ERASMUS UNIVERSITEIT ROTTERDAM

Erasmus University Rotterdam, the Netherlands
CSC PhD 2015 Project Description

School/Department:	Department of Internal Medicine Section Nephrology and Transplantation
Project Title:	Delivery of immunomodulatory and regenerative signals to the injured kidney
Abstract:	Cell therapy is one of the most promising developments in medicine for treatment of immunological and degenerative diseases. Mesenchymal stem cells (MSC) are candidates for cell therapy, as they have immunosuppressive ability and tissue repair properties via the secretion of soluble factors and via cell membrane protein interactions. MSC are easy to isolate from bone marrow or fat tissue and can be expanded manifold *in vitro*. Therefore, research efforts centre around cultured MSC (cMSC). Recent studies, however, show that intravenously infused cMSC get trapped in the lungs because of their large size and show poor engraftment in tissues, which may limit their therapeutic effect. We want to examine the effect of cMSC on kidney injury in *in vitro* and *in vivo* assays and make comparisons with freshly isolated MSC (fMSC), which are smaller and probably better adapted to the *in vivo* microenvironment, and with the secretome and membrane fragments of MSC. *In vitro*, the effect of MSC and derivatives on kidney tubular cell survival, proliferation and salt resorption capacity will be examined. *In vivo*, the homing, retention and survival of cMSC and fMSC after infusion will be examined and the effects of MSC and derivatives on kidney function studied in an ischemic kidney injury model. This study will demonstrate how the delivery regenerative and immunomodulatory signals to the injured kidney can be improved and will contribute to the development of regenerative and immunomodulatory therapy for kidney injury.
Requirements of candidate:	Background: The candidate should have a research interest in cellular therapy for organ transplantation. Cell biology and immunology knowledge will be required. Laboratory experience and small animal handling skills are an advantage. Master degree: Yes IELTS Grade: 7.0 *(minimal 6.0 per component)* *or* TOEFL: *100 (minimal 20 per component)*

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Supervisor information:	Dr. M.J. Hoogduijn m.hoogduijn@erasmusmc.nl www.linkedin.com (Martin Hoogduijn) ***Hoogduijn MJ**, Verstegen M, Engela AU, Korevaar SS, Roemeling-van Rhijn M, Merino A, Franquesa M, de Jonge J, IJzermans JN, Weimar W, Betjes MG, Baan CC, van der Laan LJ. (2014). No Evidence for Circulating Mesenchymal Stem Cells in Patients with Organ Injury. Stem Cells Dev. In press* *Eggenhofer E, Luk F, Dahlke MH, **Hoogduijn MJ**. (2014). The life and fate of mesenchymal stem cells. Front Immunol. 19;5:148.* ***Hoogduijn MJ**, Betjes MG, Baan CC. (2014) Mesenchymal stromal cells for organ transplantation: different sources and unique characteristics? Curr Opin Organ Transplant. 19:0-0.* *Roemeling-van Rhijn M, Reinders MEJ, Franquesa M, Engela AU, Korevaar SS, Baan CC, Roelofs H, IJzermans JN, Betjes MGH, Weimar W, **Hoogduijn MJ**. (2013) Allogeneic bone marrow and adipose tissue derived mesenchymal stromal cells induce $CD8^+$ cytotoxic T cell reactivity. J Stem Cell Res Ther. 12;3(Suppl 6):004* *Roemeling-van Rhijn M, Khairoun M, Korevaar SS, Lievers E, Leuning DG, Baan CC, IJzermans JN, Betjes MGH, van Kooten C, de Fijter HJW, Rabelink TJ, Weimar W, Roelofs H, **Hoogduijn MJ**, Reinders MEJ. (2013) Human bone marrow- and adipose tissue-derived mesenchymal stromal cells are immunosuppressive in vitro and in a humanized allograft rejection model. J Stem Cell Res Ther. 25;Suppl 6(1):20780* ***Hoogduijn MJ**, van den Beukel JC, Wiersma LC, IJzer J. (2013) Morphology and size of stem cells from mouse and whale: observational study. BMJ. 347:f6833.* *Roemeling-van Rhijn M, de Klein A, Douben H, Pan Q, van der Laan LJ, Ijzermans JN, Betjes MG, Baan CC, Weimar W, **Hoogduijn MJ**. (2013) Culture expansion induces non-tumorigenic aneuploidy in adipose tissue-derived mesenchymal stromal cells. Cytotherapy. 15:1352-1361.* *Engela AU, Baan CC, Litjens NH, Franquesa M, Betjes MG, Weimar W, **Hoogduijn MJ**. (2013) Mesenchymal stem cells control alloreactive $CD8^+CD28^-$ T cells. Clin Exp Immunol. 174:449-458.* ***Hoogduijn MJ**, Roemeling-van Rhijn M, Engela AU, Korevaar SS, Mensah FK, Franquesa M, de Bruin RW, Betjes MG, Weimar W,*

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