



DFG Heisenbergteam for Experimental Cardiac Surgery
and Transplant Immunology

Transplant and Stem Cell Immunobiology Lab (TSI)
Director: Sonja Schrepfer, MD, PhD

Application for the Experimental Doctoral Thesis in collaboration with Stanford University 2012:

Understanding the Immunobiology of Induced Pluripotent Stem (iPS) Cells

Principal Investigator:

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Doctoral Student:

Please email your application (letter of motivation, CV, background information) to
schrepfer@stanford.edu

Duration of project: 18 months fulltime

Deadline:

February 29th, 2012

Applicant's presentations: March 1st- March 7th

Brief summary

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 pluripotency¹. The ability to differentiate into different cell types has stimulated research in generating cardiac muscle and other cell types for potential clinical applications². 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. These are fundamental challenges that must be met before stem cell therapy can become a reality.

An alternative approach to induce long-term cell engraftment is the derivation of patient-specific induced pluripotent stem (iPS) cells by transduction or transfection of pluripotency genes or proteins to reprogram somatic cells into an “ES-like” state³⁻⁶. In theory, iPS cells would not face the same histocompatibility barriers as ES cells because they derived and transplanted into the same person. However, to date no study has investigated whether iPS cells will indeed evade immune recognition if transplanted autologously. Another more practical concern is whether personalized iPS cell based therapy will be economically feasible to the population at large. Furthermore, for acute diseases such as myocardial infarction, it would most likely be more effective if off-the-shelf products (e.g., ES/iPS cell derived cardiac cells) can be administered in a timely fashion (within a short critical window of time). One way to meet some of these challenges would be to create an iPS cell “bank” using a modulated donor cell population to avoid immune responses after transplantation.

Project Goals

Our proposal addresses **three issues critical to the understanding the immunogenicity of iPS cells** and the development of strategies to induce long-term engraftment of transplanted cells. **First**, to understand the immunogenicity of iPS cells, we will profile the expression of numerous immunogenic genes and surface proteins at various stages throughout the reprogramming and differentiation process. **Second**, we will develop a “humanized” mouse model which will allow us to study how the *in vivo* environment affects the expression of the same immunogenic markers assayed prior to transplantation while concurrently monitoring the allogeneic *in vivo* immune response towards iPS cells. **Third**, to induce long-term tolerance and

engraftment, we will target the transplanted iPS cells. We will decrease the immunogenic potential of iPS cells by decreasing the MHC-I expression and increasing the expression of T-cell apoptosis inducing ligand CD95.

Successful completion of this “forward-thinking” proposal will produce important contributions to both the field of stem cells and transplantation biology.

The first part of the project started at the University Hamburg, and for the second part the TSI-lab will move together to Stanford University, California, USA.

Therefore, the successful applicant is fluent in English, and able to move to California.

Funding will be available.

