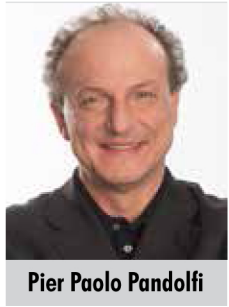


We learned how to unleash our immune system against cancer



By Pier Paolo Pandolfi

Our immune system is extremely efficient at clearing our body from any unwanted intrusions, from foreign entities such as bacteria, viruses, and parasites. Our bodies have learned, throughout evolution, how to efficiently combat foreign attacks of all sorts,

including attacks from new emerging viruses such as more recently COVID-19. We are equipped with a very sophisticated army of cells that can recognize a foreign entity and destroy it efficiently.

Our lymphocytes, the main component of our 'army', can recognize parts of a virus or microorganism as foreign and produce so-called antibodies that stick to and inactivate the target. An antibody can do the job on its own like a very precise missile that inactivates the target, the so-called neutralizing antibodies, or evoke the function of other cells that literally eat and destroy a target when tagged as foreign by an antibody. Other immune cells in our blood such as macrophages and neutrophils can recognize a foreign cell or a microorganism as foreign and eat and digest them even in the absence of neutralizing antibodies. Not only do these clear our body from infections, but they also do remember the aggressor so that at the next attack the defense is swifter and more efficient, which is at the core of vaccinations against flu, Covid, and other microorganisms.

This sophisticated system of defense has evolved and been perfected throughout our ancestral evolution. While there is little doubt that our immune system can recognize foreign intruders, for decades it was not clear whether our immune system was able to see cancer cells as foreign. This became even more puzzling when we discovered that cancer cells are often harboring mutations in their genes and molecular defects that should be recognized as "foreign."

The common mantra for decades was that if the cancer had grown in our body, the immune system had already failed. But why? Why are cancer cells not recognized by our immune system? Or why if they in fact were recognized, did they manage to overcome or evade the attack from the immune system?

Well, it took the work of many brilliant immunologists to realize that our immune system has several "brakes" built in. You need to have breaks because when the infection is eventually defeated you need to stop the attack, or you would waste the army in useless battles. An immune system that doesn't stop could even end up attacking your own organs: what we refer to as "autoimmunity."

By discovering the mechanisms that tell an immune cell to stop the fight, it became clear that cancer cells are very good and convincing at signaling 'peace' to the lymphocytes. So, when the immune system prepares for the battle against cancer cells, cancer cells send signals of non-aggression: "do not kill me" or "do not eat me." These cancer signals are very effective at putting the immune army at rest. Once these signals were understood, drugs could be developed to neutralize these breaks and reactivate the immune army against cancer.

One class of such drugs currently in the clinic is referred to as "checkpoint inhibitors," the "inhibitors of the brake." And the beauty of these drugs is that when they neutralize the cancer cells' "do not kill me" signals, the immunological army is unleashed and

the effects against cancer cells are massive and often curative.

There is still a great deal to learn on how to activate the cells against cancer that so efficiently keep us safe from microorganisms. We can by now harness the power of lymphocytes, but also of macrophages and neutrophils. They too are very potent in eradicating cancer if properly trained. We can genetically engineer cells to kill specific cancer cells, the so-called CAR-T cells of SUPERCAR-T cells. And we can even make vaccines to prevent cancer development.

All the technology and the new chemistry behind the mRNA vaccines that were rapidly developed against COVID, were originally developed to optimize the production of cancer vaccines. The explosive mRNA knowledge derived from COVID vaccines will undoubtedly offer in the years to come a panoply of new approaches for cancer prevention and therapy. The future of cancer research is truly exciting and will have a tremendously favorable impact on us all.

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