Projet MASH-FLOW

ACRONYME	**MASH-FLOW**		
INTITULE COMPLET	**Innovative combined therapies targeting Metabolic dysfunction-associated steatohepatitis**		
DUREE **DATES DEBUT/FIN**	4 ans 01/10/2025 – 30/09/2029		
APPEL A PROJET	ANR Call 2024 - PRC		
FINANCEURS	ANR		
BUDGET TOTAL	792 423 €		
PORTEUR(S) OFFICIEL(S) DU PROJET		Dr BLAISE Sébastien	
ROLE RIBP	Patenaire	**PORTEUR POUR RIBP**	Dr COUROT Eric
PERSONNELS DU LABO IMPLIQUES		COUROT Eric, Engineer to be recruited	
PARTENAIRES	UMR 7369 CNRS MEDyC Université de Reims Champagne Ardenne UMR 7242 CNRS Université de Strasbourg Laboratoire CiTCoM / Inserm U1268 / CNRS UMR 8038 Université Paris Cité		
OBJECTIFS DU PROJET	Fatty liver diseases (FLD) are common liver pathologies linked to lipid accumulation in hepatocytes (hepatosteatosis). Metabolic-Associated FLD (MAFLD) occurs when liver steatosis is unrelated to alcohol abuse. MAFLD encompasses a spectrum from benign hepatic steatosis to Metabolic dysfunction-associated steatohepatitis (MASH), characterized by steatosis, inflammation, hepatocyte ballooning, and fibrosis. MASH strongly correlates with obesity, adipose inflammation, insulin resistance, type 2 diabetes, hyperinsulinemia, atherogenic dyslipidemia, and arterial hypertension, posing a global health concern. About 20% of individuals with simple hepatosteatosis progresses to MASH, which in most severe cases, evolves to cirrhosis, potentially necessitating a liver transplant. Furthermore, about 25% of cirrhotic livers progress to hepatocellular carcinoma (HCC). MASH affects 1.5-6.4% of the global population. A quarter of French population is at MAFLD risk, with 2-3% experiencing advanced MASH. The first therapeutic approach involves lifestyle and diet changes, which are difficult challenges and very often results in failure. Therapeutic treatments, targeting the inflammatory and fibrotic pathways in the second disease stage, remain limited in effectiveness and can be explained by the non-treatment of the primary causes of the pathology (e.g., adiposity, oxidative stress...). Considering MASH's heterogeneity, lessons from trials suggest using several drugs to synergistically enhances efficacy. Combination therapies can also mitigate side effects. The MASH-FLOW project aims to develop an innovative multi-targeted therapeutic approach to combat MASH. The primary objective is to evaluate the therapeutic potential of a novel combination of three compounds:phytostilbenes, a casp2 inhibitor, and an autophagy modulator. This tri-therapy strategy is designed to simultaneously target oxidative stress, lipid metabolism dysregulation, autophagy dysfunction, and fibrosis development, which are central processes in MASH progression.		

MOT-CLES	Phytostilbenes, resveratrol, sustainable processes, bioproduction, grapevine cell cultures, MASH (Metabolic dysfunction-Associated SteatoHepatitis), autophagy modulator, caspase-2 inhibitor