

## **P52**

### **Multilineage differentiation potential of reprogrammed fibroblasts**

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#### **Objectives:**

Forced expression of the four transcription factors Oct4, Sox2, c-Myc, and Klf4 is sufficient to confer a pluripotent state upon the murine fibroblast genome, generating induced pluripotent stem (iPS) cells. Although felt to be equivalent to embryonic stem (ES) cells, the differentiation potential of these cells has not been rigorously determined. In this study, we sought to identify the capacity of iPS cells to differentiate into Flk1-positive progenitors and their mesodermal progeny including cells of the cardiovascular and hematopoietic lineages.

#### **Methods:**

To compare the *in vitro* differentiation potential of murine ES and iPS cells, we either induced embryoid body (EB) formation of each cell type or cultured the cells on collagen type IV (ColIV). Magnetic cell sorting was used to isolate ES and iPS cell-derived progenitors that were further differentiated towards cardiovascular and hematopoietic phenotypes. Immunocytochemical, gene and cell surface marker expression analysis as well as various cell functionality assays were performed.

#### **Results:**

EB formation and exposure to ColIV both induced ES and iPS cell differentiation into cells that expressed cardiovascular and hematopoietic markers. To determine if ColIV-differentiated ES and iPS cells contained a progenitor cell with cardiovascular and hematopoietic differentiation potential, Flk1-positive cells were isolated and exposed to specific differentiation conditions, which induced differentiation into functional cardiomyocytes, smooth muscle, endothelial and hematopoietic cells.

#### **Conclusions:**

Our data demonstrate that murine iPS cells, like ES cells, can differentiate into cells of the cardiovascular and hematopoietic lineages and therefore represent a valuable cell source for applications in cardiovascular regenerative medicine.