Immunolocalization of VEGF A and Its Receptors, VEGFR1 and VEGFR2, in the Liver From Patients With Biliary Atresia.

Edom PT, Meurer L, da Silveira TR, Matte U, Dos Santos JL.

Source

Laboratório Experimental de Hepatologia e Gastroenterologia do Centro de Pesquisas do Hospital de Clínicas de Porto Alegre †Department of Pathology Postgraduate Departments of ‡Gastroenterology §Pediatrics, Medicine School, Universidade Federal do Rio Grande do Sul, Porto Alegre, Rio Grande do Sul.

Abstract


In biliary atresia (BA), a cholangiopathy of elusive etiology invariably leads to cirrhosis, and a disturbed angiogenesis may be involved. We evaluated the hepatobiliary immunolocalization of vascular endothelial growth factor (VEGF) A, VEGF receptor 1 (R1), and R2 in BA. We analyzed biopsies obtained at portoenterostomy from infants with BA (n=52), including embryonic (n=14) and perinatal (n=38) types. Controls were infants with intrahepatic cholestasis (IC; n=7). In BA, VEGF A immunolocalization was also evaluated in explants (n=33) and at the porta hepatis (n=16).
Nonalcoholic fatty liver disease is currently one of the most common forms of liver disease, covering cases from simple steatosis without inflammation, to cases of steatohepatitis and fibrosis, and may lead to liver cirrhosis and hepatocellular carcinoma.
Hepatocellular carcinoma (HCC) is the sixth most common cancer in the world in terms of incidence, accounting for approximately 630 thousand new cases per year; in addition, HCC is the third most common cause of cancer death. Worldwide, the greatest risk factors for HCC are the infections caused by hepatitis B and C viruses, which increase the risk of developing the disease by about 20 times. The standard treatment in the early stages of the disease, such as surgical resection, local ablation and liver transplantation, are able to cure a proportion of patients, but most cases of HCC present in advanced stages, precluding the use of such treatments with curative intent. One such drug is Sorafenib, a kinase inhibitor with antiangiogenic and antiproliferative properties. In conclusion, Sorafenib has demonstrated survival benefits in patients with advanced HCC, thus representing a new standard reference for systemic treatment in these cases.


Bone marrow mononuclear cell therapy for patients with cirrhosis: a Phase 1 study.


Source

Internal Medicine Department, Federal University of Rio de Janeiro,

Abstract
Bone marrow-derived cell therapy has been investigated in patients with severe liver disease.

To assess the feasibility, safety and cell kinetics of autologous bone marrow-derived mononuclear cells (BMMCs) infusion in cirrhotic patients.

BMMCs were isolated from autologous bone marrow and 10% of the cells were labelled with (99m)Tc-SnCl₂. Whole body scintigraphy (WBS) was performed 3 and 24 h after infusion via the hepatic artery. Liver function and image were followed during 1 year.


Nucleoplasmic calcium regulates cell proliferation through legumain.

Andrade VA, Guerra MT, Jardim CA, Melo FM, Silva WA, Ortega MJ, Robert ME, Nathanson MH, Leite MF.

Source


Department of Biochemistry and Immunology, Federal University of Minas Gerais, Belo Horizonte.

Abstract

Nucleoplasmic Ca(2+) regulates cell growth in the liver, but the proteins through which this occurs are unknown.
We used Rapid Subtraction Hybridization (RaSH) to subtract genes in SKHep1 liver cells expressing the Ca(2+) buffer protein parvalbumin (PV) targeted to the nucleus, from genes in cells expressing a mutated form of nuclear-targeted PV which has one of two Ca(2+)−binding site inactivated. The subtraction permitted selection of genes whose expression was affected by a small alteration in nuclear Ca(2+) concentration.

RESULTS:

The asparaginyl endopeptidase legumain (LGMN) was identified in this screening. When Ca(2+) was buffered in the nucleus of SKHep1 cells, LGMN mRNA was decreased by 97%, in part by a transcriptional mechanism, and decreased expression at the protein level was observed by immunoblot and immunofluorescence. Treatment with Hepatocyte Growth Factor increased LGMN expression. Knockdown of LGMN by siRNA decreased proliferation of SKHep1 cells by ~50% as measured both by BrdU uptake and mitotic index, although an inhibitor of LGMN activity did not affect BrdU incorporation. A significant reduction in the fraction of cells in G2/M phase was seen as well. This was associated with increases in expression of cyclins A and E. Furthermore, LGMN expression was increased in hepatocellular carcinoma cells relative to normal hepatocytes in the same specimens.

CONCLUSIONS:

These findings suggest a new role for LGMN and provide evidence that nuclear Ca(2+) signals regulate cell proliferation in part through modulation of LGMN expression. Increased expression of LGMN may be involved in liver carcinogenesis.