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# Coffee restores expression of lncRNAs involved in steatosis and fibrosis in a mouse model of NAFLD

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Background and aim: Coffee intake exert protective effects against non-alcoholic fatty liver disease (NAFLD), although without fully cleared mechanisms. In this study we aimed to assess whether coffee consumption may influence the expression of long non-coding RNAs (lncRNAs) in the liver. Methods: C57BL/6J mice were fed a 12-week standard diet (SD), high-fat diet (HFD) or HFD plus decaffeinated coffee solution (HFD + coffee). Expression of specific lncRNAs involved in NAFLD was analyzed by real-time PCR. For the most differentially expressed lncRNAs, the analysis was also extended to their mRNA targets. Results: Decaffeinated coffee intake reduced body weight gain, prevented NAFLD, lowered hyperglycemia and hypercholesterolemia. NAFLD was associated with lower hepatic expression of Gm16551, a lncRNA inhibiting de novo lipogenesis, and higher expression of H19, a lncRNA promoting fibrogenesis. Coffee intake restored Gm16551 to levels observed in lean mice and downregulated gene expression of its target's acetyl coenzyme A carboxylase 1 and stearoyl coenzyme A desaturase

1. Furthermore, coffee consumption markedly decreased hepatic expression of H19 and of its target gene collagen alpha-1(I) chain;

consistently, in mice fed HFD + coffee liver expression of αSMA protein returned to levels of mice fed SD. Expression of lncRNA involved in circadian clock such as fatty liver-related lncRNA 1 (FLRL1) and fatty liver-related lncRNA 2 (FLRL2) were upregulated by HFD and were also modulated by coffee intake. Conclusion. Hepatoprotective effects of coffee may be depending on the modulation of lncRNAs involved in key pathways of NAFLD onset and progression.

#### Recent publications

- Scicali R, Piro S, Ferrara V, Di Mauro S, Filippello A, Scamporrino A, Romano M, Purrello F, Di Pino A.J Direct and Indirect Effects of SARS-CoV-2 Pandemic in Subjects with Familial Hypercholesterolemia: A Single Lipid-Center Real- World Evaluation. Clin Med. 2021 Sep 24;10(19):4363. Doi: 10.3390/jcm10194363.
- Di Pino A, Scicali R, Marchisello S, Zanoli L, Ferrara V, Urbano F, Filippello A, Di Mauro S, Scamporrino A, Piro S, Castellino P, Purrello F, Rabuazzo AM High glomerular filtration rate is associated with impaired arterial stiffness and subendocardial viability ratio in prediabetic subjects. Epub 2021 Aug 13. DOI: 10.1016/j.numecd.2021.08.030.
- Porcellati F, Di Mauro S, Mazzieri A, Scamporrino A, Filippello A, De Fano M, Fanelli CG, Purrello F, Malaguarnera R, Piro S. Glucagon as a Therapeutic Approach to Severe Hypoglycemia: After 100 Years, Is It Still the Antidote of Insulin? DOI: 10.3390/biom11091281

### **Biography**

Stefania Di Mauro has been involved in several projects concerning metabolic diseases. He conducted both benchtop and translational research. One of her main interests has been to identify circulating noncoding RNAs in several kinds of body fluids as diagnostic biomarkers of metabolic diseases, she also focused on intracellular/tissue dysregulated noncoding RNAs involved in pivotal metabolic, inflammatory and cellular stress pathways. In the context of NAFLD she developed two differential in vitro models of NAFLD where she identified intracellular and extracellular dysregulated microRNAs involved in fundamental pathways of NAFLD progression; she also analyzed through high throughput approach the whole transcriptome expressed in NAFLD NASH and control subjects. This study led to the identification of RNA panels that may be useful for NAFLD and fibrosis staging. She has also been involved in the study of hormone secretion dysregulation of pancreatic cells and intestinal cells under lipotoxic or glucotoxicity conditions.

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