

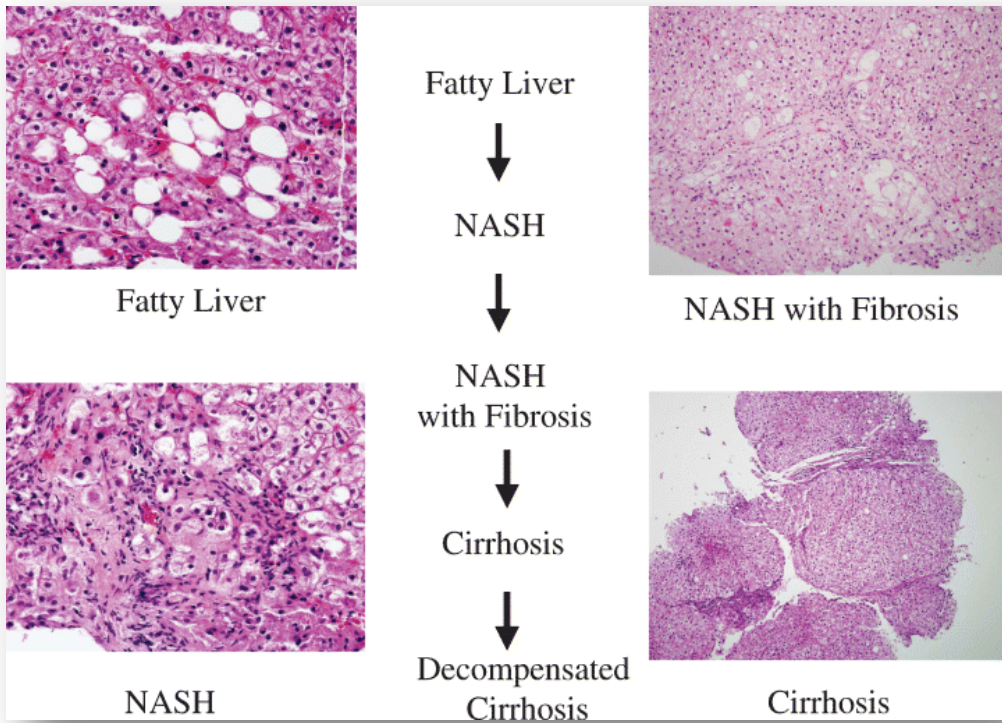
**Marie Skłodowska-Curie Actions  
Research and Innovation Staff Exchange (RISE)  
Call: H2020-MSCA-RISE-2015**

**Mastiha treatment for Healthy  
obese with NAFLD diagnosis**  
**“MAST4HEALTH”**

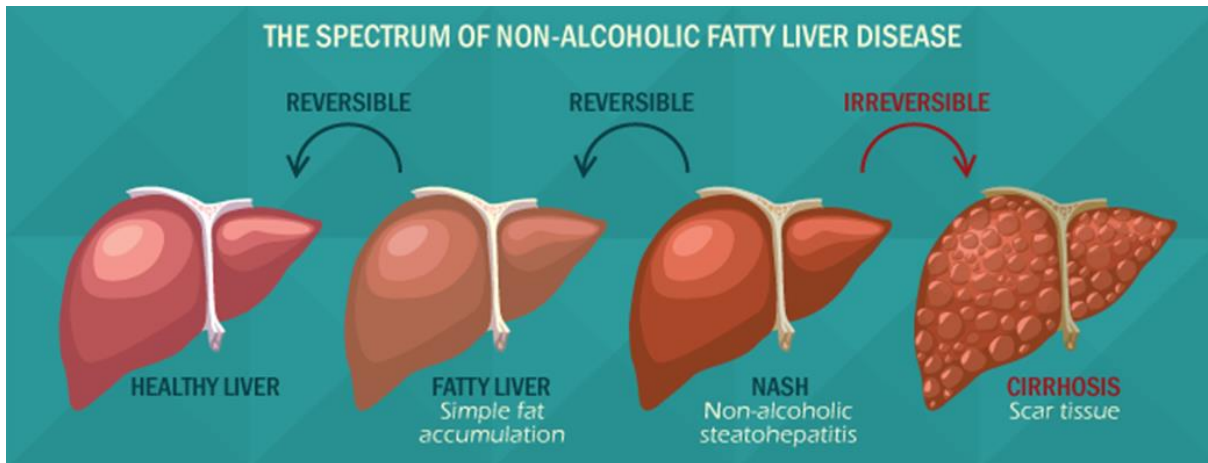
Sophie Visvikis-Siest  
Head of INSERM UMR U1122; IGE-PCV

# Nonalcoholic fatty liver disease and steatohepatitis (NAFLD/NASH)

- A spectrum of liver injury beginning from simple steatosis to nonalcoholic steatohepatitis (NASH) that leads to advanced fibrosis and cirrhosis.
- One of the most common liver disorders and a major public health problem in Europe and North America.
- One of the most common complications of obesity and diabetes mellitus in Western populations affecting approximately 50% of diabetics and 76% of obese patients



NAFLD is histologically further categorized into nonalcoholic fatty liver (**NAFL**) and non alcoholic steatohepatitis (**NASH**). NAFL is defined as the presence of hepatic steatosis with no evidence of hepatocellular injury in the form of ballooning of the hepatocytes. NASH is defined as the presence of hepatic steatosis and inflammation with hepatocyte injury (ballooning) with or without fibrosis.



# Pathogenesis

## The role of the intestinal microbiota

- The intestinal microbiota may stimulate liver steatosis through
  - the induction of obesity by harvesting energy from otherwise indigestible dietary polysaccharides
  - regulation of gut permeability and stimulation of low-grade inflammation
  - modulation of dietary choline metabolism
  - regulation of bile acid metabolism
  - stimulation of endogenous ethanol production by enteric bacteria.

# Risk factors

- Obesity (especially central type),
- Insulin Resistance,
- Type-II diabetes mellitus,
- Dyslipidaemia,
- Hyperuricaemia
- Hypertension
- Total parenteral nutrition
- Rapid weight loss
- Intestinal jejunioileal bypass surgery

# Therapeutic approach

- Weight loss through diet and exercise
- Bariatric surgery in obese NAFLD/NASH patients
- No approved specific drugs for the management of NAFLD/NASH
- Only medications to improve the aspects of metabolic syndrome

# Natural bioactive phytochemicals as an alternative treatment for NAFLD/NASH

- Some herbal remedies might result in significant improvements in liver enzymes and ultrasound scan values for NAFLD/NASH (Liu et al., 2013).
- Betulinic acid, a pentacyclic triterpene found in many plants, effectively ameliorates intracellular lipid accumulation in liver cells (Quan et al., 2013).

# Mastiha as an alternative treatment?

- Mastiha possesses **anti-bacterial activity and potent antioxidant and anti-inflammatory properties.**
- Interestingly it contains **over fifty triterpenes**, mainly **oleanolic** and **ursolic** acids and a plethora of **monoterpenes.**
- Terpenes, nowadays attract the interest of researchers and pharmaceutical companies for clinical studies and applications in the therapy of diseases due to their **antioxidant** potential but also due to their **anti-inflammatory** or **antimicrobial** properties.



# Mastiha as an alternative treatment for NAFLD?

- **Ursolic acid** ameliorates hepatic steatosis, improves lipid metabolism, lowers oxidative stress markers and reduces hepatic inflammatory factors mRNA expression in high-fat diet-induced NAFLD/NASH rats (Li et al., 2014).
- Mastiha contains **quercetin** which has been proven effective in **hepatic steatosis and oxidative stress** (Aguirre et al., 2014), as well as **gallic acid** found to ameliorate impaired glucose and lipid homeostasis in experimental NAFLD/NASH (Chao et al., 2014).

# Participants

- Harokopio University (Project Coordinator)
  - Queen Mary University of London
  - University of Leipzig
  - INSERM
  - Universita Degli Studi Magna Graecia Di Catanzaro
  - University of Novi Sad
  - University of East Sarajevo
- 
- FISABIO
  - Biotechvana
  - Randox
  - Intervideo
  - Sanofi
  - CMGA
  - Biocrates
  - Perspectum diagnostics



# Objectives

- Evaluation of Mastiha as a novel non-pharmacologic treatment for NAFLD/NASH patients
- Provision of powerful tools for the NAFLD/NASH patient management
- Establishment of network activities to support the development of new approaches in NAFLD/NASH treatment and management
- Promotion of international cooperation between research scientists working towards innovation
- Enhancement of the training of the next generation of scientists in state-of-the-art technologies and analytical techniques

# Implementation

WP No	WP Title	Activity Type	Lead Participant	Start month	End month
1	Management and Recruitment of seconded staff	Management	HUA	M1	M48
2	A multicenter randomized double blind placebo controlled (parallel arm) clinical trial on the efficacy of Mastiha supplement in NAFLD/NASH patients	Research	HUA	M6	M18
3	Potential epigenetic alterations in response to Mastiha treatment	Research	UL	M19	M40
4	Effects of Mastiha on inflammation and adhesion biomarkers and on oxidative stress indexes	Research	INSERM	M19	M40

# Implementation

WP No	WP Title	Activity Type	Lead Participant	Start month	End month
5	Blood metabolomic profiles in NAFLD patients pre- and post-intervention	Research	BIOCRATES	M19	M40
6	Genetic markers implicated in response to Mastiha treatment	Research	QMUL	M19	M40
7	Modulation of gut microbiome	Research	FISABIO	M19	M40
8	Software development for integration of metadata and omics profiles for indexing, management and interpretation.	Research	BV	M6	M47
9	Training	Training	IIWS	M6	M48
10	Dissemination and Exploitation of the results	Dissemination	SANOFI	M1	M48

**WP1**  
Management and  
Recruitment of seconded staff

**WP2:** A multicenter  
randomized double blind  
placebo controlled (parallel  
arm) clinical trial

**WP3:** Potential  
epigenetic  
alterations in  
response to  
Mastiha treatment

**WP 4:** Effects of  
Mastiha on  
inflammation

**WP5:** Blood  
metabolomic  
profiles in  
NAFLD  
patients

**WP6:** Genetic  
markers in  
response to  
Mastiha

**WP7:**  
Modulation in  
gut microbiome

**WP 8**  
Software  
development  
for integration

**WP9**  
Training

**WP10**  
Dissemination and Exploitation  
of the results

