Novel In Vitro Method for Generating Human Dendritic Cells for Immunotherapy

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SUMMARY

Researchers in the UCLA Department of Pathology and Laboratory Medicine have developed a new method for generating and expanding human CLEC9A+ dendritic cells that can be used for a wide variety of immunotherapy applications.

BACKGROUND

Immunotherapy uses specialized cells of the immune system to fight diseases such as cancer. The use of dendritic cells (DC) to present tumor-associated antigens to autologous (self) T cells has been widely investigated as an approach to cancer immunotherapy. However, while numerous strategies have been investigated, most clinical trials using DC have demonstrated only modest activity. There are several different types of DC with different abilities to present antigens to T cells to react to tumors. The majority of clinical studies have used DCs generated from blood monocytes, however the use of naturally occurring DC types may permit superior T cell immune responses through a process called cross-presentation.

CLEC9A+ DC are specialized antigen-presenting cells normally present at very low frequency in the human blood, lymph nodes, spleen, and other organs. They are highly efficient at cross-presenting antigens from cellular sources to T cells, and thus are likely involved in regulating immune responses to pathogens, anti-tumor immunity and, in certain clinical settings, autoimmunity, transplant rejection, and graft versus host disease. They are also present in the human thymus where they may be involved in the negative selection of self-reactive thymocytes and/or generation of regulatory cells.

The potential benefit of CLEC9A+ DC over monocyte-derived DC is their ability to elicit CD8+ and CD4+ T cell immunity to cellular antigens without the need for loading with MHC-specific peptides. The usual protocols used in clinical trials to generate DC from blood monocytes do not generate the CLEC9A+ type of DC. Currently there are no commercial products that produce human CLEC9A+ DC in vitro. Moreover, even experimental methods that have been reported in the literature can only generate a very limited number of CLEC9A+ DC. With a myriad of potential applications, CLEC9A+ DC can become a very important tool for developing immunotherapies if they can be produced on a large scale.

INNOVATION

Researchers in UCLA Department of Pathology and Laboratory Medicine have developed a new method for generating and expanding human CLEC9A+ DC from autologous CD34+ hematopoietic stem and progenitor cells that can be used for a wide variety of immunotherapy applications. This invention’s ability to generate large number of CLEC9A+ DC may permit the development of patient-specific immunotherapies for the treatment of a wide variety of diseases, including but not limited to cancer and chronic viral infections.

APPLICATIONS

Can be applied to create immunotherapies for cancer and chronic viral infections

ADVANTAGES

- Produces significantly larger number of CLEC9A+ DC than other comparable methods
- Produces higher purity of CLEC9A+ DC than other comparable methods
- CLEC9A+ DC produced by this method are qualitatively and quantitatively functionally superior in antigen presentation to the types of DC produced using existing methods

STATE OF DEVELOPMENT

This method has been validated and is currently being optimized. UCLA is looking for partners to explore this invention’s potential for commercialization and to help find useful applications for the method.

PATENT STATUS

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Additional Patent Pending