MINUTES OF THE 49th GENERAL ASSEMBLY OF THE EUROPEAN ASSOCIATION FOR THE STUDY OF DIABETES

held in the Pi i Sunyer Hall, Fira de Barcelona, Barcelona, Spain on Thursday 26 September, 2013 at 18:30

Present:	**Dr. Andrew J.M. Boulton**	**(President)**
	Dr. Stefano Del Prato	**(Vice President)**
	Dr. Bernard Thorens	**(Vice President)**
	Dr. Michael Roden	**(Honorary Treasurer)**
	Dr. Mark Walker	**(Honorary Secretary)**
	Dr. Cees J. Tack	**(Chair, PGEC)**
	Dr.Viktor Jörgens	**(Executive Director)**
	Dr. Monika Grüsser	**(Vice Director)**
	and 51 members	

The President, Dr. Boulton, welcomed everyone to the 49th General Assembly. He asked those present to stand in memory of the following members, who had passed away: Drs. Georg Eisenbarth, John Hutton, Harry Keen, Carol Lurie, Irina G. Obrosova, Samuel Rahbar, Jean-Louis Richard, Richard Rubin and Patrick Vexiau.

1. MINUTES 48th GENERAL ASSEMBLY 2012

Since there were no comments, the minutes were unanimously approved and officially signed as a correct record.

2. REPORTS

a) President

The President's report to the members on the activities of EASD was given in the President's Address before the Minkowski Lecture. It is available under: **http://www.easdvirtualmeeting.org/resources/6926**

The President announced the Claude Bernard Lecturer 2014: Dr. Domenico Accili.

The President announced the Medical Devices in Diabetology meeting on 26/27 February 2014. He said better post-marketing surveillance was required and the Swedish project of regulating pumps would be looked at.

The President expressed his thanks to all partners. Dr. Boulton reported that as expected the EASD Annual Meeting in Barcelona was doing very well and the number of delegates attending had slightly increased. Dr. Boulton thanked all members of the EASD Office and the Executive Committee for their commitment and hard work.

b) Honorary Treasurer

i) Result of tax audit 2008-2010/actions to be taken

In autumn 2012 for the second time, a control of the EASD by the Inland Revenue took place. These controls will always occur every three years due to the large turnover of the Association. In August 2013, EASD received the draft conclusion of this tax control. The non-profit status of the EASD is beyond all question; the main issue is the question of the taxation of the income from industry exhibition and symposia. EASD itself does not handle the industry exhibition and the symposia organized by third parties; these activities are taken care of by a professional congress organizer which is actually Interplan in Munich. In common with other medical associations in Germany, EASD has a contract, in our case with Interplan, giving them permission to organize these activities on their own responsibility without interfering with EASD concerning the organization and the fund raising. The basis of this collaboration is a loan contract and the income from such a loan contract is considered to be tax free. This legal and taxation construction is the basis of a healthy financial situation of German academic medical societies. The Düsseldorf tax authorities questioned this regulation and even asked their superiors for comments. In August 2013, they came up with the opinion that all incomes of EASD from these loan contracts, starting with 2008, are considered by the Inland Revenue as a taxable income. Taking into account corporation and local business tax, the result is that a total of Euro 5.4 million will likely have to be paid at the beginning of 2014. Following the advice of legal and

mmol/mol per risk allele (p 6.10-6 to 3.10-4). Most of these variants were low frequency variants and several were predicted to be damaging by SIFT/Polyphen2. However, due to the low frequency and power, replication in additional cohorts is necessary to reach genome wide significance. This replication is currently performed.
Conclusion: In this study we have identified a number of gene variants with relatively low frequency but a large effect on the metformin treatment response suggesting clinical usefulness in personalizing type 2 diabetes treatment. Furthermore, it identifies novel pathways modulating metformin response. However, replication in additional patients and cohorts is needed before definitive conclusions can be drawn.
Supported by: ZonMW, Priority Medicines Elderly program (project nr. 113102006)

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Insulin signalling genes exert a combined effect on all-cause mortality
C. Menzaghi[1], A. Fontana[2], M. Copetti[2], S. Rizza[3], B. Spoto[4], G. Tripepi[4], A. Marucci[1], A. Testa[4], F. Mallamaci[4], S. De Cosmo[5], S. Bacci[5], M. Federici[3], C. Zoccali[4], V. Trischitta[1];
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Background and aims: Type 2 diabetes (T2D) and cardiovascular (CV) disease are major factors increasing all-cause mortality. Both clinical entities recognize a common soil represented by insulin resistance (IR), which by itself also predicts all-cause mortality. IR is, at least partly, genetically determined. Thus, it is concievable that genetic factors, which modulate IR, play also a role in modulating T2D, CV desease and all-cause mortality. In fact, we have previously reported the combined effect of single nucleotide polymorphisms (SNPs) perturbing insulin signaling (*ENPP1* K121Q, rs1044498; *IRS1* G972R, rs1801278; *TRIB3* Q84R, rs2295490) on IR and, as a likely consequence, T2D and major CV events. Based on these encouraging results, we investigated whether a combined effect of these 3 SNPs affects also all-cause mortality.
Materials and methods: We first studied a sample comprising 742 patients (i.e. discovery sample; 238 deaths/3,520 person-years; py). Replication was assessed in a second sample of 725 diabetic patients (i.e. replication sample; 129 deaths/5,495 py).
Results: In the discovery sample, weighted genetic risk score (GRS), based on each SNP's effect size, was associated with all-cause mortality (HR=1.12, 95% CI=1.03-1.23). After stratification according to low or high genetic load (GL) (i.e. 0-1 or > 2 risk alleles), patients with high GL (n=123) were at increased risk of all-cause mortality (HR=1.36, 95% CI=1.00-1.86), as compared to those with low GL (n=619). In the replication sample, HR (95% CI) for all-cause mortality was 1.06 (0.94-1.19) for GRS and 1.58 (1.06-2.35) for GL. In a pooled analysis (1,467 individuals; 367 deaths) both GRS and GL were associated with all-cause mortality HRs (95% CI)=1.11 (1.01-1.22) and 1.41 (1.10-1.80), respectively.
Conclusion: Our finding indicates that functional non-synonymous variants affecting insulin signaling exert a joint effect on all-cause mortality and is consistent with a pathogenic role of IR on life expectancy.

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Dissecting the genetic architecture of loci with established effects on multiple cardiometabolic phenotypes and type 2 diabetes
L. Marullo[1], T.O. Kilpeläinen[2], B.K. Cornes[3], J. Dupuis[4], C. Scapoli[1], R.J.F. Loos[5], J.B. Meigs[3], A.P. Morris[6], I. Prokopenko[7], on behalf of the XC-Pleiotropy Group;
[1]Department of Life Sciences and Biotechnology, Genetic Section, University of Ferrara, Italy, [2]The Novo Nordisk Foundation Center for Basic Metabolic Research, University of Copenhagen, Denmark, [3]General Medicine Division, Massachusetts General Hospital, Boston, [4]Department of Biostatistics, Boston University School of Public Health, [5]The Icahn School of Medicine at Mount Sinai, New York, USA, [6]Department of Biostatistics, University of Liverpool, [7]Department of Genomics of Common Disease, Imperial College London, UK.

Background and aims: Genome-wide association studies (GWAS) have identified hundreds of loci associated with Type 2 Diabetes (T2D) or other cardiometabolic phenotypes, many of which overlap or map to the same genomic interval. Variants associated with multiple phenotypes, such as T2D, fasting insulin, triglycerides, HDL-cholesterol and body fat percentage influencing variants at IRS1, can provide insight into biology of correlated cardiometabolic phenotypes. However, the genetic architecture of these loci is frequently complex and needs further investigation.
Materials and methods: To disentangle association patterns of 630 associated SNPs (Dec 2012) from GWAS meta-analyses in Europeans for 19 quantitative phenotypes, T2D and hypertension, we defined sets of adjacent variants located less than 500kb apart and harboring 446 associated SNPs within 151 genomic regions (range=2-8 SNPs/region). We undertook approximate conditional analyses (ApCA) implemented in the GCTA tool to examine whether associations with multiple phenotypes within each region could be explained by LD.
Results: Across the 151 regions, we observed 14 (10%) loci in which the same SNP was associated with multiple phenotypes. Associations in 11 of these 14 loci were with epidemiologically highly correlated traits. Through ApCA, we identified 41 (27%) regions with multiple associated variants that underlie the same association signals, thus suggesting multi-phenotype effects. For 19 (13%) regions, the association with one phenotype partially explained the effect on another. Within 45 (30%) regions, multiple signals were explained by multiple non-related variants, whereas the remaining 32 (21%) regions showed complex architecture. Of the 44 regions associated with T2D, 15 contained the same association signal for other cardiometabolic phenotypes. Within 12 regions, including ANKRD55, SPRY2, DUSP8, PEPD and HNF4A, association with other phenotypes were not related to T2D variants. For 13 regions we observed complex architecture, while for the remaining 4 regions, the association with T2D partially explained the effect on another cardiometabolic phenotype.
Conclusion: Overall, a substantial number (87 or 58%) of cardiometabolic loci, of which 28 T2D loci, show potential pleiotropic effects on multiple phenotypes, which might contribute to their shared biology. Within other regions, distinct genetic effects or more complex architecture could underlie independent regulatory mechanisms.
Supported by: EFSD

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Genetic risk factors for diabetic complications in patients with type 2 diabetes from Ukraine
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Background and aims: Chronic hyperglycaemia is associated with increased risk of progression to macro (cardiovascular diseases) and microvascular complications (neuropathy, retinopathy and nephropathy). Recently, genome-wide association studies have identified a number of genetic loci for association with type 2 diabetes (T2D) and cardiometabolic traits. The effects of some of these genetic variants and the risk of diabetes progression to diabetes complications has been investigated in several populations, but has never been studied in Ukrainians, a population at high cardiovascular risk.
Materials and methods: We studied the association of a panel of 145 SNPs in loci previously reported to be associated with T2D/glycaemic traits (n=75), dyslipidemia (n=11), obesity (n=8), hypertension (n=13), cardiovascular diseases (CVD) (n=21) and microvascular complications (n=17) in approximately 3,500 subjects with T2D from the DOLCE study (M/F% 32/68, mean±SD, age-at-onset 53.5±10.6 years, BMI 31.4±5.6 kg/m^2, diabetes duration 7.1±7.4 years) (Diagnostic optimization and treatment of diabetes and its complications in the Chernihiv region). Effects of genetic loci were studied using logistic regression adjusted for sex and age-at-onset for macrovascular complications, and sex and diabetes duration for microvascular complications. The analyses were performed using R software, and genotyping was performed using Mass ARRAY iPLEX (Sequenom, San Diego, CA).
Results: We have replicated previous associations of GIPR rs10423928 (OR=1.29, P=0.005), WDR12 rs6725887 (OR=1.42, P=0.005) and MIA3 rs17465637 (OR=1.24, P=0.04) with CVD. VEGF rs2010963 (OR=1.28, P=0.02) previously reported to be associated with diabetic retinopathy (DR), was in our study associated with diabetic nephropathy (DN). The risk C-allele in TMEM26 rs1530440 (hypertension locus) was associated with increased