provides a framework for future studies investigating PBC epidemiology.

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OC-06

Serum coding and non-coding RNAs as biomarkers of NAFLD and fibrosis severity

A. Scamporrino[1,§], S. Di Mauro[1,§], S. Petta[2], F. Urbano[1], A. Filippello[1], M. Ragusa[3,4], M.T. Di Martino[5], F. Scionti[5], S. Grimaudo[2], R.M. Pipitone[2], G. Privitera[1], A. Di Pino[1], R. Scicali[1], A.M. Rabuazzo[1], A. Craxì[2], M. Purrello[3], F. Purrello[1], S. Piro[1]

[1] *Department of Clinical and Experimental Medicine, Internal Medicine, Garibaldi-Nesima Hospital, University of Catania, Catania, Italy*
[2] *Section of Gastroenterology, Di.Bi.M.I.S., University of Palermo, Palermo, Italy*
[3] *Department of BioMedical Sciences and BioTechnology, Section of Biology and Genetics Giovanni Sichel, Unit of Molecular, Genome and Complex Systems BioMedicine, Catania, Italy*
[4] *IRCCS Associazione Oasi Maria S.S., Institute for Research on Mental Retardation and Brain Aging, Troina (EN), Italy*
[5] *Department of Experimental and Clinical Medicine, Magna Graecia University, Catanzaro, Italy*

Background and aims: Non Alcoholic Fatty liver Disease is a global health threat. Diagnosis of NASH and stage liver fibrosis is based on liver biopsy. This study principally aimed to identify circulating differentially expressed coding and non-coding RNAs in serum samples of biopsy-proven mild and severe NAFLD patients respect to controls and respect to each other.

Methods: We firstly performed a whole transcriptome analysis through microarray ($n = 12$: 4 CTRL; 4 mild NAFLD: NAS ≤ 4 F0; 4 severe NAFLD NAS ≥ 5 F3), followed by a second stage validation of selected coding/non-coding RNAs through single Real Time PCR assays in a larger independent patient cohort (88 subjects: 63 NAFLD, 25 CTRL). A similar analysis was also performed in cellular NAFL/NASH models both at intracellular and extracellular level. RNAs diagnostic performance and their correlation with histological/clinical data were also analysed.

Results: The first step of the study led to the identification of many differentially expressed coding/non-coding RNAs in each group comparison. We validated the up-regulation of UBE2V1, BNIP3L mRNAs, and TGFB2/TGFB2-OT1 coding/non-coding RNA both in patients with NAS ≥ 5 (versus NAS ≤ 4) and in patients with Fibrosis stages = 3-4 (versus $F = 0$-2). HBA2 mRNA and RP11-128N14.5 lncRNA were up-regulated respectively only in $F = 3$-4 or NAS ≥ 5 patients. UBE2V1 and RP11-128N14.5 were also up-regulated in NASH *in vitro* model respect to NAFL *in vitro* model and controls. Extracellular RNA expression partially reflected serum sample results. UBE2V1, RP11-128N14.5, BNIP3L, and TGFB2/TGFB2-OT1 were associated with histological scores and biochemical data. Combinations of TGFB2/TGFB2-OT1 + FIB-4 (AUC = 0.891, p-value = 0.000003) or TGFB2/TGFB2-OT1 + Fibroscan (AUC = 0.892, p-value = 0.000002) improved the detection of $F = 3$–4 with respect to $F = 0$-2 fibrosis stages.

Conclusions: We identified specific serum coding/non-coding RNA profiles in severe and mild NAFLD patients that possibly mirror molecular mechanisms underlying NAFLD progression towards NASH/fibrosis. TGFB2/TGFB2-OT1 detection improves FIB-4/Fibroscan diagnostic performance for advanced fibrosis discrimination.

[§]Equal contribution.

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OC-07

ATG7 genetic variant and defective autophagy: a novel risk factor for non-alcoholic fatty liver disease progression in patients with type 2 diabetes mellitus

S. Pelusi[1,2], G. Baselli[1], A. Cespiati[1,2], P. Dongiovanni[2], M.V. McCain[3], M. Meroni[1], R. Romagnoli[4], S. Petta[5], A. Grieco[6], L. Miele[6], G. Soardo[7], E. Bugianesi[8], S. Fargion[1,2], R. De Francesco[9], S. Romeo[10,11], A.L. Fracanzani[1,2], H.L. Reeves[12], L. Valenti[1,2]

[1] *Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[2] *Internal Medicine and Metabolic Diseases, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy*
[3] *Northern Institute for Cancer Research, The Medical School, Newcastle University, Newcastle upon Tyne, UK*
[4] *Department of Surgical Sciences, Liver Transplantation Center, University of Turin, Turin, Italy*
[5] *Section of Gastroenterology, DIBIMIS, University of Palermo, Palermo, Italy*
[6] *Internal Medicine and Gastroenterology Area, Fondazione Policlinico Universitario A. Gemelli, Catholic University of Rome, Rome, Italy*
[7] *Clinic of Internal Medicine-Liver Unit, Department of Experimental and Clinical Medical Sciences, University of Udine, Udine, Italy*
[8] *Division of Gastroenterology, Department of Medical Sciences, University of Torino, Italy*
[9] *Istituto Nazionale di Genetica Molecolare (INGM), Romeo ed Enrica Invernizzi, Bioinformatic group, Milan, Italy*
[10] *Sahlgrenska Center for Cardiovascular and Metabolic Research, Wallenberg Laboratory, Cardiology Department, University of Gothenburg, Gothenburg, Sweden*
[11] *Clinical Nutrition Unit, Department of Medical and Surgical Sciences, Magna Graecia University, Catanzaro, Italy*
[12] *Newcastle upon Tyne NHS Foundation Trust, Newcastle upon Tyne, UK*

Introduction: Genetic factors play an important role in nonalcoholic fatty liver disease (NAFLD) and NAFLD-related hepatocellular carcinoma (HCC).

Aim: To evaluate the burden of rare or novel mutations predicted to impair protein function on NAFLD progression.

Materials and methods: We performed whole exome sequencing (WES) in 142 NAFLD-HCC cases, 59 patients with NAFLD and advanced fibrosis, and 50 healthy individuals. Phenotypic characterization in carriers and non carriers of the rs143545741 *ATG7* variant was performed.