

Results: Median BMI was 30,4 [28,7–33,4] kg/m², T2D and PNPLA3 GG were present in 31% and 21,8% of cases. PRO-C4 levels fell significantly in group B ($p=0,041$) and C ($p=0,015$), but not in group A ($p=0,147$). TSP2 levels fell substantially in group B ($p=0,046$) and in group C ($p=0,004$) but not in group A ($p=0,714$). FIB-4 and VCTE did not show clinically significant changes. Delta PRO-C4 showed a stepwise negative increase across the 3 groups: from mean -71,7 (SD 510,3) ng/ml to mean -228,7 (634,2) ng/ml to mean -695,5 (1735,8) ng/ml (ANOVA $p=0,011$). Delta TSP2 varied from mean -0,2 (13,5) ng/ml to mean -4,2 (14,5) ng/ml to mean -12,6 (15,8) ng/ml (ANOVA $p=0,004$). PRO-C4 and TSP2 showed significant association with delta weight changes: R^2 0,05 ($p=0,003$) and 0,08 ($p=0,0002$). Delta TSP2 > -1,96 ng/ml and delta PRO-C4 > -703 ng/ml (both by Youden Index) were associated with WL >5% after adjustment for age, male sex, obesity, T2D and PNPLA3 GG: aOR 0,16 (0,04–0,63, $p=0,008$) and aOR 0,29 (0,29–0,96, $p=0,043$) respectively.

Conclusion: In patients with MASLD without advanced fibrosis undergoing dietary intervention, serum TSP2 and PRO-C4 levels fell significantly in correlation to WL and were associated with WL >5%. This evidence suggests their clinical utility to monitor attenuation of hepatic fibrogenesis.

doi: [10.1016/j.dld.2026.01.049](https://doi.org/10.1016/j.dld.2026.01.049)

T-07

Involvement of the hERG1 potassium channel in cholangiocarcinoma cell biology

Giada Alla Viligiardi¹, Claudia Duranti¹, Chiara Capitani¹, Rossella Colasurdo¹, Tiziano Lottini¹, Paola Ostano², Alessia Tani¹, Jessica Iorio¹, Daniele Nosi¹, Daniele Bani¹, Annarosa Arcangeli¹, Chiara Raggi¹, Elena Frediani³, Francesca Margheri³, Mirella Pastore¹, Fabio Marra¹, Laura Maggi¹, Anna Vanni¹, Daniele Guasti¹

¹ Department of Experimental and Clinical Medicine, University of Florence, 50137, Florence, Italy

² Cancer Genomics Laboratory, Edo and Elvo Tempia Valenta Foundation, 13900, Biella, Italy

³ Department of Experimental and Clinical Biomedical Sciences, University of Florence, 50134, Florence, Italy

Background and Aim: hERG1 is a voltage-gated potassium channel normally found in excitable cells, but it is often overexpressed in tumors, where it interacts with β 1 integrin and activates cancer-related pathways. Intrahepatic cholangiocarcinoma (iCCA) is an aggressive liver malignancy with limited treatment options. This study aimed to investigate the role of hERG1 and its downstream signaling in iCCA biology.

Methods: hERG1 expression was assessed in three iCCA cell lines, and functional studies were performed using siRNA-mediated silencing (si hERG1) and pharmacological inhibition. Cellular behavior was evaluated through standard assays, and molecular and structural changes were analyzed using qRT-PCR, Western blotting, electron microscopy, and transcriptomics.

Results: hERG1 silencing led to a 75–80% reduction in mRNA and protein expression but did not impact proliferation or viability. In contrast, both genetic silencing and pharmacological inhibition significantly reduced cell motility and impaired angiogenesis, as shown by reduced tube formation in HUVECs exposed to si hERG CCA conditioned media. Gene expression analyses revealed downregulation of epithelial mesenchymal transition (EMT) and angiogenesis markers. Key oncogenic pathways, including FAK, PI3K, and AKT, were notably suppressed. Ultrastructural analysis showed endoplasmic reticulum swelling and increased vesicular traffic, in-

dicating cellular stress and altered membrane turnover. Transcriptomic profiling confirmed dysregulation in vesicle trafficking and exocytosis, highlighting a broader impact of hERG1 on intracellular dynamics.

Conclusion: hERG1 plays a critical role in supporting motility and angiogenic potential in iCCA cells without affecting proliferation. Its inhibition alters key oncogenic and cellular processes, positioning hERG1 as a promising therapeutic target in iCCA.

doi: [10.1016/j.dld.2026.01.050](https://doi.org/10.1016/j.dld.2026.01.050)

T-08

Portal-Peripheral miRNA Signature Reveals a Chronic Pro-Inflammatory Trap in the Portal District linked to local Increased Endothelial NLRP3 Inflammasome Activity in Cirrhosis

Kymentie Ferdinande¹, Alberto Zanetto², Michele Carron³, Giulio Barbiero⁴, Michele Battistel⁴, Stefano Groff⁴, Sarah Shalaby⁵, Romilda Cardin¹, Marco Senzolo⁶

¹ Department of Surgery, Oncology, and Gastroenterology, University of Padova, Italy

² Department of Surgery, Oncology, and Gastroenterology, University of Padova, Italy; Gastroenterology/Multivisceral Transplant Unit, Padova University Hospital, Italy

³ Department of Medicine, University of Padova, Italy

⁴ Unit of Interventional Radiology, Radiology 2 Unit, Department of Integrated Diagnostic Services, University Hospital of Padua, Padua, Italy

⁵ Barcelona Hepatic Hemodynamic Laboratory, Liver Unit, Hospital Clinic, Institut de Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain

⁶ Gastroenterology/Multivisceral Transplant Unit, Padova University Hospital, Italy

Introduction and aims: The presence of a distinct pro-inflammatory milieu within the portal circulation and its role in fibrosis progression and portal hypertension complications, including portal vein thrombosis (PVT), remains debated. Protein-based inflammatory markers are often downstream products and subject to hepatic clearance, limiting their interpretability. MicroRNAs (miRNAs) act as early, stable regulators of inflammatory and immune signaling and may provide a more accurate reflection of local vascular immune activity. This study consists of two parts: 1) Profiling of miR-21-5p, miR-146a-5p, miR-155-5p, and miR-223-3p in paired portal and peripheral blood samples from patients with cirrhosis, in order to characterize the portal-peripheral inflammatory signature; and 2) Western blot analysis to assess the expression levels of NLRP3, the inflammasome component correlating with the miRNAs of interest, in protein extracts from portal and suprahepatic veins obtained during liver transplantation in patients with cirrhosis.

Methods: 1) Adult patients with cirrhosis undergoing transjugular intrahepatic portosystemic shunt (TIPS) placement (N=13) were prospectively enrolled. Paired peripheral and portal blood samples were obtained during the procedure. miRNA expression levels were quantified, and peripheral measurements were compared with those from healthy controls (N=10). 2) Adult patients with cirrhosis undergoing liver transplantation were prospectively enrolled (N=3). Paired samples from the portal and suprahepatic veins were processed for protein extraction to assess NLRP3 expression by Western blot analysis in order to evaluate portal compartment-specific inflammasome activation.

Results: Compared with healthy controls, cirrhotic patients exhibited significantly elevated circulating miR-21-5p levels (median 1.41 [1.05–1.97] vs. 0.96 [0.76–1.06], $p=0.04$), consistent with enhanced fibrogenic and inflammatory activity. Within patients,