

Methods: As models of hypercholesterolemia and Smith-Lemli-Opitz-syndrome, we treated THP1, JY cells or human PBMC with cholesterol or 7-dehydrocholesterol (7DHC), respectively. To test the beneficial effects of Mediterranean diet, we treated cells with polyunsaturated fatty acids. Then we measured the magnitude of DP with our novel emission ratiometric approach using flow cytometry.

Results: Loading of cells with cholesterol or 7DHC resulted in dose-dependent increases in DP. As demonstrating the importance of diet, ω -3 fatty acid decreased, while ω -6 or saturated fatty acid increased the magnitude of DP. In our ongoing studies, we are determining alterations in the DP in samples from hypercholesterolemic and hypertriglyceridemic patients compared to control individuals.

Conclusions: In conclusion, we determined the effects of changes in membrane composition on DP in in vitro disease models with our novel technique.

M/6 DRUG CANDIDATE BGP-15 IMPROVES CARDIAC FUNCTION BY ACTIVATING THE PROTEIN KINASE G PATHWAY

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Keywords: Heart failure, Dyslipidemia, BGP-15, Echocardiography, cGMP-PKG

Aims: Pharmacological treatment of heart failure represents a major unmet need. Recent evidence suggests that hidroximic-acid derivative small molecule BGP-15 improves muscle function and strength, restores cardiac function, and reduces arrhythmic episodes in animal models of muscular dystrophy, heart failure or diabetic cardiomyopathy. Our aim in this present study was to evaluate the effects of BGP-15 in a rabbit model of atherosclerotic cardiovascular disease.

Methods: New-Zealand male rabbits were divided into 3 groups: (I) healthy control (normal chow); (II) dyslipidemic (DD) group (atherogenic chow); (III) atherogenic chow+BGP-15-treatment (DD+BGP-15 group, 10 mg/kg, p.o.), for 16 weeks. Serum parameters were determined at the endpoint of the study, and echocardiography was carried out to estimate cardiac function. Western Blot and ELISA assays were carried out to determine myocardial cGMP levels and VASP protein phosphorylation to determine the activity of the cGMP-PKG signaling pathway.

Results: Serum parameters were unaffected by BGP-15-treatment. The drug candidate restored diastolic function (E and A wave, DecT, e'/a', E/e', IVRT) and improved Tei-index compared to untreated DD rabbits. Myocardial cGMP levels, along with the phosphorylation of VASP protein was significantly elevated in the left ventricle samples of BGP-15-treated rabbits in comparison to the DD animals.

Conclusions: Even though BGP-15 treatment did not affect serum parameters, it considerably enhanced diastolic function, partly by modulating the cGMP-PKG pathway. As BGP-15 has excellent safety profile, it may offer a new therapeutic approach in atherosclerotic cardiovascular disease.

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M/7 IMPACT OF PER OS ANTIBIOTIC TREATMENTS ON THE GASTROINTESTINAL COLONIZATION WITH A MULTIRESTANT KLEBSIELLA PNEUMONIAE STRAIN

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Keywords: AMR, microbiota, gene transfer, colonization, in vivo

Aims: Colonization resistance refers to the ability of microbiota to prevent expansion and persistence of exogenously acquired bacterial species. Antibiotic therapy can damage this ability. Our goal was to determine the effect of different per os antibiotic treatments on colonization rate and resistance gene copy numbers in intestinally carried *K. pneumoniae* (KP5825) in mice. This strain expressed a PMQR gene, an ESBL gene (CTX-M-15) as well as a carbapenemase enzyme.

Methods: C57BL/6 mice were colonized with 5×10^6 CFU of KP5825 orally after 2 weeks of ampicillin pretreatment. Then mice were divided into 6 groups receiving antibiotic treatments for 15 days: 0.5g/L and 0.1g/L of ampicillin (AMP), ceftazidime (CAZ), ciprofloxacin (CIP) was administered in the drinking water (6th group: control). Every three days fresh fecal pellets were collected. In the second phase of our experiments the V3-V4 region of the 16S rRNA gene was sequenced to determine the microbiota composition in the animals. We used qPCR technique to determine the KP5825 DNA quantities and assess the resistance gene copy numbers.

Results: Our results show a significant perturbation in the microbiota. We could also observe that after 15 days KP5825 decreased significantly ($p < 0,004$) in the control group and in the CIP treatment groups ($p < 0,0001$, $p < 0,002$). Furthermore, qPCR results show that higher dose CAZ treatment lead to 4-fold increase in CTX-M plasmid quantities.

Conclusions: Thus, the CAZ had higher power on the dissemination of resistance genes than CIP. This raises the possibility of in vivo plasmid transfer, which we intend to investigate in our future experiments.

N. Multidisciplinary poster session III. –ANATOMY -PATHOLOGY - RADIOLOGY - PHARMACOLOGY

N/1 CHANGES IN NOTCH SIGNALING IN THE TEETH OF PITUITARY ADENYLATE CYCLASE-ACTIVATING POLYPEPTIDE (PACAP)-DEFICIENT MICE

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Keywords: PACAP, teeth development, signaling, Notch

Aims: PACAP is a regulatory neuropeptide of the glucagon/secretin/VIP peptide family affecting tooth development partly via Shh (Sonic hedgehog) signaling cascade. The role of Notch signaling in tooth development is well described. We wanted to elucidate the possible connection between PACAP and Notch signaling pathway during tooth development.

Methods: We applied immunohistochemistry of Notch receptors (Notch1, 2, 3, 4), their ligands (DLL1, 3, 4,