The Importance of Stem Cells and Bioengineering in Regenerative Medicine

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The field of regenerative medicine is focused on the creation of functional human tissue to either model, repair or replace the damaged body part. This provides promise that in the future scientists will be able to bioengineer human tissue in vitro [1,2] that may allow the identification of novel medicines and has the potential for cell based therapies. If successful, such approaches could have a significant impact on the problem donor organ shortage for transplantation and improve patient treatment and medication.

The liver is a fascinating organ, performing many processes necessary for life. In addition to its broad functional repertoire, the liver is the only human organ capable of large scale regeneration. Only 20-30% of healthy liver mass is required liver regeneration. The primary regenerative response of the liver is provided by its principal cell type, the hepatocyte. However when the liver is overloaded or chronically damaged, the hepatocyte response is inhibited, prompting the activation of a resident stem cell population. In both cases, acute and chronic liver injury may result in irreparable loss of human liver function marking the onset of liver disease. Presently the only real treatment strategy for critically failing liver function is organ transplantation. While highly successful, the shortage of donor organs limits its widespread implementation. The generation of liver tissue from a renewable resource therefore holds great promise for the development of extra-corporeal liver support devices and transplantation procedures.

In addition to cell based therapies, the field of regenerative medicine also offers the ability to engineer tissue to model human biology in a dish. Moreover, with modern stem cell technology, it is now possible to select the genotype of interest which has sophisticated the study of human health and disease [9]. The bioengineering of such a resource in 3-dimensions holds great promise and has already led to the construction of predictive human prototypes for the testing of drug safety and efficacy [1]. In the future this type of approach will undoubtedly lead to the development of novel and more specific classes of drugs for human use. Presently, the process for bringing a new drug to market is estimated to take over 12 years and cost between $800m and $2b [3]. A substantial amount of this cost is incurred through attrition or failure. Unsurprisingly, the later a compound fails in this process, the greater the cost reinforcing the need for front loading of more accurate and predictive toxicity assays in preclinical drug development.

Given the scarcity of human liver and the instability of the hepatocyte, research has focussed on the provision of renewable and scalable sources of human hepatocytes. Stem cells are a cell type which offer great promise in this area [4] and are found in all multi-cellular organisms. Stem cells are capable of cell division and produce identical copies of themselves or differentiate into specialized cell types. With an understanding of the basic biology, stem cells represent an unlimited resource to develop novel medicines and cell based therapies. The work in my laboratory is focussed on generating and engineering human hepatic tissue for these purposes. We have published extensively in this field [1,2,4-15] and have developed stable human resources from pluripotent stem cells. Our goal in the future is to further stabilise and mature these human resources to better interrogate the basic biology. This will result in the development of higher fidelity human hepatocytes for drug development and a clinical grade resource capable of providing liver support.

References


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