

**Erasmus University Rotterdam, the Netherlands**  
**CSC PhD 2015 Project Description**

<b>School/Department:</b>	<p>Dept. of Gastroenterology and Hepatology  Erasmus Medical Center</p> <p>(Research school: Erasmus Postgraduate School Molecular Medicine)</p>
<b>Project Title:</b>	Unveiling virus-drug interactions in hepatitis E cell culture system
<b>Abstract:</b>	<p>Globally, hepatitis E virus (HEV) infection is the most common cause of acute viral hepatitis. Mortality rates range from 0.2% to 4.0% but are higher in infants under 2 years of age and it reaches 10% to 25% in pregnant women and recipients of solid organ transplantation. Unfortunately, no specific treatment is available and studies are hampered by the lack of a good model system.</p> <p>Our laboratory has implemented a most robust HEV cell culture system that was recently developed in NIH, US. In this project we aim to characterize the molecular details of HEV infection employing infection of untransformed hepatocytes generated from patient-derived Induced pluripotent stem cells. The biological effects of infection and the cellular consequences of immunosuppressants that are commonly used in organ transplant patients thereon will be characterized by kinome profiling. Thus, we hope to identify novel avenues for the rational treatment of this disease.</p>
<b>Requirements of candidate:</b>	<p>Master degree: Yes</p> <p>Background: Molecular Biology/Cell biology/Virology</p> <p>IELTS Grade: 7.0 (<i>minimal 6.0 per component</i>)  or  TOEFL: 100 (<i>minimal 20 per component</i>)</p>
<b>Supervisor information:</b>	<p><b>Prof.dr. H.J. Metselaar</b>  Dept. Of Gastroenterology and Hepatology  Erasmus MC University Medical Center Rotterdam  T: +31 10 7035942  E: <a href="mailto:h.janssen@erasmusmc.nl">h.janssen@erasmusmc.nl</a>  <a href="http://www.erasmusmc.nl/mdl/organisatie/?lang=en">http://www.erasmusmc.nl/mdl/organisatie/?lang=en</a></p> <p>Selected recent publications (from &gt;180 peer-reviewed publications):</p>

	<ul style="list-style-type: none"> <li>▪ van der Woude CJ, <b>Metselaar HJ</b>, Danese S. Management of gastrointestinal and liver diseases during pregnancy. <u><b>Gut</b></u>. 2014 Jun;63(6):1014-23. (IF : 13)</li> <li>▪ 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, <b>Metselaar HJ</b>. Genetic variance in ABCB1 and CYP3A5 does not contribute toward the development of chronic kidney disease after liver transplantation. <u><b>Pharmacogenet Genomics</b></u>. 2014 Sep;24(9):427-35. (IF: 3.5)</li> <li>▪ Wang Y, Zhou X, Debing Y, Chen K, Van Der Laan LJ, Neyts J, Janssen HL, <b>Metselaar HJ</b>, Peppelenbosch MP, <b>Pan Q</b>. Calcineurin inhibitors stimulate and mycophenolic acid inhibits replication of hepatitis E virus. <u><b>Gastroenterology</b></u>. 2014 Jun;146(7):1775-83. (IF: 13.9)</li> <li>▪ Zhou X, Wang Y, <b>Metselaar HJ</b>, Janssen HL, Peppelenbosch MP, <b>Pan Q</b>. Rapamycin and everolimus facilitate hepatitis E virus replication: Revealing a basal defense mechanism of PI3K-PKB-mTOR pathway. <u><b>J Hepatol</b></u>. 2014 May 22. (IF: 10.4)</li> <li>▪ Verhoeven CJ, Farid WR, de Jonge J, <b>Metselaar HJ</b>, Kazemier G, van der Laan LJ. Biomarkers to assess graft quality during conventional and machine preservation in liver transplantation. <u><b>J Hepatol</b></u>. 2014 May 4. pii: S0168-8278(14)00294-3. (IF: 10.4)</li> <li>▪ Verhoeven CJ, Farid WR, de Ruiter PE, Hansen BE, Roest HP, de Jonge J, Kwekkeboom J, <b>Metselaar HJ</b>, Tilanus HW, Kazemier G, van der Laan LJ. MicroRNA profiles in graft preservation solution are predictive of ischemic-type biliary lesions after liver transplantation. <u><b>J Hepatol</b></u>. 2013 Dec;59(6):1231-8. (IF: 10.4)</li> <li>▪ Saliba F, De Simone P, Nevens F, De Carlis L, <b>Metselaar HJ</b>, Beckebaum S, Jonas S, Sudan D, Fischer L, Duvoux C, Chavin KD, Koneru B, Huang MA, Chapman WC, Foltys D, Dong G, Lopez PM, Fung J, Junge G; H2304 Study Group. Renal function at two years in liver transplant patients receiving everolimus: results of a randomized, multicenter study. <u><b>Am J Transplant</b></u>. 2013 Jul;13(7):1734-45. (IF : 6.2)</li> <li>▪ <b>Metselaar HJ</b>, van Campenhout MJ, van der Eijk AA. The best way to prevent cytomegalovirus infection after liver transplantation: the debate goes on. <u><b>Transpl Int</b></u>. 2013 Jun;26(6):590-1. (IF : 3.1)</li> <li>▪ van der Laan LJ, Hudson M, McPherson S, Zondervan PE, Thomas RC, Kwekkeboom J, Lindsay AS, Burt AD, Kazemier G,</li> </ul>
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	<p>Tilanus HW, Bassendine MF, <b>Metselaar HJ</b>. Results of a two-center study comparing hepatic fibrosis progression in HCV-positive liver transplant patients receiving cyclosporine or tacrolimus. <u><b>Transplant Proc.</b></u> 2010 Dec;42(10):4573-7. (IF : 1)</p> <ul style="list-style-type: none"> <li>Tjon AS, Sint Nicolaas J, Kwekkeboom J, de Man RA, Kazemier G, Tilanus HW, Hansen BE, van der Laan LJ, Tha-In T, <b>Metselaar HJ</b>. Increased incidence of early de novo cancer in liver graft recipients treated with cyclosporine: an association with C2 monitoring and recipient age. <u><b>Liver Transpl.</b></u> 2010 Jul;16(7):837-46. (IF : 3.7)</li> </ul> <p>Co-supervision: <b>Dr. Q. Pan</b> Dept. Of Gastroenterology and Hepatology Erasmus MC University Medical Center Rotterdam T: +31 10 7037502 E: <a href="mailto:g.pan@erasmusmc.nl">g.pan@erasmusmc.nl</a> <a href="http://www.erasmusmc.nl/gastrolab/">http://www.erasmusmc.nl/gastrolab/</a></p> <p>Selected recent publications:</p> <ul style="list-style-type: none"> <li>Wang Y, Zhou X, Debing Y, Chen K, Van Der Laan LJ, Neyts J, Janssen HL, Metselaar HJ, Peppelenbosch MP, <b>Pan Q</b>. Calcineurin inhibitors stimulate and mycophenolic acid inhibits replication of hepatitis E virus. <u><b>Gastroenterology.</b></u> 2014 Jun;146(7):1775-83. (IF: 13.9)</li> <li>Zhou X, Wang Y, Metselaar HJ, Janssen HL, Peppelenbosch MP, <b>Pan Q</b>. Rapamycin and everolimus facilitate hepatitis E virus replication: Revealing a basal defense mechanism of PI3K-PKB-mTOR pathway. <u><b>J Hepatol.</b></u> 2014 May 22. (IF: 10.4)</li> <li>Zhou X, de Man RA, de Knegt RJ, Metselaar HJ, Peppelenbosch MP, <b>Pan Q</b>. Epidemiology and management of chronic hepatitis E infection in solid organ transplantation: a comprehensive literature review. <u><b>Rev Med Virol.</b></u> 2013 Sep;23(5):295-304. (IF: 5.8)</li> <li>Hernanda PY, Pedroza-Gonzalez A, van der Laan LJ, Bröker ME, Hoogduijn MJ, Ijzermans JN, Bruno MJ, Janssen HL, Peppelenbosch MP, <b>Pan Q</b>. Tumor promotion through the mesenchymal stem cell compartment in human hepatocellular carcinoma. <u><b>Carcinogenesis.</b></u> 2013 Oct;34(10):2330-40. (IF: 5.3)</li> <li><b>Pan Q</b>, Nicholson AM, Barr H, Harrison LA, Wilson GD, Burkert J, Jeffery R, Alison MR, Looijenga L, Lin WR, McDonald SA, Wright NA, Harrison R, Peppelenbosch MP, Jankowski JA. Identification</li> </ul>
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	<p>of lineage-uncommitted, long-lived, label-retaining cells in healthy human esophagus and stomach, and in metaplastic esophagus. <b><u>Gastroenterology</u></b>. 2013 Apr;144(4):761-70. (IF: 13.9)</p> <ul style="list-style-type: none"> <li>▪ <b>Qiuwei Pan</b>, Petra E. de Ruiter, Herold J. Metselaar, Jaap Kwekkeboom, Hugo W. Tilanus, Harry L.A. Janssen and Luc J.W. van der Laan. Mycophenolic acid augments interferon-stimulated gene expression and inhibits hepatitis C virus infection in vitro and in vivo. <b><u>Hepatology</u></b>. 2012 Jun;55(6):1673-83. (IF: 11.7)</li> <li>▪ <b>Qiuwei Pan</b>, Vedashree Ramakrishnaiah, Scot Henry, Suomi Fouraschen, Petra de Ruiter, Jaap Kwekkeboom, Hugo W. Tilanus, Harry L.A. Janssen and Luc J.W. van der Laan. Hepatic cell-to-cell transmission of small silencing RNA extends the therapeutic reach of RNAi against hepatitis C infection. <b><u>Gut</u></b>. 2012, Sep;61(9):1330-9. (IF: 13)</li> <li>▪ <b>Qiuwei Pan</b>, Hugo W. Tilanus, Herold J. Metselaar, Harry L.A. Janssen and Luc J.W. van der Laan. Virus-drug interactions-molecular insight into immunosuppression and HCV. <b><u>Nature Reviews Gastroenterology &amp; Hepatology</u></b>. 2012 Apr 17;9(6):355-62. (IF: 10.8)</li> </ul>
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