

PhD Project Description

School/Department:	Department of Biochemistry, Erasmus MC
Supervisor information:	<p>Prof. dr. Tokameh Mahmoudi, PhD, t.mahmoudi@erasmusmc.nl</p> <p><u>Selected personal grants:</u> ERC StG laureate (2014)</p> <p><u>Selected publications:</u></p> <p>2019 BioRxiv (and under review eLife) de Crignis E et al. Human liver organoids; Modelling HBV Infection, Replication and Related Tumorigenesis. doi: https://doi.org/10.1101/568147</p> <p>2012 <i>Cell</i> Li VS, Ng SS, Boursma P, Karthaus RW, Gerlach JP, Mohammed S, Heck AJ, Maurice MM, Mahmoudi T*, and Clevers H*. Wnt pathway activation through inhibition of proteosomal b-catenin degradation within the intact endogenous Axin1 complex. 149(6):1245-56.</p>
Project Title:	Liver organoid-tumoroid platform in study of HBV infection and tumorigenesis
Abstract:	<p>Project Summary Persistent Hepatitis B virus (HBV) infection remains the leading cause of liver cirrhosis and hepatocellular carcinoma world-wide. However, identification and study of the molecular events that occur as consequence of HBV infection and which mediate onset of hepatocellular carcinoma have been greatly hindered because of the lack of a relevant primary untransformed model system. The stem cell based liver organoid / tumoroid technology for the first time allows the culturing, expansion, banking, differentiation of hepatocytes from healthy donors or infected patients at various stages of disease (Huch M et al., 2015). My group has also recently developed a primary HBV infected and patient-derived human liver organoid model system (de Crignis et al, 2019) which for the first time allows long term culturing and analysis of HBV infected patient livers providing a platform suitable for antiviral drug screening and examination of HBV-induced mechanisms of liver pathogenesis and HCC. We have generated HBV infected patient and healthy liver organoid culture lines seeded from surgically explanted tissue. Human liver organoids are infected with both recombinant virus as well as HBV infected patient serum and determinants of infection and viral replication are examined. We will perform drug and toxicity screens using the HBV infected liver organoid platform and also examine the role of various pathways implicated in liver cancer such as Wnt-beta-catenin (Li VS et al <i>Cell</i> 2012), p53 and Ras in the organoid model. Transgenic liver organoid lines including those that exogenously express the HBV receptor NTCP or the viral gene HBX, E and core Antigens are also generated and molecular determinants of infection and oncogenesis are investigated using these tools.</p> <p>Main methodology and techniques 3D liver organoid cultures from healthy donor, HBV infected and hepatocellular carcinoma patients, Next generation sequencing analysis of chromatin and gene expression (ChIP-seq and RNA-seq) , High resolution imaging (OIC-confocal, fluorescence microscopy), Flow Cytometry Activated Cell Sorting, Lentiviral transduction and gene editing</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 Molecular Virology or Molecular Biology who also has some basic training or interest in bioinformatics to join our research team. The student should be fluent in English (<i>English speaking countries & Netherlands</i>: no requirement; <i>Other countries</i>: IELTS 7.0 (<i>min 6.0 for all subs</i>), TOEFL 100 (<i>min 20 for all subs</i>). 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. For more information regarding this vacancy, please contact t.mahmoudi@erasmusmc.nl.

Application requirements & Deadlines:

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

* Erasmus MC, ranked world no32 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>