EC Cancer Editor's Column - 2016

Immunotherapy as a Tool to Improve the Immune Response against Cancer

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COLUMN ARTICLE

Have you ever imagined that the cure for cancer could be your own immune system? A personalized treatment for cancer patients? This new approached was considered the breakthrough of the year in 2013, bringing tons of hope for several patients in need for a new cancer treatment. If I ask you how cancer is being treated today you would give the exact same answer as 50 years ago. Don't you think it's time for something new? We are developing new therapies! No more chemicals, radiation, aggressive surgeries, only our own cells. Immunotherapy records a pivotal moment in cancer as long sought attempt to promote the immune system against tumors. Cancer is a major public health problem in the world and currently the second leading cause of dead in USA. Several efforts have been made to find a cure for cancer or should get as close to cure by increasing research to enhance the understanding of cancer biology. The war on cancer began in 1971 with National Cancer Act by U.S President Richard Nixon. Unfortunately many factors have generated a less optimistic scenario and have been presented as blocking progress in finding a cure for cancer. Some examples of this biological complexity: cancer heterogeneity, genetic and epigenetic alterations, risk of factors, challenges of early detection and diagnosis, drug approval process, tumor vasculature, subversion of immune system by tumor cells, apoptosis resistance, improvement of drug resistance in cancer chemotherapy, tumor microenvironment and the list could be endless. In this context, why is it so hard to make a global cancer vaccine? Why cancer vaccines are hard to target and how to handle them to reach a targeted immune response? A plently of researchers have tried to develop cancer vaccines for decades but unfortunately this achivement does not translate into success in clinical trials. This complexity is also due to the compromise nature of how the evoultion selects our immune system to respond not only against strange particles or different cells but normal cells as well. Cancer cells are able to escape and avoid detection and destruction by the immune system. These cells can recruit diversity of cell types, including endothelial cells, fibroblasts and immune cells, and through production and secretion of stimulatory growth factors. This collection of cells and molecules together compose the tumor microenvironment. We know that microenvironment plays a major role during the initiation and development of tumor progression. This finding has enabled for the logical design of drugs. Several studies have investigated the immune system of cancer patients, and they suffer from large immunosuppression mainly due to decrease lymphocyte proliferation and cytotoxic activity. This means that the immune system, responsible for immunosurveillance now becomes weak, inactive and inefficient. Immunotherapy is one of the best therapies compared to traditional therapies that may cause potential toxicities such as chemotherapy and radiation. For several reasons the cancer patient's immune system stops fighting and gives up the battle. So we have to reverse this situation. The potential use of immunotherapy is to restore the immune system of patients in attempt to stimulate it to reject and destroy tumors. Some strategies such mono-

Citation: Jorge Augusto Borin Scutti. "Immunotherapy as a Tool to Improve the Immune Response against Cancer". EC Cancer ECO.01 (2016): 01-02.

clonal antibodies to block immune checkpoints (α-CTLA, α-PD-L1 and α-PD-1), dendritic cell-based immunotherapy, T cell adoptive transfer, autologous immune enhancement therapy, cytokines, peptides, oncolytic immunotherapy and genetically engineered T cells (CAR T cells) are being, with positive results, developed to improve the quality of life and increase survival of cancer patients. Furthermore, novel immunologic targets for cancer immunotherapy on regulation of immune system have led to the identification of a several potential molecules such LAG-3, VISTA, TIM-3, ICOS, 4-1BB and OX-40. Immunotherapy represents a novel and promising approach for targeted therapy of cancer patients and clinical trials have already shown clinically significant anti tumor activity in neuroblastoma, breast, prostate, melanoma, pancreatic tumors, chronic lymphocytic leukemia and B cell lymphoma. Are we closer to a cancer cure?

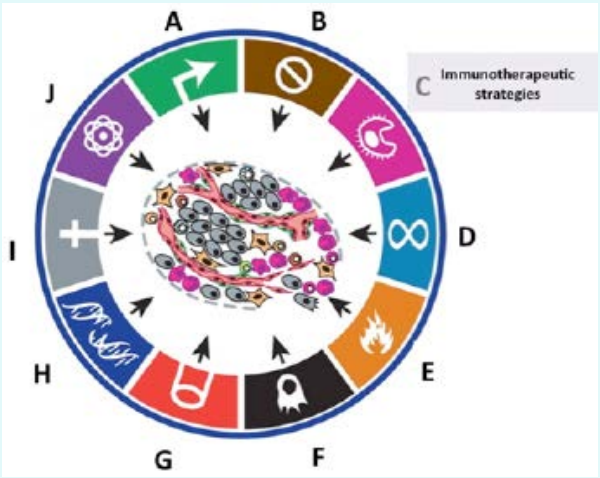

Figure 1: Biological capacities and therapeutic targeting of the Hallmarks of Cancer.

A plenty of drugs are able to interfere with each specific stage of the acquired capabilities for tumor growth development and progression. Some cancer biological capacities are defined as: A) Sustaining proliferative signaling; B) Evading growth suppressors; C) Avoid immune destruction; D) Enabling replicative immortality; E) Tumor promoting inflammation; F) Activating invasion and metastasis; G) Inducing angiogenesis; H) Genome instability and mutation; I) Resisting cell death and J) Deregulating cellular energetics. With recent approvals for multiple therapeutic immunotherapies (C) strategy in several types of cancer they are being targeted clinically with positive results such CAR T cells and immune checkpoint blockade (α-CTLA and α-PD-1).

(Hanahan D and Weinberg R. "Hallmarks of Cancer: The Next Generation". Cell 144.4 (2011): 646-674).