Towards a bioartificial liver

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What is the vision that led to the establishment of a research consortium between EILF and Research Centers in Europe and USA?

The goal and vision of the consortium: working towards the development of a bio-artificial liver by launching and promoting a compelling and dedicated fundraising program; special target focus children.

The EASL Foundation is proud to announce a most innovative program aiming at pursuing the dream of creating a 'bioartificial liver'.

There are presently hundreds thousands of people on the organ wait list, many of whom will die before finding a compatible donor. Even those fortunate enough to receive an organ in time face ongoing medical difficulties, often for the rest of their lives.

Recent technical achievements in stem cell research, tissue engineering and whole organ regeneration and preservation offer potentially powerful solutions to this public health problem. Regenerative medicine is advancing towards the final frontier, i.e. the assembly of vital organs to definitively solve the organ donor shortage.

However, tissue engineering research and regenerative medicine research is currently underfunded, receiving less than $500 million annually in the U.S. compared to $5 billion for cancer and $2.8 billion for HIV/AIDS.

The aim of the EASL Foundation program is to accelerate academic research in Europe to address key challenges in this field and resolve the remaining technical problems in order to bring this life saving technology to all of the people who desperately need it.

Two key programs will be addressed by the Consortium established after the first EASL Foundation meeting held in Paris on May 2nd 2017:

1. Regeneration of 5% liver mass
2. Regeneration of 30% of liver mass

These ambitious programs bring together international renowned experts and pioneering in the field of hepatology, hepatocyte transplantation in paediatric patients, stem cells, biomaterials and tissue engineering coming from the most prestigious universities.

The first program aims at recreating in the lab up to 5% of the liver mass in order to develop "tissue-patches" for the treatment of inherited metabolic **paediatric** patients. Liver-based inborn errors of metabolism such as urea cycle defects, Crigler–Najjar syndrome type 1, factor VII deficiency, glycogen storage disease type I, and infantile Refsum's disease are life- threatening conditions with a complex and expensive management. These conditions require liver transplantation even though the metabolic defects are typically the result of a single enzyme deficiency in a liver that otherwise functions normally. Although outcomes following liver transplantation are excellent, this is not an ideal solution. More than 35,000 patients currently await liver transplantation in Europe and the United States and 20%-15% of patients die on the waiting list. Patients would therefore benefit from development of novel approaches to liver replacement due to the lack of donors and the procedure being particularly risky in some patient groups (e.g. mortality over 50% in patients with organic acidaemias).

The novel approach proposed by the Consortium relies on the development of tissue-patches composed of human ECM hydrogels or other biomaterials as 3D scaffolds combined with primary human hepatic cells and stem cells as shown in Figure 1.

Figure 1. Schematic view of the tissue-patches approach

The second program aims at recreating 30% of the liver mass corresponding to the same amount of hepatic mass used for living-donor transplant. In living donor liver transplant a section of liver is removed from a living donor; because the liver can regenerate itself, both the transplanted section and the remaining section of the donor's liver are able to regrow into a normal-sized liver.

Deaths from chronic liver disease caused by viral infections, alcohol and metabolic conditions are increasing worldwide. According to the World Health Organisation, the total deaths caused by cirrhosis and liver cancer have increased by 50 million/year since 1990. At present, liver transplantation is the only successful treatment for patients with end stage liver disease. However, 20%-15% of patients die on the waiting list due to a shortage of organ donors. Therefore, novel strategies are needed in order to meet the demand of organs for liver transplant. Several studies published from members of this Consortium reported the development of liver 3D whole organ scaffolds from both animal and human tissues. The resulting 3-dimensional ECM scaffolds have been shown to provide an excellent environment for the *in vitro* growth of multiple liver cell types retaining excellent functionality as well as in vivo biocompatibility after transplantation in animals.

The novel approach proposed by the consortium is based on the development of whole organ biological scaffolds repopulated with different types of human cells as shown in Figure 2.

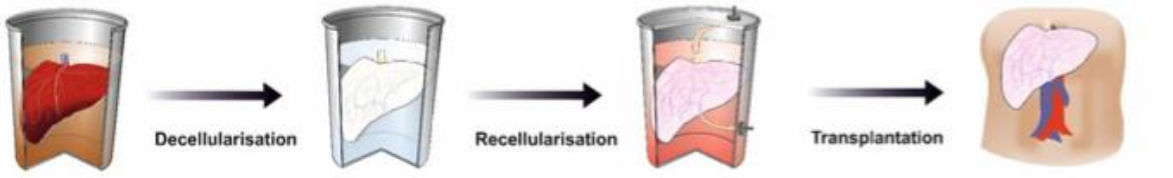

Figure 2. Schematic view of the whole organ engineering approach