

Study shows potential of differentiated iPS cells in cell therapy without immune rejection

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A new study from Boston University School of Medicine (BUSM) shows that tissues derived from induced pluripotent stem (iPS) cells in an experimental model were not rejected when transplanted back into genetically identical recipients. The study, published online in *Cell Stem Cell*, demonstrates the potential of utilizing iPS cells to develop cell types that could offer treatment for a wide range of conditions, including diabetes, liver and lung diseases, without the barrier of immune rejection.

Ashleigh Boyd, DPhil, and Neil Rodrigues, DPhil, the study's senior authors, are assistant professors of dermatology at BUSM and researchers at the Center for Regenerative Medicine (CRoM) at Boston University and Boston Medical Center (BMC). They also are lead investigators at the National Institutes of Health's Center of Biomedical Research Excellence (COBRE) at Roger Williams Medical Center, a clinical and research affiliate of BUSM.

iPS [cells](#) can be developed from adult cell types, such as skin or blood, by returning them to a stem cell state using [genetic manipulation](#). iPS cells are capable of maturing (differentiating) into all the specific cell types in the body, making them a powerful tool for biological research and a source of tissues for transplantation based therapies. Given that iPS cells can be made in a patient-specific manner, there should be great potential for them to be transplanted back into the same patient without rejection. Yet a study published in *Nature* in 2011 demonstrated that iPS cells transplanted in the stem cell state were rejected in genetically

identical recipients.

"The Nature study provocatively suggested that tissues derived from patient-specific iPS cells may be immunogenic after transplantation. However, it never directly assessed the immunogenicity of the therapeutically relevant cell types that could be utilized in regenerative medicine and transplantation," said Rodrigues.

The BUSM researchers evaluated this matter by taking [adult cells](#) from an [experimental model](#) and deriving iPS cells from them. They then differentiated the iPS cells into three cell types: neuronal (nerve); hepatocytes (liver); and endothelial (blood vessel lining) cells. These three [cell types](#) represent each of the three germ layers present during embryonic development – mesoderm, ectoderm and endoderm. Cells from these layers differentiate and ultimately develop into the body's tissue and organ systems. Using experiments to mirror the potential clinical use of patient-specific iPS cells in cell therapy, the team transplanted each of the differentiated cells into a genetically identical experimental model and found no signs of an elevated immune response or indications of rejection.

The study results suggest that using patient-specific iPS cells should overcome issues of immune rejection in transplantation, which will be a significant problem for potential embryonic stem cell-derived therapies. [Immune rejection](#) in transplantation is treated clinically by immunosuppressive drugs but they can have serious side-effects, including the risk of developing cancer.

"If the use of immunosuppressive drugs can be avoided, as may be the case for patient-specific iPS cell based therapies, it would be preferable. Our results are very promising and future work should be directed at assessing whether tissues derived from human iPS cells will similarly lack [immunogenicity](#)," said Boyd.

Provided by Boston University Medical Center

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