

The Importance of Hepatocyte Transplantation

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Abstract

To overcome the complication of Orthotopic Liver Transplantation (OLT) the techniques of hepatocyte transplantation has been taken into consideration. Comparing to OLT, hepatocyte transplantation is cost-effective, less invasive, cryo-preservable and can be distributed to multiple recipients from the single donor. There is the number of clinical studies that showed the survival rate of the patient transplanted with hepatocyte is significantly higher comparing to non-transplanted patients. Therefore, this short communication enlightens the importance of hepatocyte transplantation.

Keywords: Hepatocyte; Transplantation; Liver Transplantation

Introduction

Liver is the center for metabolism of every foreign substance. Almost all the drug and xenobiotics are lipophilic and liver enables them to cross the membranes of intestinal cells [1]. Because of its central role in metabolizing the drugs and xenobiotics, it possesses toxicity threats leading to hepatic injury [2]. Though the liver is the organ of unique potential to auto regenerate but repeated liver injury leads the organ towards chronic liver injury and liver failure. OLT is the therapy of choice for the patient with end-stage liver disease but the unavailability of compatible organ donor, increase mortality of organ recipient, complex surgical procedure, expensive operating cost and life-long use of immune-suppressive drugs limits the usefulness of liver transplantation [3]. Moreover it is estimated that in united states alone 2200 patients die while awaiting for liver transplantation [4].

Hepatocytes are widely used for numerous clinical and research applications but their short life span and limited capacity of replication limits the usefulness of the culture of primary hepatocytes. Hepatocytes can be isolated from whole liver, wedge fragments of liver unsuitable for liver transplantation and mostly from the primary and secondary tumor or some other diseased part. Hepatocytes isolated in this way exhibits the identical functions and structures with *in vivo* counterparts but losses specialized membrane domains like bile canaliculi and inter cellular junctions and have very short life span in suspension. For long survival, a substratum

is needed for attachment. When the primary hepatocytes plated in a culture condition, they reconstitute bile canaliculus like structure by re-aggregating and exhibit early phenotypic alteration by showing the short life span of few days [5].

Despite achieving considerable improvement in the cryopreservation and storage of primary hepatocytes, The requirement of large amount of primary hepatocytes for clinical and research purpose limits the availability [6-9]. Since the standards in drug testing are strict, the demand of primary hepatocytes has been continually increasing [10,11]. Moreover the source of primary hepatocytes is limited and the time of procurement is lengthy, expensive and logistically demanding, to overcome this shortage of primary hepatocytes animal cell source and immortalized human hepatocytes have been purposed for alternative clinical approach [12]. Many laboratory animals (rat, mouse, pig) have common characteristic features with human hepatocytes [13,14] and are frequently available on demand and have higher rate of proliferation of hepatocytes *in vivo* [15]. Though some characteristics features are similar with human hepatocytes, it is difficult to extrapolate the data from animal experiment to functional mechanism of human. Immortal human hepatocytes shows the specific advantage but in comparison of primary hepatocytes, the immortalized hepatocytes exhibit the functional limitations, although the number of studies showed the positive impact [16-18]. The cell line which possess high cytochrome P450 activity for detoxification, ability of synthesizing the

higher level of glutamine synthase, can expand in-vivo, and the cell line with no risk of xenogeneic antigenicity and zoonosis are considered as ideal hepatocytes cell line [19].

Hepatocytes are responsible for protein synthesis, they manufacture the main component of cytoskeleton e.g. albumin, prothrombin, fibrinogen and clotting factors, additionally, hepatocytes synthesize lipoprotein, ceruloplasmin, transferrin and glycoproteins, they also manufacture their own structural proteins and enzyme. Furthermore, carbohydrate and lipid metabolism, detoxification of exogenous and endogenous compounds are also the main functions of hepatocytes [20]. Before transplantation of the immortalized hepatocytes the hepatocyte specific characteristics must be examined. The cell line having sufficient hepatocytes specific functions are suitable for transplantation [21].

Conclusion

OLT is the therapy of choice for end-stage liver disease, the unavailability of the compatible organ donor, complex surgical procedure, increased mortality of organ recipient limits the applicability of OLT. Therefore, the necessity of hepatocyte transplantation arises as a potential alternative for the patient with end-stage liver disease. Thus hepatocyte cell lines that are identical with in-vivo counterpart can be used for the patient waiting for liver transplantation. There are a significant number of clinical studies which showed that the survival rate of a patient with hepatocyte transplantation is significantly higher as compared with the non-transplanted patient.

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