Let’s fix the cancer brakes

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Cancer therapy is based on surgery, irradiation, chemotherapy and immunotherapy. These methods are eventually pushing the inbuilt existing mechanisms to start the work that prevent/cure us of the diseases. There are two known anti-cancer mechanisms: apoptosis inside the cell and immune system outside of it. In cancer both of them are damaged due to mutations. So, the rational way to treat cancer is to fix the existing cancer brakes that perfectly work in majority of us during lifetime.

Irradiation and chemotherapy can damage DNA. During DNA replication/cell division apoptosis system erase the cells with unrepairable mutations. Billions of cells go into apoptosis every day in our body. Cancer cells accumulate mutations in apoptosis pathways and by this way avoid execution. Elephants who have apoptosis system in working conditions due to numerous p53 “guardian of the genome” copies have less cancer frequency than humans with >50% cancers having non-functional p53 [1]. So, to beat cancer we need to restore apoptosis system inside cancer cells. One of the ways to do this is cancer cells-targeted delivery of apoptosis inducer that acts “downstream” of p53 in the intrinsic apoptosis pathway [2]. Nature does nothing in vain. This way is “approved” by the mechanism which cytotoxic T-cells use to kill the cell: they “inject” granzyme B that directly activates caspases – the final participants in apoptosis pathway and, hence, p53 conditions are not important at all.

Immune system protects us from invaders and mutated cells. Cancer cells accumulate “indulgence” mutations that gave them opportunity to grow without punishment [3]. Due to these mutations’ cancer cells can avoid T-cells attack or create tumor immune-suppressive microenvironment. To struggle with cancer modern immunotherapy recruited mainly executive T, NK and B-cells, while regulatory cells are important at all.

Oncofetal antigens are proteins which are typically present during fetal development and are found in adults with certain kinds of cancer. There are several oncofetal antigens: alpha-fetoprotein (AFP), carcinoembryonic antigen, beta-human chorionic gonadotropin, trophoblast glycoprotein precursor, etc. They are synthesized not for our convenience to help detect, diagnose, and manage some types of cancer. Two main oncofetal proteins: AFP and AFP receptor (AFPR) were attributed as nutrient delivery system to serve embryo and cancer cells. AFPR was recently discovered on MDSC [5] and hence, these cells also use AFP for nutrient delivery and protect embryo [6] and tumor from immune rejection. It is not a coincidence that AFPR is the most widespread tumor marker (>80%). Mutations that leads to AFPR expression are the main “indulgence” mutations in cancer cells. It is obvious that regulatory MDSC depletion in cancer patients is a hot topic of immunotherapy [7]. One of the tools for this purpose is AFP-toxin drugs that are specifically targeted to AFPR [8].

So, AFP-toxin drugs can fix the cancer brakes both inside and outside the cells. Regulatory MDSC-targeted immunotherapy has a more powerful effect on cancer eradication than targeted chemotherapy, it needs low drug doses and is safe for the patient. Cancer treatments with AFP-toxin medicines were successfully used in humans and have a bright future.

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