Results: PCSK9 dose-dependently reduced LDLr expression in control and FH fibroblasts to similar extents, by up to 77±8% and 82±7%. Likewise, PCSK9 reduced LDLr abundance by 39±8% in non-FH and by 45±10% in HeFH lymphocytes, irrespective of their LDLr mutation status. We found positive correlations of the same magnitude between PCSK9 and LDLr-C in controls (b=0.022, p=0.0003), 2D06E (b=0.20, p=0.0002), V408M (b=0.24, p=0.0002), and D154N (b=0.25, p=0.0048) HeFH patients. The strengths of these associations were all similar.

Conclusion: Elevated PCSK9 levels are equally detrimental for HeFH and non-FH patients: a 100ng/mL increase in PCSK9 will lead to an increase in LDL-C of 0-20-0.25mmol/L, in controls and HeFH alike, irrespective of their LDLr mutation. This explains why non-FH and HeFH patients respond equally well to monoclonal antibodies targeting PCSK9.

0169
Paraoxonase 1 activity, in the fructose-fed rats, in the presence and in the absence of an antioxidant treatment with alpha-lipoic acid

Steliania Ghibiu (1), Cristina Cricău (2), Claudiu Morogovan (3), Cristina Mogosan (1), Maria Dronca (4)
(1)Université de Médecine et Pharmacie, Pharmacologie, Cluj Napoca, Roumanie – (2) Université de Médecine et Pharmacie, Biochimie pharmaceutique et laboratoire clinique, Cluj Napoca, Roumanie – (3) Université “Vasile Goldis”, Arad, Roumanie – (4) Université de Médecine et Pharmacie, Biochimie médicale, Cluj Napoca, Roumanie

Introduction: Paraoxonase 1 (PON1) is an esterase synthesized by the liver and secreted into the plasma, where it is associated with high density lipoproteins (HDL). Its role is to protect LDL and HDL from oxidation, thus preventing atherosclerosis. A decreased level of plasma PON1 activities has been found in diabetes mellitus, cardiovascular disorders and chronic liver diseases; but, it can also be influenced by diet and lifestyle. The purpose of this study was to assess the PON1 activities in the insulin-resistant rats fed with a fructose-enriched diet, in the presence and in the absence of an antioxidant treatment with alpha-lipoic acid (AL).

Methods: 48 male Sprague-Dawley rats were randomized into two series: rats fed for 3 months with standard chow (Control) or with standard chow supplemented with fructose (60%). In each series, a group of rats was treated intraperitoneally during 14 days/month with NaCl 0.9% and another group with 50 mg/kg/day AL. At the end of the 3 months, we assessed: 1) peripheral tissue resistance to insulin (HOMA-IR) and plasma lipid profile, 2) paraoxonase, arylesterase and lactonase activities of PON1, 3) plasma homocysteine level were significantly (p>0.05) enhanced in the fructose group. The AL dis-

Results: The fructose intake increased peripheral tissue resistance to insulin (HOMA-IR) and plasma lipid profile, less the HDL. Also, transaminase and PON1 activities increased in association with a decrease in plasma transaminase activities, of the plasma and the liver. The fructose intake also significantly (p<0.05) enhanced the fructose group. The AL dis-

Conclusions: In our experimental conditions, the fructose intake induced a decrease in plasma transaminase and PON1 activities in the presence of a hyperhomocysteinemia. The AL treatment restored the enzymes’ activities and had a hepatoprotective effect, but without influence on Hcy level.

0211
Prevention of cardiovascular, renal and metabolic abnormalities by soluble epoxide hydrolase inhibition in a murine model of type 2 diabetes

Clothilde Roche (1), Marie Besnier (1), Roméo Cassel (2), Najah Harouti (1), David Coquereil (1), Dominique Guerrot (1), Lionel Nicol (1), Sylvanie Renet (1), Emmanuelle Loison (2), Christophe Morisseau (3), Paul Mulder (1), Antoine Ouvrard-Pascaud (1), Anne-Marie Madec (2), Vincent Richard (1), Jeremy Bellien (1)
(1) Inserm U1096, Rouen, France – (2) Inserm U1060 – CarMeN, Lyon, France – (3) University of California, Davis, Etsats-Unis

Objective: Epoxysicosatradioic acids (EETs) are synthesized from arachidonic acid, notably in endothelial cells, and display attractive metabolic, vasodilatory and anti-inflammatory properties. We demonstrated previously that inhibiting EET degradation mediated by soluble epoxide hydrolase (sEH) reduces hypertension and heart failure, and others reported that it improves glucose homeostasis in type 2 diabetes. However, the impact of such strategy on target organ damage in diabetes remains to be clarified.

Materials and methods: The pharmacological sEH inhibitor t-AUCB (10 mg/l in drinking water) was administered for 8 weeks in mice subjected to a high fat diet (HFD, 60% fat) for 16 weeks. Mice on control chow diet (10% fat), non-treated HFD mice and HFD mice treated with glibenclamide (80 mg/ml) served as controls.

Results: Glibenclamide and t-AUCB similarly prevented the increased fasting glycemia in HFD mice (Control: 5.4±0.2; HFD: 8.0±0.8; HFD+G: 5.1±0.3; HFD+t-AUCB: 5.6±0.2 mmol/L; p<0.05). However, only t-AUCB improved glucose tolerance and decreased gluconeogenesis. In parallel, t-AUCB prevented adi-

Discussion: These results demonstrate that beyond its glucose-lowering effects sEH inhibition improves coronary endothelial function, diastolic dys-

Aim: Tea is one of the most consumed beverages in the world and its health-