

# 1

*by* Pratika Y

---

**Submission date:** 10-Jun-2020 02:29AM (UTC+0300)

**Submission ID:** 1340964764

**File name:** 4.\_Human\_Liver\_Carcinomas\_Recruit.pdf (64.36K)

**Word count:** 1064

**Character count:** 6239

treated patients with low pretreatment miR-223 expression is longer in comparison to those with high miR-223 expression. This suggest that miR-223 might predict the success of Sorafenib treatment.

Acknowledgement: This work was supported by grants from the Hungarian Scientific Research Found OTKA K101435 and OTKA T75468.

#### 1049

##### **microRNA EXPRESSION DIFFERS IN EMBRYONAL AND FETAL SUBTYPES IN HUMAN HEPATOBLASTOMA**

M. Gyugos<sup>1</sup>, G. Lendvai<sup>1</sup>, I. Kenessey<sup>1</sup>, K. Schlachter<sup>1</sup>, A. Kiss<sup>1</sup>, P. Nagy<sup>2</sup>, M. Garami<sup>3</sup>, Z. Bab<sup>3</sup>, Z. Schaff<sup>1</sup>. <sup>1</sup>2nd Department of Pathology, <sup>2</sup>1st Department of Pathology and Experimental Cancer Research, <sup>3</sup>2nd Department of Pediatrics, Semmelweis University, Budapest, Hungary

E-mail: gyugosmonika@gmail.com

**Background and Aims:** Hepatoblastoma (HB) is the most common primary liver cancer in childhood, which has epithelial, mixed (epithelial and mesenchymal) and non specified types, based on tissue components. Since the prognosis of the two epithelial subtypes, embryonal and fetal, is different, we aimed to examine whether these differences were present at microRNA (miRNA) expression level as well.

**Methods:** Total RNA was isolated from 56 formalin fixed paraffin-embedded samples consisting of 15 embryonal, 22 fetal and 19 non-tumorous surrounding liver samples taken from 26 patients. Following DNase treatment, the expression of 14 microRNAs was determined using TaqMan MicroRNA Assays. Relative expression was calculated applying the average of miR-140 and miR-328 expressions as the reference. Statistical analysis was performed using Wilcoxon matched pairs, Kruskal-Wallis and Log-Rank tests.

**Results:** In 56 samples, elevated expression levels of miR-18a, miR-96 and miR-224 were found in the embryonal component compared to fetal. As compared to non-tumorous surrounding liver samples, decreased miR-17-5p, miR-122, miR-195, miR-210, miR-214 levels and increased miR-221 level were detected in fetal subtypes, furthermore decreased miR-122 and miR-214 levels were found in the embryonal components.

Survival analysis revealed low expression level and better Overall-Survival (OS) and Event Free Survival (EFS) in case of miR-224. These results were statistically significant ( $p < 0.05$ ).

**Conclusion:** The results indicate that different miRNA expression patterns exist in the epithelial hepatoblastoma subtypes. Interestingly, the up- and downregulation of miR-17-5p and miR-210 in HB differed from that reported in hepatocellular carcinoma. Acknowledgement: This study was supported by grant OTKA T75468 from the National Scientific Research Foundation.

#### 1050

##### **HUMAN LIVER CARCINOMAS RECRUIT MESENCHYMAL STEM/STROMAL CELLS THAT CAN PROMOTE TUMOR GROWTH VIA PARACRINE SIGNALING**

P. Hernanda<sup>1</sup>, A. Pedroza-Gonzales<sup>1</sup>, L.J.W. van der Laan<sup>2</sup>, H.L.A. Janssen<sup>1</sup>, M.P. Peppelenbosch<sup>3</sup>, Q. Pan<sup>1</sup>. <sup>1</sup>Gastrology and Hepatology, Erasmus Medical Centre, <sup>2</sup>Department of Surgery and Laboratory of Experimental Transplantation and Intestinal Surgery, <sup>3</sup>Gastrology and Hepatology, Erasmus MC University Medical Center, Rotterdam, The Netherlands

E-mail: p.hernanda@erasmusmc.nl

**Background and Aims:** Bone marrow mesenchymal stem/stromal cells (MSCs) can migrate to tumor sites and contribute to the tumor microenvironment. However, it is still hotly debated whether MSCs have a positive or negative effect on tumor growth. This study aims to investigate whether human liver carcinomas contain MSCs and whether MSCs may affect tumor growth.

**Methods:** MSCs were cultured from surgical resected hepatocellular carcinoma (HCC) (n=6) and liver metastatic colorectal tumor (LM-CRC) (n=7). Immunohistochemical staining of STRO-1 (the best-known MSCs marker for in vivo detection) was performed in paraffin-embedded patient HCC and LM-CRC tissues (n=24). The effects of MSCs on tumor growth were evaluated in immune-deficient mice.

**Results:** Solid tumors formed in mice by subcutaneous engraftment of human hepatoma Huh7 cells were able to recruit MSCs. MSCs were also found in patient liver tumors (successfully cultured from 11 out of 13 liver tumors). Their MSC properties were characterized by adipocyte and osteocyte differentiation and common mesenchymal markers. Notably, in situ staining showed that STRO-1 positive cells are significantly enriched in the tumor, in particular the tumor-stromal region, compared with the adjacent area in HCC and LM-CRC tissues (n=24,  $p < 0.01$ ). In mice, co-implantation of Huh7 and MSCs resulted in significant larger tumors than engraftment of Huh7 alone (tumor weight  $1.56 \pm 0.27$  g Vs  $0.44 \pm 0.19$  g, Mean $\pm$ SEM, n=8,  $p < 0.01$ ). Consistently, co-culturing Huh7 with irradiated MSCs significantly increased the number ( $196 \pm 29$  Vs  $123 \pm 36$  clones/5000 Huh7, Mean $\pm$ SD, n=5,  $p < 0.01$ ) and the size ( $1329 \pm 258$  Vs  $270 \pm 155$  pixels, n=5,  $p < 0.01$ ) of formed colonies. This effect was also observed by treatment of MSCs conditioned medium (MSC-CM), suggesting secreted tropic factors contributing to the tumor promoting effect. Genome-wide gene expression array and pathway analysis confirmed the up-regulation of cell growth and proliferation-related processes and down-regulation of cell death-related pathways by treatment of MSC-CM in Huh7 cells.

**Conclusion:** Human liver carcinomas recruit MSCs, which in turn can promote tumor growth. These results shed new light on the crosstalk between MSCs with liver cancer cells but also caution stem cell therapy of using MSCs for liver cancer and other liver diseases with high risk of developing malignancy.

#### 1051

##### **THE MAGNITUDE OF THE RESPONSE OF HEPATOCELLULAR CARCINOMA AND CHOLANGIOCARCINOMA TO SORAFENIB IS AFFECTED BY THE EXPRESSION OF INACTIVATING VARIANTS IN THE SLC22A1 GENE**

E. Herráez<sup>1</sup>, O. Briz<sup>1,2</sup>, E. Lozano<sup>1</sup>, R.I.R. Macías<sup>1,2</sup>, V.S. Robledo<sup>1</sup>, J. Hernandez-Iglesias<sup>1</sup>, A. González-Hernández<sup>1</sup>, L. Bujanda<sup>2,3</sup>, J. Banales<sup>2,4</sup>, J.J.G. Marin<sup>1,2</sup>. <sup>1</sup>Laboratory of Experimental Hepatology and Drug Targeting (HEVEFARM), Biomedical Research Institute of Salamanca (IBSAL), Salamanca University, Salamanca, <sup>2</sup>National Institute for the Study of Liver and Gastrointestinal Diseases (CIBEReh), Barcelona, <sup>3</sup>Department of Gastroenterology, Donostia Hospital, Instituto Biodonostia, University of the Basque Country EHU/UPV, <sup>4</sup>Department of Gastroenterology, Donostia Hospital, Instituto Biodonostia, University of the Basque Country EHU/UPV, San Sebastian, Spain

E-mail: elisah@usal.es

**Background and Aims:** Reduced efficacy of pharmacological treatment of cancer is due in part to decreased intracellular content of active drugs. Thus, lowering uptake is an important mechanism of tumour chemoresistance. In this respect, down-regulation of SLC22A1 encoding the organic cation transporter-1 (OCT1) may affect the response of hepatocellular carcinoma (HCC) and cholangiocarcinoma (CGC) to sorafenib, which is taken up in part by OCT1. The aim of the present study was to investigate whether SLC22A1 variants may contribute to chemoresistance of the primary liver tumours HCC and CGC to sorafenib.

**Methods:** Gel-electrophoresis-based complete sequencing and selective variant identification by RT-PCR was performed to detect SNPs in SLC22A1 cDNA. Modifications in the wild-type sequence of the OCT1 ORF were mimicked by directed mutagenesis and used

## ORIGINALITY REPORT

21%

SIMILARITY INDEX

16%

INTERNET SOURCES

21%

PUBLICATIONS

0%

STUDENT PAPERS

## PRIMARY SOURCES

1

[www.falk-foundation-symposia.org](http://www.falk-foundation-symposia.org)

Internet Source

9%

2

[medfeeds.sunway.dk](http://medfeeds.sunway.dk)

Internet Source

7%

3

Mónika Gyugos, Gábor Lendvai, István Kenessey, Krisztina Schlachter et al. "microRNA expression might predict prognosis of epithelial hepatoblastoma", *Virchows Archiv*, 2014

Publication

5%

Exclude quotes Off

Exclude matches &lt; 5%

Exclude bibliography Off