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Hepatocytes produced from human tooth pulp into swine with cirrhosis: two transplantations with time interval

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We treated the liver cirrhosis by two step transplantations of hepatocyte produced from human exfoliated deciduous tooth (SHED) into the swine with cirrhosis. SHED at three passages was separated by magnetic sorting with CD117 antibody. For hepatic differentiation, CD117+SHED was grown in DMEM supplemented with insulin-transferrin-selenium-x (ITS-x), embryo-tropic-factors (ETF) and hepatocyte-growth-factor (HGF) for five days; IMDM supplemented with ITS-x, ETF, HGF, dexamethasone and oncostatin for another 11 days. F344-Nude rats were employed for this study. Carbon tetrachloride (CCl₄) was administrated by intraperitoneal injection for 15 weeks to induce cirrhosis. Hepatocyte-like-cells (2x10⁶ cells/animal) suspended in Hank's Balanced Salt Solution were transplanted into the spleen. The vehicle was injected to the positive control group. Non-cirrhosis-models were used as negative control group. Animals were sacrificed for four weeks after the transplantation. Then five weeks later, the second transplantation was carried out, and then the swine were euthanized. Immunocytochemistry observation of the hepatically differentiated cells strongly demonstrated positive staining for albumin, IGF-1, α -feto-protein, HNF4 α and CPS-1. The histopathological analysis, HE and Masson's trichrome staining, indicated a significant decrease of fibrous tissue in the transplantation group with comparing to the positive control group. Healthy liver tissues were recovered by the transplantation. Moreover, serological test results revealed significance differences between the groups. Serum ALT levels of the test group dramatically decreased to one third compared to the positive control group. Activities of albumin, bilirubin, BUN, HA levels were also recovered. By only one transplantation albumin value was improved, but two steps showed much better improvement. The two steps transplantations of hepatocyte-like cells from human tooth transplanted into the liver with severe failure demonstrated their capacity to preform positively because of drastic decreasing fibrous tissues. Together, these findings suggested that two steps transplantation is a future potential protocol for treating chronic liver injuries such as cirrhosis.

Biography

Yaegaki K has received his Doctor of Dental Science and then completed his PhD in Medicine from Kurume University (Medical Biochemistry) and Post-doctoral studies from University of British Columbia. He was trained as an Oral Maxillofacial Surgeon at School of Medicine Kurume University. His specialty was facial injuries. He is the Director and Head of Oral Health at Nippon Dental University, which is the oldest dental school in Asia. He is also a Dean of PhD program and has published more than 100 papers and 20 books

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