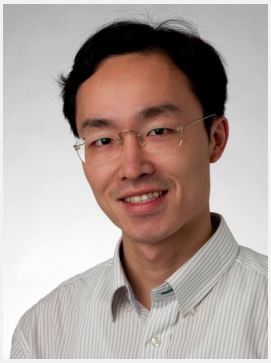
ImmunoTools IT-Box-139 Award 2012



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INVESTIGATING THE ADAPTIVE IMMUNE RESPONSE AFTER iPS CELL TRANSPLANTATION

Today's most urgent problem in transplantation is the lack of suitable donor organs and tissues. One alternative to organ transplantation is cell therapy whereby the aim is to replace, repair, or enhance the biological function of damaged tissue or diseased organs. Thus, the primary goal of cell transplantation has been to find a renewable source of cells that could be used in humans to regenerate damaged tissues and organs. In recent years, there is much interest in using embryonic stem (ES) cells to regenerate tissues and organs. In contrast to adult stem cells, ES cells possess unlimited self-renewal and pluripotency[1]. The ability to differentiate into different cell types has stimulated research in generating neurons, cardiac muscle, hematopoietic progenitor cells, hepatocytes, pancreatic beta cells, and other cell types for potential clinical applications[2-4]. However, despite the excitement surrounding ES cell research, important issues surrounding immunogenicity have not been fully addressed and strategies to avoid rejection remain largely untested[5]. An alternative approach to induce long-term pluripotent cell engraftment is the derivation of pluripotent cells by reprogramming somatic cells (such as skin fibroblasts). Therefore, induced pluripotent stem **(iPS) cells** are generated from adult fibroblasts. In theory iPS cells would not face the same histocompatibility barriers as ES cells because they could autologously transplanted. However, their autologous use is restricted by high cost, limited availability, and ethical issues.

To understand the immunogenicity of allogeneic iPS cells, I will use immunotools supplies, which will be used for immune profiling. This strategy will enable accurate determination of the number of distinct antigen receptors, as well as the frequency of cells within each receptor, in any defined population of lymphocytes.

BIBLIOGRAPHY

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PROJECT GOAL

Our group recently identified the adaptive immune system being involved in ES cell rejection (published in "Circulation"):

Deuse T, Seifert M, Phillips N, Fire A, Tyan D, Kay M, Tsao M, ***Hua X****, Velden J, Eiermann T, Volk HD, Reichenspurner H, Robbins RC, Schrepfer S. HLA I knockdown human embryonic stem cells induce host ignorance and achieve prolonged xenogeneic survival. Circulation 2011 (Oct); 124 (Suppl1).*

Similar to ES cells, it is likely that therapeutic allogeneic transplantation of iPS cells will face immunological rejection if transplanted across histocompatibility barriers. We therefore propose to analyze T cells and B cells with unprecedented depth and specificity after human iPS transplantation.

TECHNIQUES, WHICH WILL BE USED TO INVESTIGATE THE ADAPTIVE IMMUNE RESPONSE

In Vivo bioluminescence imaging (BLI)

Longitudinal *in vivo* assessment of iPS cell survival after transplantation will be performed by bioluminescence at day 0, 1, followed by every other day until disappearance of the BLI signal.

This elegant method allows to demonstrate adaptive immune responses, was developed at Stanford University and is available in our lab. After re-transplantation of iPS cells, transplanted cells will get rejected significant faster resulting in an even faster disappearance of the BLI signal.

Immunological Assays

Immunological assays, such as ELISPOT Assays, Cell-mediated lympholysis (CML) chromium-release assay, donor-specific antibodies, are established in our lab and will be used in the study.

Confocal Immunofluorescence

Most importantly, we are aiming to use confocal immunofluorescence for co-localization of graft infiltrating lymphocytes, NK cells, B cells, and macrophages.

Details of how the ImmunoTools antibodies from the IT-Box-139 are intended to be used within your project

This proposal is designed to achieve a better understanding of the adaptive immune reaction to human iPS cells. The first important milestone will be to identify adaptive immune system after iPS cell transplantation into x allogeneic (humanized) mice.