HU
HUMANITAS UNIVERSITY

RESEARCH TOPIC MEM6

Dissecting the role of Tumor Endothelial Cells in HCC with VETC+ angiogenesis provides potential targets of treatment
Curriculum MEM Clinical

Clinical Unit name and address
Pathology Department - IRCCS Humanitas Research Hospital

Laboratory name
Humanitas Research, IRCCS Humanitas Research Hospital

Clinical Supervisor
Massimo Roncalli
massimo.roncalli@hunimed.eu

Pre-clinical Supervisor
Ana Lleo De Nalda
ana.lleo@humanitas.eu

Abstract
The candidate will investigate the biology of endothelial cells in hepatocellular Carcinoma (HCC). In particular, we will focus on tumoral endothelial cells (TEC) in HCC cases showing Vessel that Encapsulate Tumor Cluster tumors (VETC+). VETC is a type of vascular HCC phenotype favoring metastases (renne et al Hep 2020).

The hypothesis of the project is that TECs in VETC + cases can play a "pro-active" role in the tumor microenvironment, conditioning the biological behavior of the tumor and its prognosis.

In particular, the study aims to:
-to characterize the molecular profile of TECs;
- to define the interactions of TECs with the other cells of the tumor micro-environment, in particular the immune ones, and secondly the tumor cells;
- to clarify whether the phenomenon of the endothelial-mesenchymal transition is involved in the process of metastasis, clinically characterizing VETC + cases.

Main technical approaches
The candidate should have an excellent knowledge of the morphological and phenotypic features of hepatocarcinomas. In particular, he should be able to recognize and adequately characterize the vascular profile of these lesions.

In addition, the candidate should have basic knowledge of laboratory techniques such as

www.hunimed.eu

semi-quantitative real-time RT-PCR, Western Blot analysis, immunohistochemical analysis, Luciferase reporter assay, data mining and bioinformatics analysis.

The candidate should be able to integrate the results of molecular analysis with morphological and clinical information through appropriate data mining and bioinformatics analysis skills.

Scientific references

1) Renne SL, Woo HY, Allegra S, et al. Vessels Encapsulating Tumor Clusters (VETC) Is a Powerful Predictor of Aggressive Hepatocellular Carcinoma. Hepatology. 2020;
2) Kurebayashi Y, Ojima H, Tsujikawa H, et al. Landscape of immune microenvironment in hepatocellular carcinoma and its additional impact on histological and molecular classification. Hepatology. 2018; 68:1025-1041.
3) Sulas P, Di Tommaso L, Novello C, et al. A Large Set of miRNAs Is Dysregulated from the Earliest Steps of Human Hepatocellular Carcinoma Development. Am J Pathol. 2018;188:785-794
4) Zhang H, Hu J, Liu L. MiR-200a modulates TGF-β1-induced endothelial-to-mesenchymal shift via suppression of GRB2 in HAECs. Biomed Pharmacother.2017; 95:215222.
5) Ma Z, Shuai Y, Gao X, Wen X, Ji J. Circular RNAs in the tumour microenvironment. Mol Cancer. 2020;19:8.

Type of contract

PhD scholarship of € 22.400 gross per year awarded by Humanitas University. This sum is exempt from IRPEF income tax according to the provisions of art. 4 of Law no. 476 of 13th August 1984, and is subject to social security contributions according to the provisions of art. 2, section 26 and subsequent sections, of Law no. 335 of 8th August 1995 and subsequent modifications.

Borsa di dottorato pari a € 22.400 annui lordi erogata da Humanitas University. Importo non soggetto a tassazione IRPEF a norma dell'art. 4 della L. 13 agosto 1984 n. 476 e soggetto, in materia previdenziale, alle norme di cui all'art. 2, commi 26 e segg., della L. 8 agosto 1995, n. 335 e successive modificazioni.