

PhD Project Description

School/Department:	Erasmus MC, Department of Surgery
Supervisor information:	<p>Prof. dr. Luc van der Laan & dr. Monique Verstegen l.vanderlaan@erasmusmc.nl / m.verstegen@erasmusmc.nl</p> <p>Selected publications:</p> <ul style="list-style-type: none"> - <i>Materials Science & Engineering</i>, 2020, Willemse, van der Laan & Verstegen, et al - <i>Transplantation</i>, 2020, Verstegen & van der Laan, et al - <i>Cancers</i>, 2019, van Tienderen, van der Laan & Verstegen, et al. - <i>Nature Medicine</i>, 2017, Broutier, Verstegen, van der Laan & Huch, et al. - <i>Nature</i>, 2016, Blokzijl, Verstegen, van der Laan & van Boxtel et al.
Project Title:	Exploring the regenerative potential of liver organoids in liver transplantation
Abstract:	<p>Although the adult liver is well-known for its regenerative capacity, the cellular events that drive this repair are pleiotropic and not fully elucidated. The two liver epithelial cell types, hepatocytes and cholangiocytes, have self-renewal capacity to maintain homeostasis and in response to liver injury. Moreover to the plasticity of epithelial cells, bipotent progenitor cells are found within the canals of Hering, the smallest branches of the biliary tree in the liver. These bipotent progenitor cells can differentiate into both mature hepatocytes and cholangiocytes. In larger bile ducts, including in the extrahepatic bile ducts, typical peribiliary glands harbor biliary progenitor cells which provide a proliferative response upon damage of the bile duct providing new cholangiocytes to restore the biliary lining. With the development of the 3D organoid culture technique, epithelial cells, including those found in the liver can be expanded <i>in vitro</i> (Huch et al, Cell, 2015) and used as model for stem cell biology and liver diseases such as Metabolic Associated Fatty Liver Disease (MAFLD) or primary liver cancer.</p> <p>The projects in our lab involve the use of biliary organoids to model liver-related disease (MAFLD, Allagile Syndrome, Cystic Fibrosis), study liver and bile duct regeneration (by developing liver-on-a-chip technology), and liver and bile duct tissue engineering (decellularisation techniques and extracellular matrix analysis).</p> <p>During liver transplantation performed in Erasmus MC, biopsies are collected from liver and extrahepatic bile duct from donor and recipient (explanted liver) to be used in research projects. These biopsies are analyzed using histological techniques (immunohistochemistry, immunofluorescence, conventional, confocal and light-sheet microscopy) and molecular biological techniques (qPCR, RNA-expression arrays and whole genome sequencing). In addition, the LGR5-positive, Wnt-responsive adult stem cells from liver and the extrahepatic bile duct, will be cultured and expanded as organoids to be used as (patient-specific) models for liver regeneration and/or disease, including primary liver cancer.</p> <p>Main methodology and techniques: 3D biliary organoid cultures from healthy donor and patient biopsies (NASH, primary liver cancer). Gene expression analysis (single cell RNA sequencing, RT-qPCR), high resolution imaging (OIC-confocal, fluorescence microscopy), protein expression analysis (FACS, Immunohistochemistry, Western blotting).</p>
Requirements of candidate:	<ul style="list-style-type: none"> • We are looking for a highly motivated PhD student who has received excellent scientific and practical training in the areas of stem cell biology, transplantation medicine and/or regenerative medicine to join our research team. • The student should be fluent in English (IELTS <i>min</i> 6.0), TOEFL 100 (<i>min</i> 20 for all subs). • We offer: Supervision, lab facilities and infrastructure, and training. We will cover Laboratory costs. As a candidate PhD student at Erasmus MC, your salary and living expenses will be covered by your University or Scholarship Council.

Application requirements & Deadlines:

<https://www.eur.nl/en/about-eur/erasmus-university-china-centre/csc-scholarship>

Erasmus MC, ranked world

* No.32 for Clinical Medicine US News 2020:

<https://www.usnews.com/education/best-global-universities/clinical-medicine?page=3>

* No. 30 Nature Index for Biomedical Sciences 2019:

<https://www.natureindex.com/supplements/nature-index-2019-biomedical-sciences/tables/healthcare>