# ImmunoTools *special* Award 2014

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## The Immune Response to Induced Pluripotent Stem Cells (iPS) in Autologous Cell Therapy

**Proposal Overview**

Today, we live longer and mostly better; however, medicine has not brought yet the cures of many major pathological conditions. An important breakthrough in stem cell research in 2006 revealed that human somatic cells such as skin cells are reprogrammed into induced pluripotent stem cells (IPS). These cells can give rise to any kind of cell of the human body that could potentially treat many human diseases that could benefit from cell replacement transplantation. A pressing assumption in the field of iPS cells that remains to be defined is that because iPS derived cells will be autologous, coming form the same person that they will be used for, there will be no immune-cell response. Previous studies that have successfully treated mouse models with iPS derived progenitor cells have used immune suppressive methods. We will first make high quality mouse and human iPS cells from primary fibroblasts (Fibro-1) then derive a second fibroblasts cell line (Fibro-2) that will be comprehensively characterised. Then we will then compare the immune response of fibroblast cell lines Fibro-1 and Fibro-2 for; MHC1 expression levels in response to interferon and in vitro T cell kill assays. The use of ImmunoTools antibodies and growth factors will be essential for this aspect of the work. For the mouse work we will engineer grafting of tetraploid complementation made chimera mouse skin on the original mouse to determine any in vivo graft-host immune issues.

If we can demonstrate the absence of any immune response induced by iPS-derived cells, this will have an enormous impact on the quality of life of future patients undergoing autologous cell therapy. Conversely, if we identify differences of peptides presented by MHC-I molecules it will provide the ground breaking and pivotal knowledge to move forward with for the eventual clinical application of iPS cells in regenerative medicine. The clarification of whether or not there is an iPS-specific immune reaction in autologous iPS cell therapy is a critical point in the stem cell field for future clinical trials. The use of ImmunoTools antibodies and growth factors will be part of this discovery.

**Objective of the Project**

To define the elements involved in any immune response against human and mouse iPS-derived cells that can cause rejection in autologous stem-cell therapy.

**Methodology**

We will make three new iPS cell lines from mouse and human fibroblasts, using modified RNA transfection methods that are detailed below. For human work we will take skin biopsies from 3

male volunteers. The human iPS cell lines will be made in clinical grade conditions, meaning using animal free (xeno-free) cell culture products, transgene and virus-free RNA transfection methods and the use of the newly developed "Sala Blanca" or "white room", GMP grade cell culture facilities at the Faculty of Medicine, University of Barcelona, where Dr. Michael Edel is based. These cell culture facilities are for the preparation of stem cells for clinical stem cell-therapy and will be rented at the University of Barcelona. We will compare three mouse and human primary fibroblast cell lines, termed **Fibro-1** and make iPS cells that will then be differentiated back to fibroblasts cells termed **Fibro-2** using both retrovirus method and RNA transfection (virus and transgene free) method. Fibroblasts and iPS cells made from retrovirus methods have already been made and are available for this study. The cell lines will then be exhaustively tested for their immune status and immune response using ImmunoTools reagents.