

Toward a Melanoma Dendritic Cell Vaccine using Neoantigens

Editorial

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The Venezuelan biologist Beatriz M. Carreno from the Department of Pathology & Immunology at Washington University in St. Louis, USA, leads a team, along Professor Gerald P. Linette, that seeks alternatives to develop an immunotherapy for melanoma.

In April 2015, the group published in Science, a therapy with dendritic cells sensitized with neoantigens that are mutated peptides derived from melanomas, which are patient-specific. These mutations are missense that is, generated by changing a nucleotide, causing the appearance of a codon encoding a different amino acid, a protein product that the immune system recognizes as foreign.

Dendritic cells are the first and only cells capable of inducing a primary immune response activating resting naïve T cells in secondary lymphoid tissues (ie. lymph nodes) from antigens that they capture in the epithelia. Dendritic cells are called immature when they are in the epithelium functioning as phagocytes, and mature when they act as antigen-presenting cells in the lymph nodes.

In the study, the inoculation of dendritic cells pulsed with neoantigens produced a robust immune response in three adult patients with advanced cutaneous melanoma. These melanomas were IIIc, resected and had not responded to prior therapy with anti-CTLA-4 (Ipilimumab), which stimulates the proliferation and activation of T cells that facilitate the destruction of tumor cells.

The aim of the study was to determine safety, tolerability, and immune responses to neoantigens in a therapy with modified dendritic cells, paving the way for a phase I trial in the coming months.

This cell therapy is different from other customized therapies against neoplasms in two main aspects: 1) The use of mature dendritic cells, which produce important growth factors for the generation of a vigorous immune response, as demonstrated earlier by the group; and 2) The administration of the cell therapy by infusion, rather than by injection.

An interesting result was the high diversity of T cells responding to dominant and subdominant neoantigens, indicating the existence of a large pool of naïve tumor-specific T cells that are activated with the cell therapy. Recent observations showed that the use of antibodies to CTLA-4 also alter TCR diversity in melanoma patients.

According to the authors, the results are too premature to conclude that the treatment has produced some therapeutic benefit to patients. However, it appears that therapy with neoantigen-sensitized dendritic cells may be an effective treatment for melanomas in the coming years.

References

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