Immunotherapy bullets for the clinic

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The immune system comprises specific cell types, proteins and organs to protect the body against danger and is essential in the defense of infections. Among these specific cell types we found the T cells, which when active can kill damaged or infected cells, as well as cancer cells. T cells require specific signals to be activated. Then dendritic cells (DCs) get involved. These cells are very specialized in the capture of antigens, any substance produced by the body or the environment, their processing and presentation in a simpler fashion to the T cells. Dendritic cells express molecules and release some proteins, as CD86 and IL-12, respectively, which activate T cells.

In this study, we have analyzed if dendritic cells could be activated by antigen-antibody complexes: immunotherapy bullets. Antibodies recognize specific regions of antigens, hence being very specific. Antigens bound to antibodies are called antigen-antibody immune complexes (ICs) and have been studied as a possible therapy. The most abundant protein in the white egg, ovalbumin, was used as a model to study if administered with an antibody against it, forming immune complexes, could trigger higher stimulation of the dendritic cells than the ovalbumin alone. In 4 of 11 donors an increased stimulation was observed in comparison to soluble ovalbumin. Additionally, high variation among donors was found, which can be due to intrinsic differences between donors on the receptors that recognize this antigens and immune complexes.

Additionally, a second construct was also examined. This second antigen was a synthetic peptide, a small protein synthetically formed. This strategy has been previously used in clinical therapy for treatment of human papillomavirus and has showed promising results. Moreover, these peptides can be formed from almost any protein found suggesting that might be used as a possible strategy for the treatment of many diseases, as cancer. Thus, fusing immune complexes with synthetic peptides might be an important strategy for the clinic, since they might drive increased stimulation of T cells. Immune complexes formed with this construct elicited higher stimulation of dendritic cells on 66% of the donors with respect to the free peptide, indicating that the enhanced stimulation depends on the antibody binding. These findings demonstrate that antigen-antibody immune complexes are more efficient than soluble antigens to trigger functional activation of DCs, which can improve vaccine development and treatment for many diseases.

Human dendritic cells are difficult to isolate in large amounts. Therefore, they can be derived from monocytes, immune cells that are in a much larger amount in the blood. After culture with different proteins that differentiate them into dendritic cells, they behave like these cells and present their characteristics. Thus, they are called monocyte-derived dendritic cells (MoDCs). This is one of the most common models used in immunotherapy to analyze properties of dendritic cells.

However, MoDCs might not behave completely as human DCs. Therefore, further studies are required on natural unmodified cells to understand how immune complexes can stimulate different cell subsets from the immune system and how this approach can be used in the clinic. Moreover, the use of synthetic peptides in conjunction with immune complexes might be an effective strategy for immunotherapy of different diseases. The high variation among donors is a factor that should be studied in the future to know how these constructs can be used in treatment.

Degree project in Biology, Master of Science (1 year), 2013
Examensarbete i biologi 30 hp till magisterexamen, Uppsala universitet, 2013
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