clinical application of β-blocker agents requires patient and disease oriented approaches.

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Is NLRP3 inflammasome a new pharmacological target in myocardial ischemia/reperfusion injury?

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Objectives: Recently it has been documented that the NLRP3 inflammasome plays a pivotal role in the inflammatory response to tissue injury. The NLRP3 inflammasome is a large multimeric danger-sensing platform that induces activation of the caspase-1 and mediates the cleavage of inactive pro-IL-1β, among other proteins, into its active form. We have shown that the activation of the NLRP3 inflammasome exacerbates myocardial ischemia/reperfusion (I/R) injury in diabetic mice. Moreover, our group previously demonstrated that INF-4E inhibits NLRP3, ATPase and caspase-1 activities in THP-1 cells. Here we test in an ex-vivo model whether INF-4E inhibiting NLRP3 may positively affect I/R injury, post-ischemic cardiac function and molecular response in the rat hearts.

Materials and methods: Isolated hearts from male Wistar rats (body weight 450,550 g; n = 7) underwent perfusion without ischemia (Sham) or I/R (30-min ischemia plus 20-min or 60 min reperfusion) with and without IFN-4E treatment (50 M for 20-min before ischemia). Coronary perfusion pressure and left ventricular pressure (LVP) were monitored, and dP/dtmax assessed during the entire period of perfusion. Biopsies obtained at the end of reperfusion were used for Western blotting evaluations of NLRP3 and caspase-1 (apoptosis index) levels/activities and for assessment of RISK pathway involvement. At the end of 60 min reperfusion infarct size was measured with nitro-blue-tetrazolium technique by an independent observer.

Results: In this preliminary study, the 20 min IFN-4E pre-ischemic administration induced a significant reduction of infarct size and an improvement in post-ischemic LVP recovery. Western blot analysis demonstrated NLRP3 and caspase-1 activation by I/R procedure, which were strongly attenuated after IFN-4E pre-treatment. Moreover, an important modulation of RISK kinase phosphorylation was observed, though a clear-cut correlation between the reduction in infarct size and phosphorylation of RISK kinases was not observed.

Conclusions: These preliminary results demonstrate that the IFN-4E inhibits the formation of the NLRP3 inflammasome in the rat heart and ameliorates the response to myocardial I/R injury, confirming the ability of this drug to affect NLRP3 inflammasome complex activation.

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Spread bio oil diet and cardiac response to ischemia/reperfusion: A preliminary study in mice

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Objectives: The role of diet is of paramount importance in the prevention and development of cardiovascular disease (CVD). A diet high in saturated fat increases the risk of heart disease and stroke, in particular it causes about 31% of coronary heart disease and 11% of stroke worldwide. The Mediterranean diet is the symbol of the Italian style and is considered able to reduce the burden of CVD, but this protective alimentary modality is frequently neglected for incorrect life style. Recently it has been suggested that "spread bio oil" (SBO), an innovative food product, at hard fat phase, mainly based on olive oil, may be beneficial, thus in the present study we aimed to compare three different diets, standard, high fat and SBO diet, in terms of cardiac response to the ischemia/reperfusion (I/R).

Materials and methods: Male mice were fed with standard diet (SD), high fat (HF) or spread SBO diet for 4 weeks. Before, during and at the end of these diets blood samples were collected and the anthropometric parameters, such as body mass index (BMI), weight, height and abdominal circumference, were evaluated. The hearts of each group were randomly assigned to two different protocols: only Tyrode perfusion (Sham) or I/R (30 min ischemia and 60 min reperfusion), at the end of experiments the infarct size was evaluated with nitro-blue tetrazolium techniques.

Results: While HF diet did not induce significant variations of anthropometric parameters (BMI, weight, and abdominal circumference), left ventricular weight resulted significantly higher in comparison to SD animals. Also, the infarct size resulted higher in HF than in SD hearts (infarct size 65 ± 5% and 43 ± 5%, respectively). Although, the animals fed with SBO diet displayed a significant increase of abdominal circumference with respect to SD only, surprisingly enough, their hearts had a smaller infarct size (26 ± 6%) with respect to both SD and HF animals.

Conclusions: These preliminary data suggest that the SBO increases the resistance of heart to I/R challenge, despite partial modifications of anthropometric parameters. To explain these preliminary results further investigations and analyses of cardioprotective pathways are necessary.

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Obestatin exerts post-conditioning-like cardioprotective effects via nitrosative/oxidative signaling

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Objectives: Obestatin (Obe), a 23-amino acid peptide derived from preproghrelin, affects several neurometabolic and cardiac physiological functions. A preconditioning-like effect of obestatin in limiting apoptosis and ischemia/reperfusion (I/R) injury in both isolated rat heart and cultured adult cardiomyocytes has been recently demonstrated. We hypothesized an obestatin-postconditioning-like cardioprotective effect via a nitrosative/oxidative mitochondrial signaling (NO/ROS/PKCε/mitoKATP channel).

Materials and methods: Isolated hearts underwent the following protocols: control group (I/R, 30 min global ischemia followed by 120 min reperfusion); Obe group (obestatin 75 nM, for 20 min immediately after ischemia and 100 min reperfusion). Other hearts received obestatin plus different antagonist of NO/ROS/PKCε/mitoKATP channel pathway. Each inhibitor was given during the last 5 min of stabilization and the initial 20 min reperfusion. Developed left ventricular pressure