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Conclusions: In the background of ALPPS-induced faster and higher regeneration, miRNA-mediated regulation can play an important role.

M/4 THE MOLECULAR BASIS OF THE INTERACTION BETWEEN COAGULATION FACTOR XIII AND FIBRINOGEN

Eniko Sebestyen, Krisztina Péntes-Daku

Division of Clinical Laboratory Science, University of Debrecen, Faculty of Medicine

Keywords: FXIII, fibrinogen, coagulation, thrombosis, interaction

Aims: Coagulation factor XIII (FXIII) consists of two A and two B subunits, its active form stabilizes the clot by crosslinking fibrin chains. Fibrinogen is made of three pairs of chains (α , β , γ). Plasma fibrinogen can be separated by ion exchange chromatography into 3 fractions: Peak1 containing γ A/ γ A chains (85%), Peak2 with γ A/ γ' (15%) chains and γ'/γ' (0.5%) fraction. The plasma FXIII circulates in the blood bound to fibrinogen. By characterizing this interaction, we may be able to synthesize a peptide that binds to FXIII and decreases its activity and consequently thrombus formation.

Methods: Our aim was to characterize the binding of FXIII to the different fibrinogen isoforms by surface plasmon resonance technique (SPR) and isothermal titration calorimetry (ITC). We used Biacore systems for the SPR measurements and we immobilized FXIII-B and Peak1 fibrinogen as the ligand. As analyte, we used FXIII-B, Peak1, Peak2, and a 9-amino-acid long γ A (γ A9) peptide, which we made by peptide synthesis. We studied the interaction between FXIII and γ A9 on a microcalorimeter (Microcal ITC 200).

Results: Peak1 and Peak2 fibrinogen bind to FXIII-B with almost the same affinity (K_d in the range of 10^{-6}) and the γ A9 binds to FXIII-B with a two magnitudes higher affinity (K_d in the range of 10^{-8}).

Conclusions: In conclusion, we can confirm that the FXIII-B subunit is associated with fibrinogen. The binding is a complex mechanism involving both γ A and γ' chains.

M/5 THE MEASUREMENT OF THE DIPOLE POTENTIAL WITH A NOVEL HIGH-THROUGHPUT FLOW CYTOMETRIC METHOD

Máté Szabó, Florina Zákány MD, Bence Cs. Szabó, Zoltán Varga PhD DSc, Péter Nagy MD PhD DSc, Tamás Kovács MD PhD

Department of Biophysics and Cell Biology, Faculty of Medicine, University of Debrecen, Debrecen, Hungary

Keywords: dipole potential, hypercholesterolemia, polyunsaturated fatty ac

Aims: The least-known component of membrane potentials, the dipole potential (DP) originates from the preferential alignment of molecular dipoles at the membrane-water interface, generating a large positive (~300mV) potential creating an immensely strong intramembrane electric field. Consistently, DP influences a multitude of membrane-coupled events, including ion channel gating, ErbB activation, etc. The magnitude of DP is mainly determined by the lipid composition of cell membrane. Since it is entirely located within the membrane, it is difficult to measure in living cells, however, we developed a flow cytometric technique to determine DP. Our aim was to examine effects of changes in the composition of cell membrane in disease models and human samples.

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

Ticián Wilisicz 1, Zoltán Szilvássy 2, Béla Juhász 2, Mariann Bombicz 2, Dániel Priksz 2, Balázs Varga 2

1 Faculty of Medicine, University of Debrecen, 2 Department of Pharmacology and Pharmacotherapy, University of Debrecen

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

Ferenc Balázs Farkas, Judit Domokos, Béla Kocsis, Eszter Ostorházi, Dóra Szabó