



Samenvatting proefschrift Geert Nibourg

‘Human liver cell lines for the AMC-bioartificial liver’

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Promotor:

Prof. dr. T.M. van Gulik

Co-promotor:

Dr. R.A.F.M. Chamuleau

Dr. R. Hoekstra

Acute liver failure (ALF) is a devastating disease and liver transplantation is the only lifesaving treatment. However, each year many patients die on the waiting list for liver transplantation, as there is a shortage of donor livers. A bioartificial liver (BAL) can temporarily support the failing liver and thereby bridge patients with ALF to liver transplantation, or preferably, to liver regeneration. A BAL comprises a bioreactor that is loaded with a biocomponent (cells) that can be connected to the patient's blood stream outside the body. This way, the BAL takes over the function of the failing liver. A critical factor in BAL development is the biocomponent, which should be expandable, from human origin, and be able to take over all of the liver's many functions. In eleven chapters, this PhD thesis describes this search for a suitable biocomponent, which led to the human liver cell line HepaRG. Firstly, we analysed monolayer cultures of HepaRG extensively for a broad spectrum of hepatic functions most relevant for BAL therapy and improved the hepatic functionality by optimizing the culture protocol. Subsequently, we cultured the HepaRG cells in the AMC-BAL and likewise optimized the hepatic functionality of this HepaRG-AMC-BAL. The AMC-BAL culture increased the viability and hepatic functionality of the HepaRG cells to unique high levels. Subsequently, we tested the HepaRG-AMC-BAL for efficacy in a rat model of ALF and demonstrated that treatment of these rats with the HepaRG-AMC-BAL increased their survival time with 50%. In addition, we studied the effects of toxic ALF plasma and of medium flow rate on the functionality of the HepaRG-AMC-BAL. The studies in this thesis have led to a HepaRG-AMC-BAL with proven efficacy and have paved the way for clinical studies with the HepaRG-AMC-BAL in patients with ALF, planned in 2015. ◀

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