Conclusions: Effect of CA + ACEI (ARB) and HCTZ + ACEI (ARB) on lipids profile and IR depends on polymorphisms of ÀÑÅ (I/D), AGTR1 (A1166C), eNOS (T894G), PPARγ2 (Pro12Ala) [3] ADRβ1 (Arg389Gly) genes.

PP.21.325 FUNCTIONAL EFFECTS OF COMMON NADPH OXIDASE POLYMORPHISMS ON PERIPHERAL AND CENTRAL PRESSURES

P. Xaplanteris, C. Vlachopoulos, K. Baou, C. Vassiliadou, I. Dima, N. Ioakeimidis, C. Stefanadis. *Hippokration Hospital, 1st Department of Cardiology, Athens Medical School, Athens, Greece*

Background: The nicotinamide adenine dinucleotide phosphate (NADPH) oxidase system produces superoxide, thus regulating redox state in the vessel wall. Three single nucleotide polymorphisms (SNPs) of the p22phox subunit (-930A/G, C242T, A640G) have been associated with increased oxidative stress in hypertensives; however, the role of these polymorphisms on peripheral and central pressures in normotensive individuals has not been addressed.

Methods: 210 normotensive individuals were studied. The -930A/G, C242T and A640G SNPs were determined by polymerase chain reaction. Peripheral pressures were measured by mercury sphygmomanometer and aortic pressures by a validated device employing applanation tonometry.

Results: Prevalence of genotypes was AA:27.6% AG:44.3%, GG:28.1% for -930A/G; CC:33.3%, CT:49.5%, TT:17.2% for C242T and AA:29.5%, AG:47.6%, GG:22.9% for A640G.

Peripheral and central pressures did not vary across genotypes for the C242T and A640G SNPs. However, the -930A/G SNP influenced blood pressures:G allele carriers demonstrated higher levels of peripheral systolic blood pressure (PSBP) (AA: 113 ± 12, AG: 118 ± 13, GG: 119 ± 11 mmHg; $p < 0.01$) and diastolic blood pressure (PDBP) (AA: 70 ± 9, AG: 73 ± 10, GG: 74 ± 9 mmHg; $p < 0.01$). Regarding central pressures, AA homozygotes had lower central systolic blood pressure (CSBP) (AA: 103 ± 12, AG: 107 ± 13, GG: 108 ± 11 mmHg; $p < 0.01$) and diastolic blood pressure (CDBP) (AA: 71 ± 9, AG: 74 ± 10, GG: 75 ± 10 mmHg; $p < 0.01$). In multiple linear regression analysis, presence of the G allele (AG or GG) independently predicted periperal and central blood pressures.

Conclusion: The -930A/G SNP of the p22phox promoter is an independent determinant of peripheral, as well as of central pressures, in normotensive individuals. The G allele is associated with higher blood pressure in the brachial artery, as well as in the aorta. These findings further elucidate the role of this polymorphism in the regulation of blood pressure.

PP.21.326 PARACRINE STIMULATION OF VASCULAR SMOOTH MUSCLE PROLIFERATION BY DIADENOSINE

V. Jankowski, W. Zidek, J. Jankowski. *Med. Klinik IV, Charite, Berlin, Germany*

Objectives: The purinergic receptor system plays an important role in the regulation of both vascular and tubular functions within the kidney; however, the release of purinergic agonists other than ATP by renal tissue is not known. In this investigation, we determine if kidney tissue a source of diadenosine polyphosphates, which have high affinity for the P(2X) and P(2Y) receptors.

Methods and Results: Both diadenosine pentaphosphate and hexaphosphate were identified by matrixassisted laser desorption ionization-mass spectrometry in extracts purified from both whole porcine kidney and from cloned cells of the LLC-PK1 cell line. Both polyphosphates in nanomola concentrations were found to significantly stimulate the proliferation of vascular smooth muscle cells derived from rat thoracic aortas. The purinergic-receptor antagonist, suramin, did not significantly affect the growth-stimulatory properties of the polyphosphates. The growth stimulation of vascular smooth muscle cells by platelet-derived growth factor was potentiated by both diadenosine polyphosphates.

Conclusion: We conclude that diadenosine polyphosphates are endogenous purinergic agonis of the kidney that have physiologic and pathophysiologic relevance. These epithelial cell metabolic products have vasoregulatory properties while linking the energy supply and tubular function.

PP.21.327 A46G AND C79G POLYMORPHISMS IN BETA2-ADRENERGIC RECEPTOR GENE (ADRB2) AND ESSENTIAL HYPERTENSION RISK: A META-ANALYSIS

S. Wen[1], Y. Lou[1], J. Liu[2], Y. Huang[3], J. Liu[1], Z. Wang[1], Y. Liu[1], Z. Li[2], Y. Li[3], Y. Xie[3]. [1]*Department of Hypertension Research, Beijing Anzhen Hospital, CMU, and Beijing Institute of Heart Lung and Blood Vessel Diseases, Beijing, China,* [2]*Department of Cardiology, Beijing Anzhen Hospital, Capital Medical University, Beijing, China,* [3]*State Key Laboratory of Genetic Engineering, Institute of Genetics, School of Life Science, Fudan University, Shanghai, China*

Objective: No clear consensus has been reached on the β2-adrenergic receptor polymorphisms (A46G and C79G) and essential hypertension risk. We performed a meta-analysis to summarize the possible association.

Methods From 301 reports, we included 18 articles (20 studies) at the inclusion criteria. The fixed-effects model and the random-effects model were applied for dichotomous outcomes to combine the results of the individual studies.

Results: There was no statistical association between A46G and hypertension risk in all subjects, Asians or Caucasians. However, the association was observed in dominant genetic model (AA vs. (AG + GG)) ($P = 0.04$, OR = 1.38, 95% CI [1.01 - 1.87], Pheterogeneity = 0.98) in the subgroup of the mixed Africans. No statistical association could be found between C79G and hypertension risk in overall or any ethnic subgroup. In the research conducted on the severe hypertension (SBP ≥160mmHg and/or DBP≥95mmHg hypertensive population), significant association could be found in dominant genetic model (CC vs. (CG + GG)) ($P = 0.04$, OR = 1.38, 95% CI [1.02 - 1.86], Pheterogeneity = 0.03), and there was also a boardline significance between the C79 allele and severe hypertension ($P = 0.05$, OR = 1.26, 95% CI [1.00 - 1.57], Pheterogeneity = 0.04). No association could be found in the study between these two polymorphisms and stage 2 hypertension.

Conclusion Significant association between ADRB2 A46G polymorphism and hypertension was found in the population of the mixed African. The ADRB2 C79G polymorphism has significant association with the SBP ≥160 mmHg and/or DBP ≥95 mmHg hypertensive population.

PP.21.328 ACE (I/D) AND ENOS (T894G) GENES' POLYMORPHISMS INFLUENCE NEW CARDIOVASCULAR (CV) EVENTS: PHARMACOGENOMIC UPDATE ON THERAPY

J.V. Ursuliak[1], K.M. Amosova[2], V.P. Pishak[1], L.P. Sydorchuk[1], R.A. Volkov[3], I.I. Sydorchuk[1], R.I. Sydorchuk[1]. [1]*Bukovinian State Medical University, Chernivtsi, Ukraine,* [2]*National State Medical University, Kyiv, Ukraine,* [3]*Chernivtsi State University, Chernivtsi, Ukraine*

Objective: To determine the association between ACE (I/D) and eNOS (T894G) genes polymorphisms and new CV events in hypertensive patients with coronary artery disease (CAD) and acute coronary syndrome (ACS) in response to pharmacogenetically determined treatment.

Design/Methods: 249 mild-severe hypertensive patients (126 female, 123 male, age 50.5 ± 10.4), 70 – CAD (27 – ACS, 43 – stable angina (SA) participated in prospective pharmacogenetic study based on individual genotype-dependent BP reduction, according to ESH/ESC (2007). Genotyping of ACE and eNOS genes – PCR test. CV risk – by SCORE and Framingham scales.

Results: Age, gender, risk area of living, systolic BP, dyslipidemia, heart rate, left ventricular hypertrophy, residual ischemia, smoking, diabetes mellitus, WBC, claudicating, fibrinogen and electrical myocardial instability were independent risk factors for CV events. Baseline fatal and non-fatal CV risks for the next 10-years (SCORE and Framingham10) and 4-years (Framingham4) were significantly higher in D-homozygous patients than in I-allele carriers of ACE gene: 10.54 ± 3.70% ($p < .05$), 32.59 ± 5.67% ($p = .048$) and 17.99 ± 3.29% ($p = .01$), DD, ID and II, accordingly. Differences in CV risks were generally independent on eNOS (T894) gene polymorphism ($p > .05$), but associated with CAD (not ACS) in TT-genotype carriers: 14.76 ± 6.15% ($p < .05$), 33.76 ± 6.54% ($p < .05$) and 13.47 ± 4.35 ($p = .05$). The median reduction of CV risk in response to 12 months therapy (SCORE/Framingham10/Framingham4) was reliable in all genotypes carriers of ACE gene: II-(−55.1/−29.0/−47.3%, $p < .05$), ID- (−47.7/−31.4/−31.3%, $p < .05$), DD-(−50.2/−24.0/−47.9%, $p < .02$), with some deviation according to eNOS gene: fatal CV risk decreased significantly in all genotypes (in GG −62.0, TG −45.8, TT −41.8%, $p < .02$), non-fatal Framingham10 in TG-carriers (−20.7%, $p < .05$), Framingham4 – in G-allele carriers (−42.8/ −38.3%, $p < .05$).

Conclusions: DD-genotype of ACE gene has direct association with increased CV risks in hypertensive patients. eNOS (T894G) gene didn't influence CV risks, but TT-genotype is associated with CAD and new CV events in hypertensive patients. Pharmacogenetically modified treatment caused reliable reduction of patients with fatal CV risk (SCORE > 5.0%) by 42.8% and non-fatal (Framingham10/4 >20.0/15.0%) by 31.3% and 30.3%, accordingly ($p < .001$).