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Cancer Immunotherapy as a new treatment option

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Introduction

As we know, cancer can coaptate the immune control. However, some medications can disrupt immunological checkpoints and \'\'release\'\' anti-tumor immunity. This complex biological process still contains many mysteries and is currently the subject of an intense study. By making the most of this, cancer immunotherapy could be a key part of the clinical management of cancer in a specific way: in cancer patients, the cancer immunity cycle does not perform optimally so the goal of cancer immunotherapy is to initiate itself – sustaining cycle of cancer immunity enabling it to amplify, propagate and generate unrestrained autoimmune inflammatory responses to overcome the negative feedback mechanisms of cancer; also, important inflection points in the history of cancer therapy: durable monotherapy responses are being reported (in different human cancers with several different ages), new drugs and implement clinical strategies are indicated in melanoma (a disease thought to be atypically immunogenic) and immunology therapy of cancer could report safety and more manageable profiles tan traditional cancer therapies (they act specifically). A successful approach will be to find a common rate – limiting step in the tumor micro-environment so that we can act selectively targeting it in any given patient (because amplifying the entire cycle may provide anticancer activity but also could damage normal cells and tissues, as chemotherapy).

Objectives

The main objective is to assess the status of antitumor immunotherapy in order to conclude whether, as of now or in the future, immunotherapy can be considered as a viable treatment option.

Methodology

The conduction of this narrative review will be based on the conference about cancer immunotherapy ‘’Medicina de Precisión e Inmunoterapia: retos y oportunidades para el tratamiento del cáncer’’ *Dr. Mariano Barbacid*. Also, we contacted Pedro Romero, who works at Ludwig Cancer Research at University of Lausanne, 1066 Epalinges, (Switzerland); and who recommended us some important articles releated with this topic.

Results

Cancer rejection is a 7-step process

The manipulation of the second activating signal could abrogate anti-cancer immune reactions (who apparently blocks B7 expression and over-express CTLA-4). The scientific community soon realized that this swarm of stimulatory and inhibitory molecules inter-playing in the anti-tumor immune response could be able manipulated to improve such response. This approach has been termed Immune Checkpoint Blockade, in other words, “molecules than can be blocked to free the immune system to destroy tumor cells”.

Monoclonal Antibodies

The lack of CD28 activation by binding CTLA-4 is a physiological phenomenon since it reacts with B7 with much higher affinity than CD28. So, it interrupts the second activating signal, and T cells enter in a state of anergy.

PD-1 has a role in controlling the suppressive function of treg playing a role in T cell recognition of antigens presented to T cells in secondary lymphoid organs.

Tremelimumabis a fully human IgG2 anti CTLA-4. It posed hopes in early melanoma.

Nivolumabis a fully human IgG4 anti PD-1, and it showed good responses in human melanoma, kidney and rectal cancers.

Ipilimumabis a fully human IgG1 anti CTLA-4. Phase III trials showing improved survival,so it was approved in 2011 in USA and Europe for the treatment of unresectablemelanoma and a meta-analysisshowed extendedsurvival in 20% of patients, reaching 10 years in some cases.

Cancer Vaccines

Cancer vaccines seek to target a tumor-specific antigen and distinct from self-proteins. Tumor antigens have been divided into two categories: shared tumor antigens (expressed by many tumors) and Unique Tumor Antigens (resulting from mutations induced through physical or chemical carcinogens, so they are expressed only by individual tumors). One approach could be vaccines containing whole tumor cells, but these vaccines have been less effective. Defined tumor antigens decrease the risk of autoimmunity, but tumors can evade destruction through antigen loss variance. A process called ‘’epitope spreading’’ or ‘’provoked immunity’’ may mitigate this weakness.

Chimeric Antigen Receptor T Cells (CARTS)

Many tumor cells do not express HLA molecules, hence T cells cannot recognize them. CAR T-cell therapy employs gene transfer techniques to reprogram endogenous T cells to target a specific tumor antigen. Patients typically receive chemotherapy, the goal is to induce lymphodepletion and thereby enhance car t-cell expansion and persistence in vivo, lymphodepletion may have the additional benefit of tumor cytoreduction, which can potentially improve CAR T-cell treatment efficacy and minimize toxicity.

Conclusion

In conclusion, immunosuppression is the natural history of cancer and multiple mechanisms are known that may work together or in parallel; consequently, there is a need to pursue other potential agents which must act in a synergy way.

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