Erasmus MC, ranked world no13-36 for clinical fields by USNews 2021, no 30 Nature Index for Biomedical Sciences 2019

PhD Project Description

School/Department:	***Department of Biochemistry, Erasmus MC***
Supervisor information: Selected grants: ERC StG laureate (2014), Health Holland, ZonMW (2019) 	Prof. dr. Tokameh Mahmoudi, PhD, t.mahmoudi@erasmusmc.nl Selected publications: 2021 Elife 10:e60747. de Crignis E, Hossain T, Romal S, Carofiglio F, Moulos P, Khalid MM, Rao S, Bazrafshan A, Verstegen MM, Pourfarzad F, Koutsothanassis C, Gehart H, Kan TW, Palstra RJ, Boucher C, IJzermans JN, Huch M, Boj SF, Vries R, Clevers H, van der Laan LJ, Hatzis P, Mahmoudi T. Application of human liver organoids as a patient-derived primary model for HBV infection and related hepatocellular carcinoma. doi: 10.7554/eLife.60747. 2021 Nature Communications. doi: 10.1038/s41467-021-22608-z. Rao S, Lungu C, Crespo R, , Steijaert TH, Palstra R-J , Prins HAB , van IJcken W, Mueller Y, van Kampen JA, Verbon A , Katsikis P, Boucher CAB, Rokx C, Gruters RA. Mahmoudi T.Selective cell death in HIV-1-infected cells by DDX3 inhibitors leads to depletion of the inducible reservoir 2021 Cell Death Dis. Clark MP, Huynh T, Rao S, Mackiewicz L, Mason H, Romal S, Stutz MD, Ahn SH, Earnest L, Sozzi V, Littlejohn M, Tran BM, Wiedemann N, Vincan E, Torresi J, Netter HJ, Mahmoudi T, Revill P, Pellegrini M, Ebert G. Clinical stage drugs targeting inhibitor of apoptosis proteins purge episomal Hepatitis B viral genome in preclinical models. 12(7):641. 2021 Cancer Lett. 3D human liver organoids: An in vitro platform to investigate HBV infection, replication and liver tumorigenesis. Rao S, Hossain T, Mahmoudi T. 506:35-44. 2012 Cell 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 bcatenin degradation within the intact endogenous Axin1 complex.149(6):1245-56.
Project Title:	Human liver organoid-tumoroid platform in study of HBV infection and tumorigenesis
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 (confocal, fluorescence microscopy), Flow Cytometry Activated Cell Sorting, Lentiviral transduction and gene editing, molecular biology and molecular virology techniques. Lab webpage: Mahmoudilab.com	**Project Summary** Persistent Hepatitis B virus (HBV) infection remains the leading cause of liver cirrhosis and hepatocellular carcinoma world-wide. However, the molecular events that occur as consequence of HBV infection and which mediate onset of hepatocellular carcinoma have remained elusive because of lack of a relevant primary untransformed model system. My group, in collaboration with the HUB has recently developed a patient-derived HBV infected human liver organoid model system (de Crignis 2021), using the adult stem cell human liver organoid/tumoroid technology (Huch 2015), which allows long term culturing and analysis of HBV infected patient or healthy donor livers providing a platform suitable for antiviral drug screening and examination of HBV-induced mechanisms of liver pathogenesis and HCC. 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 generate transgenic organoids to study the function of viral and host factors and perform drug and toxicity screens using the HBV liver organoid platform and examine the role of various pathways implicated in liver cancer such as Wnt-bcatenin (Li VS 2012), and epigenetic regulators 
Requirements of candidate: contact t.mahmoudi@erasmusmc.nl.	• 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 (*English speaking countries & Netherlands:* no requirement; *Other countries:* IELTS 7.0 *(min 6.0 for all subs)*, TOEFL 100 *(min 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. For more information, please contact prof Mahmoudi