

Erasmus University Rotterdam, the Netherlands
CSC PhD 2015 Project Description

School/Department:	Erasmus MC, Department of Surgery
Project Title:	Working title: Liver graft engineering: Stem cell repopulation in liver extracellular matrix
Abstract:	<p>As the shortness in liver donors severely limits the number of patients that receive a transplant, alternative approaches need to be explored. One of these alternatives is to construct transplantable liver tissue on the bench by using liver extracellular matrix (ECM) and repopulate this, or parts of this, with cultured liver (stem) cells. Preliminary results show that explanted porcine (whole) livers and human (whole) livers, can efficiently be de-cellularized using a perfusion set-up (Baptista <i>et al</i>, Hepatology. 53(2):604-17). A part of the project includes creating the ECM, characterizing and evaluating its use in liver-tissue engineering.</p> <p>In parallel, several cell culture systems are set up to produce cells to repopulate the a-cellular ECM. Pilot experiments are performed to culture LGR5 positive stem cells into so-called liver organoids from healthy and diseased liver tissue (Huch <i>et al</i>, Nature. 494:247-50 and Regen Med. 8(4):385-7). These human liver organoids, as well as other cell cultures of f.i. liver-derived mesenchymal stem cells (MSC), will be further characterized and used for re-seeding in liver ECM to study the possibility to repopulate the EMC with new liver cells. The ultimate goal of this project is to construct a transplantable (part of the) liver to function as graft and/or bridging therapy for patients that are on the waiting list for liver transplantation. The Erasmus MC, Department of Surgery is well equipped to perform this innovative research and have a close collaboration with leading stem cell researchers in the Netherlands and UK.</p>
Requirements of candidate:	<p>Master degree: Yes</p> <p><u>Background:</u> the candidate should have a Master's degree in Biology, Medicine or a related field. He/she should be interested in translational and basic research with a strong interest in liver regenerative medicine. Preferably he/she has some experience in working in an academic laboratory. We are looking for a reliable colleague with good communication and social skills and speaks and writes English well.</p> <p>IELTS Grade: 7.0 (<i>minimal 6.0 per component</i>) or</p>

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	TOEFL: 100 (minimal 20 per component)
Supervisor information:	<p>Dr. L.J.W. van der Laan, (Phone +31 10 703 7557, l.vanderlaan@erasmusmc.nl)</p> <p>Dr. J. de Jonge (j.dejonge.1@erasmusmc.nl)</p> <p>Dr. M.M.A. Verstegen (m.verstegen@erasmusmc.nl)</p>
Publication list (last 2 years):	<ul style="list-style-type: none"> - Fouraschen SM, Hall SR, de Jonge J, van der Laan LJ., 2014, Support of hepatic regeneration by trophic factors from liver-derived mesenchymal stromal/stem cells., <u>Methods Mol Biol.</u> 2014;1213:89-104. - Hoogduijn MJ, Verstegen MM, 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., No Evidence for Circulating Mesenchymal Stem Cells in Patients with Organ Injury., 2014, Stem Cells Dev. [Epub ahead of print] - Tapirdamaz O, Hesselink DA, El Bouazzaoui S, Azimpour M, Hansen B, van der Laan LJ, Polak WG, Kwekkeboom J, van Schaik RH, van Gelder T, Metselaar HJ., Genetic variance in ABCB1 and CYP3A5 does not contribute toward the development of chronic kidney disease after liver transplantation., 2014, Pharmacogenet Genomics.;24(9):427-35. - Farid WR, Verhoeven CJ, de Jonge J, Metselaar HJ, Kazemier G, van der Laan LJ., The Ins and Outs of MicroRNAs as Biomarkers in Liver Disease and Transplantation., 2014, Transpl Int. [Epub ahead of print] - van der Laan LJ, de Ruiter PE, van Gils IM, Fieten H, Spee B, Pan Q, Rothuizen J, Penning LC., Canine hepatitis virus and idiopathic hepatitis in dogs from a Dutch cohort., 2014, J Viral Hepat., [Epub ahead of print]

<p><i>Continued:</i></p>	<ul style="list-style-type: none"> - Tjon AS, van Gent R, Jaadar H, Martin van Hagen P, Mancham S, van der Laan LJ, te Boekhorst PA, Metselaar HJ, Kwekkeboom J., Intravenous immunoglobulin treatment in humans suppresses dendritic cell function via stimulation of IL-4 and IL-13 production., 2014, J Immunol.;192(12):5625-34. - Verhoeven CJ, Farid WR, de Jonge J, Metselaar HJ, Kazemier G, van der Laan LJ., Biomarkers to assess graft quality during conventional and machine preservation in liver transplantation., 2014, J Hepatol.;61(3):672-84. - Verhoeven CJ, Metselaar HJ, van der Laan LJ., Barking up the wrong tree: MicroRNAs in bile as markers for biliary complications., 2014, Liver Transpl. ;20(6):637-9 - Ramakrishnaiah V, van der Laan LJ., Hepatitis virus hijacks shuttle: exosome-like vesicles provide protection against neutralizing antibodies. 2014, Hepatology; 59(6):2416-8. - Fouraschen SM, de Ruiter PE, Kwekkeboom J, de Bruin RW, Kazemier G, Metselaar HJ, Tilanus HW, van der Laan LJ, de Jonge J., mTOR signaling in liver regeneration: Rapamycin combined with growth factor treatment., 2013, World J Transplant. 3(3):36-47. - Pan Q, Fouraschen SM, de Ruiter PE, Dinjens WN, Kwekkeboom J, Tilanus HW, van der Laan LJ., Detection of spontaneous tumorigenic transformation during culture expansion of human mesenchymal stromal cells., 2014, Exp Biol Med (Maywood);239(1):105-15. - 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, Culture expansion induces non-tumorigenic aneuploidy in adipose tissue-derived mesenchymal stromal cells., 2013, Cytotherapy; 5(11):1352 - Boor PP, Metselaar HJ, Mancham S, van der Laan LJ, Kwekkeboom J., Rapamycin has suppressive and stimulatory effects on human plasmacytoid dendritic cell functions., 2013, Clin Exp Immunol.;174(3):389-401. - Verhoeven CJ, Farid WR, de Ruiter PE, Hansen BE, Roest HP, de Jonge J, Kwekkeboom J, Metselaar HJ, Tilanus HW, Kazemier G, van der Laan LJ., MicroRNA profiles in graft preservation solution are predictive of ischemic-type biliary lesions after liver transplantation., 2013, J Hepatol.
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- Verhoeven CJ, Farid WR, de Ruiter PE, Hansen BE, Roest HP, de Jonge J, Kwekkeboom J, Metselaar HJ, Tilanus HW, Kazemier G, van der Laan LJ., MicroRNA profiles in graft preservation solution are predictive of ischemic-type biliary lesions after liver transplantation., 2013, J Hepatol.;59(6):1231-8.
- Ramakrishnaiah V, Thumann C, Fofana I, Habersetzer F, Pan Q, de Ruiter PE, Willemsen R, Demmers JA, Stalin Raj V, Jenster G, Kwekkeboom J, Tilanus HW, Haagmans BL, Baumert TF, van der Laan LJ., Exosome-mediated transmission of hepatitis C virus between human hepatoma Huh7.5 cells., 2013, Proc Natl Acad Sci U S A.;110(32):13109-13.
- Farid WR, de Jonge J, Zondervan PE, Demirkiran A, Metselaar HJ, Tilanus HW, de Bruin RW, van der Laan LJ, Kazemier G., Relationship between the histological appearance of the portal vein and development of ischemic-type biliary lesions after liver transplantation., 2013, Liver Transpl.;19(10):1088-98.
- Hernanda PY, Pedroza-Gonzalez A, van der Laan LJ, Bröker ME, Hoogduijn MJ, Ijzermans JN, Bruno MJ, Janssen HL, Peppelenbosch MP, Pan Q., Tumor promotion through the mesenchymal stem cell compartment in human hepatocellular carcinoma., 2013, Carcinogenesis. ;34(10):2330-40.
- Tjon AS, Tha-In T, Metselaar HJ, van Gent R, van der Laan LJ, Groothuisink ZM, te Boekhorst PA, van Hagen PM, Kwekkeboom J., Patients treated with high-dose intravenous immunoglobulin show selective activation of regulatory T cells., 2013, Clin Exp Immunol. ;173(2):259-67.
- van der Meer AJ, Farid WR, Sonneveld MJ, de Ruiter PE, Boonstra A, van Vuuren AJ, Verheij J, Hansen BE, de Knecht RJ, van der Laan LJ, Janssen HL., Sensitive detection of hepatocellular injury in chronic hepatitis C patients with circulating hepatocyte-derived microRNA-122., 2013, J Viral Hepat. 2013 Mar;20(3):158-66.
- de Mare-Bredemeijer EL, Mancham S, Utomo WK, de Canck I, van Thielen M, de Meester E, Rossau R, van der Laan LJ, Hansen BE, Tilanus HW, Kazemier G, Janssen HL, Metselaar HJ, Kwekkeboom J., Genetic polymorphisms in innate immunity receptors do not predict the risk of bacterial and fungal infections and acute rejection after liver transplantation., 2013, Transpl Infect Dis.;15(2):120-33.