the first well-known one. Its "scans" damaged DNA and tell the cells to undergo apoptosis in order to avoid the formation of mutant-Cancer cells, or they repair DNA damaged regions and put them proper for the normal "genetic messages".

The issue with a tumor suppressor gene, is that Cancer forming -related is due to a lack of it, an abnormal expression or a mutant analog that can´t suppress correctly the damages.

To correct something that is mainly missing is not an easy task. Anyway, many advances are currently ongoing with novel-P53-targeted compounds, undergoing Phase 1 and 2 Clinical Trials [2,3].

Who we choose as more important mechanism of tumor formation and maintenance? we think both.

Even when we are happier tackling oncogenes such as KRAS or its derivate kinase pathways (NRAS, MEK), the future restoration of the abnormal DNA-repair processes will highlight P53 activities and perhaps become as so essential as oncogenes-tackling, in the whole biologic Cancer process.

Why, because if we think that millions of years ago, the DNA-damaging agents were not many or less than today, activations of oncogenes were surely lesser also. Oncogenes were occupied in other cellular activities. Tumor suppressor repairing duties were so probably also some "quite lazy" or with minimal, if activity at that time.

But, consider both were working: dinosaurs have had Cancers as far is known and found (bone tumor ones for e.g.).

Nowadays, tumor suppressor activities such as those that comport P53, is waiting a "father Christmas Drug" to finally arrive. This will make P53 scans proper ones and leave DNA normal activities and not to "think" on tumor re-constructing activities [3].

While the before-mentioned happens, KRAS and its "kinase friends" will continuously being tackled with novel drugs, not only to block the process, but also to overcome tumor resistance that is the still "big foe" in Cancer treatment [4].

Conflicts of Interest

The authors declared that they have no conflicts of interest.

Bibliography

1. Punekar SR., *et al*. "The current state of the art and future trends in RAS-targeted cancer therapies". *Nature Reviews Clinical Oncology* 19 (2022): 637-655.

2. Einsenstein M. "Restoring the guardian of the genome". *Nature Outline* 603 (2022).

3. Hassin O., *et al*. "Drugging p53 in cancer: one protein, many targets". *Nature Reviews Drug Discovery*; October 10, (2022).

4. Longo D., *et al*. "Targeting Oncogenic RAS protein". *The New England Journal of Medicine* 387 (2022): 184-186.