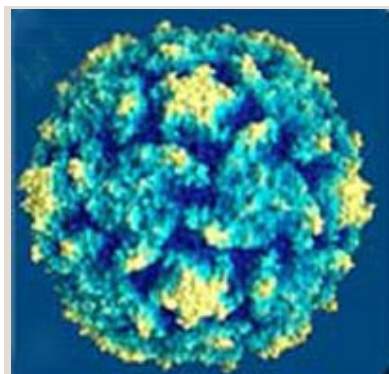


Generation of EBV-specific T-cells using virus-like particles facilitates adoptive treatment of EBV-associated diseases

Reference Number: TO 01-00758

Challenge

Epstein-Barr virus (EBV)-specific T-cell lines generated by repeated stimulation with EBV-immortalized lymphoblastoid B-cell lines (LCL) have been successfully used to treat EBV-associated post-transplant lymphoproliferative disease (PTLD) in hematopoietic stem cell transplant recipients. However, because of the laborious and lengthy procedure of preparing EBV-specific T cell lines and the often rapid progression of PTLD, this form of adoptive immunotherapy still has a limited role in the management of virus-associated complications in transplant recipients. To implement this treatment as a conventional and efficacious therapeutic option, generic and more direct approaches for the generation of EBV-specific T-cell lines enriched in disease-relevant specificities need to be developed.



EBV

Source: NASA

Technology

CD4⁺ T cells play an important role in establishing antiviral immunity. In immunosuppressed patients, low numbers of endogenous CD4⁺ T cells have been identified as risk factor for the development of PTLD. To rapidly generate T-cell lines enriched in EBV-specific CD4⁺ T cells, the inventors developed a fast and standardized stimulation protocol. Virus-like particles (VLP) of EBV, incapable of transforming primary human B cells, are pulsed onto human PBMC, which are subsequently used to reactivate and expand EBV-specific CD4⁺ T cells from peripheral blood.

Commercial Benefit and Opportunity

EBV-VLP stimulated T cells are suggested to be much more efficient in eliminating newly EBV-infected B cells and thus in controlling EBV infection. A new option to treat EBV-associated diseases like PTLD, nasopharyngeal carcinoma or Hodgkin's-Disease might approach.

In addition, stimulation with VLP will obviate the lengthy and costly procedure of generating LCL and thus significantly shorten the process of preparing T cells for adaptive T-cell therapy. Furthermore, safety concerns because of EBV wild-type virus in the T cell preparations are no longer an issue.

The technology is available for (non-)exclusive licensing. Parties interested in collaborative research and development are highly welcomed.

Developmental Status

An in vitro proof-of-concept has been provided demonstrating that EBV-antigen specific CD4⁺ T cells are efficiently expanded from peripheral blood of EBV-positive donors using PBMC pulsed with EBV-VLP as stimulators. Experiments to use such EBV-VLP as a vaccine are ongoing.

Patent Situation

An EP and PCT patent application has been filed.

Relevant Publication

Adhikary et al. (2008), J. Virol. 82, 3903-3911.

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