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MINUTES OF THE 48th GENERAL ASSEMBLY OF THE EUROPEAN ASSOCIATION FOR THE STUDY OF DIABETES

held in Berlin Messe, Germany, Thursday 4 October 2012 at 18:00

Present:	**Dr. Andrew J.M. Boulton**	**(President)**
	Dr. Fatima Bosch	**(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 49 members	

The President, Dr. Boulton, welcomed everyone to the 48th General Assembly. He asked those present to stand in memory of the following members, who had passed away: Drs. Angelika Bierhaus, Artur Czyzyk, Keith Taylor and Ulrich Vischer.

1. MINUTES 47th GENERAL ASSEMBLY 2011

Since there were no comments, the minutes were approved unanimously 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/2694

The President reported on the various activities and expressed his thanks to all partners. Dr. Boulton reported that as expected the EASD Annual Meeting this year in Berlin 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

Dr. Roden reported that the income from membership fees had decreased in 2011 and income from registration fees had increased slightly. There was a decrease in donations which was due to the fact that Merck had paid for two Final Programmes (2009 and 2010) in the year 2010. In 2011 only the Final Programme for 2011 was paid for. Donations for courses increased substantially. The total income of the Association was in the same frame as in 2010.

Regarding expenditure, Dr. Roden reported that Travel/ Meeting Expenses included expenses for more than one Meeting. EASD transferred more than 3 million Euro to the Foundation.

Dr. Roden summed up by saying the accounts of EASD remained healthy.

c) Honorary Auditors

The President asked the Honorary Auditor, Dr. Peter Diem for his report. Dr. Diem confirmed that the accounts had been checked carefully by Dr. Luis Gardete-Correia and were in perfect order. Dr. Boulton asked for the vote to accept the accounts.

The Honorary Treasurer was unanimously discharged (38 votes for and 1 abstention).

Conclusion: Genotype imputation using dense reference panels such as the 1KG allowed the identification of novel candidate genes as well as fine-mapping of already known associated regions using less sample sizes. These results, which we will confirm in independent populations, will lead to a better description of the genetic basis of T2D, allowing a better exploitation from the previously spent resources in large GWAS datasets.

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Large-scale genome-wide association meta-analysis of the 1000 genomes project imputed data identifies 19 novel lipid loci and new variants in previously known loci

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Background and aims: Hyperlipidemia is a frequent companion to T2D, reflecting shared insulin resistance, and contributes to diabetes-related complications. Genome-wide association (GWA) studies have been successful in detecting numerous associations with blood lipids (high and low density lipoprotein cholesterols (LDL/HDL), total cholesterol and triglycerides), through a substantial proportion of the genetic contribution to trait variances remains unexplained.
Materials and methods: In order to find more loci and to approach potential causal variants by fine-mapping in already known loci, we performed GWA meta-analysis of studies imputed from high density reference panel provided by the June 2011 release of 1000 Genomes project. This reference allows us to analyze markers with minor allele frequency as low as 0.5%. 17 population-based studies of European origin were used with total sample size up to 51,204 individuals.
Results: In a fixed-effects meta-analysis following imputation, we found 79 loci associated with at least one of the lipid measures with $P<5\times10^{-8}$, 19 of these were previously unreported (>2Mb from known loci) and lead variant at 7 of them had minor allele frequency less than 5%. We could replicate previously-reported associations at 3 missense SNPs (*APOE, ANGPTL4* and *PCSK9*, with MAFs 16.5%, 3.0% and 1.9% respectively) identified from candidate-gene resequencing efforts, and 3 others (*APOB, GCKR* and *HNF4A*, with MAFs 23.8%, 35.9% and 4.1%) found in GWA studies as the new lead SNPs. Initial fine-mapping analyses have identified at least two coding variants (*ABCA6/8* and *MOSC1,* with MAFs 1.9% and 28.0%) being lead SNPs at those loci and several other examples of low frequency lead SNPs.
Conclusion: Our results highlight the potential for the identification of novel associations using existing GWAS genotyping data, supplemented with imputation from high-density reference panel of 1000 Genomes Project without the need for costly re-sequencing experiments.
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Pleiotropic effects of obesity-susceptibility loci on metabolic traits: a meta-analysis of up to 37,874 individuals

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Background and aims: Obesity is a key risk factor for a number of metabolic diseases, including type 2 diabetes, dyslipedimia and cardiovascular disease. Although the exact biological mechanisms linking obesity to these co-morbidities are not fully understood, a set of common genetic factors with pleiotropic effects (i.e. affecting multiple traits) might in part explain the observed associations. We aimed to investigate whether the currently established obesity-susceptibility loci that were identified through genome-wide associations studies for body mass index (BMI) and waist-to-hip-ratio (WHR) are also associated with metabolic traits, independently of obesity-related traits.
Materials and methods: We systematically assessed associations of the 32 BMI and 14 WHR loci, individually and combined in two genetic predisposition scores (GPS-BMI, GPS-WHR), with glycaemic traits, blood lipids, and blood pressure (BP) by meta-analyzing data of up to 37,874 individuals of European ancestry from six population-based studies. We also examined whether these associations were influenced by (central) adiposity.
Results: The meta-analyses showed associations of both the individual obesity-susceptibility loci and the genetic predisposition scores with metabolic traits that were not driven by the obesity-related phenotypes. We observed significant associations of BMI-increasing alleles at five BMI-loci with lower levels of 2-hr glucose (RBJ, QPTCL: effect sizes -0.068 and -0.107 SD, respectively), HDL-cholesterol (SLC39A8: -0.065 SD, MTCH2: -0.039 SD), and diastolic BP (SLC39A8: -0.069 SD), and higher and lower levels of LDL- and total-cholesterol (QPTCL: 0.041 and 0.042 SD, respectively, FLJ35779: -0.042 and -0.041 SD, respectively) (all Ps<2.4x10-4), independently of BMI. The WHR-increasing alleles at two WHR-loci were significantly associated with higher proinsulin (GRB14: 0.069 SD) and lower fasting glucose levels (CPEB4: -0.049 SD), independently of BMI and WHR. A higher GPS-BMI was associated with lower systolic BP (-0.005 SD), diastolic BP (-0.006 SD) and 2-hr glucose (-0.013 SD), while a higher GPS-WHR was associated with lower HDL-cholesterol (-0.015 SD) and higher triglyceride levels (0.014 SD) (Ps<2.9x10-3), independently of BMI and/or WHR.
Conclusion: Our results provide evidence that obesity susceptibility loci have pleiotropic effects on metabolic traits, independently of adiposity. These findings bring a novel insight into mechanisms that link obesity with metabolic abnormalities and highlight that the genetic variants predisposing to obesity might also predispose to, or protect from, other metabolic disorders.
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Dissecting the pleiotropic effects of established type 2 diabetes and other cardiometabolic trait loci to define pathways and gene networks involved in type 2 diabetes pathogenesis

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Background and aims: Recent genome-wide association studies (GWAS) for human complex phenotypes have identified hundreds of genetic variants for cardio-metabolic traits and risk of disease. At many loci or specific variants associations are observed with multiple epidemiologically correlated traits. We formed the Cross-Consortia Pleiotropy Group to investigate the patterns of multi-cardio-metabolic trait associations across the genome. We aimed (a) to examine the associations of cardio-metabolic trait loci with epidemiologically correlated traits by grouping shared patterns of individual trait effects; (b) to define pathway and gene networks involved in the trait variability within the association pattern groups.
Materials and methods: We evaluated the genetic effects of 544 independent variants ($r^2<0.8$) from a total of 687 SNPs from published GWAS meta-analyses (thru Sep 2012) of 20 quantitative cardio-metabolic traits, including systolic/diastolic blood pressure, 8 glycaemic, 6 obesity/anthropometric, 4 lipid traits, and 2 diseases (Type 2 Diabetes (T2D), hypertension). We applied a complete hierarchical cluster analysis, which grouped variants according to their impact on the cardio-metabolic traits. We combined these data with annotated pathways, protein-protein interactions and semantic relationships from the published literature using GRAIL and DAPPLE software tools, which estimated the significance of connections between putative genes.
Results: We identified 33 groups of variants with shared patterns of associations with cardio-metabolic traits. Of these, 22 clusters contained groups of variants showing association with one or a group of highly correlated phe-

notypes. In the other 11 clusters, genetic variants were grouped according to their patterns of phenotypic effects. A group of 17 BMI/WC loci, such as *MC4R, TMEM18, BDNF, TFAB2B, NEGR1*, were related to BMI, lower HDL, higher triglycerides (TG), T2D risk, insulin resistance and obesity traits, the latter two being insignificant after BMI adjustment. 19 loci from another cluster were related to "healthy obesity/unhealthy leanness" by association with higher BMI and HDL, lower TG, glycaemic traits and risk of T2D, where three growth factors, *GRB14, PDGFC, VEGFA* showed significant connectivity ($p<0.001$). A cluster of 23 loci primarily associated with lower height or higher total cholesterol were also related to lower skeletal growth and higher HDL, accompanied by significant direct ($p=0.05$) and indirect ($p=0.001$) physical gene interactions. A cluster containing *CDKAL1, THADA, IGF2BP2, RREB1, DGKB, PROX1* and 6 other loci were related to beta cell function and glucose homeostasis traits and higher T2D risk.
Conclusion: This approach shows great promise for dissecting genetic effects on cardio-metabolic traits.

PS 014 Nutrition and mechanisms in diabetes: observational studies

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Anti-obesity and anti-diabetic effect of chronic coffee consumption in mice

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Background and aims: Chronic coffee consumption is correlated with a substantially lower incidence of type 2 diabetes. Apparently the association does not depend on race, gender or geographic distribution of the study populations. For the experimental exploration of the underlying mechanisms the demonstration of this effect in a mouse model of type 2 diabetes is needed.
Materials and methods: From week 10 on, male C57BL/6NCrl mice consumed regular coffee (i.e. coffee containing a natural content of caffeine) as filtered brew of 20 g ground coffee per litre (mean caffeine concentration 327 ± 30 mg/l, n = 29) or 40 g/ litre *ad libitum* or continued to drink tap water. The development of obesity and diabetes caused by a high fat diet (55% lipids, HFD) was observed for 35 weeks in comparison with mice feeding on normal chow (9% lipids, ND). In addition to parameters of metabolism, the morphology of the endocrine pancreas was quantified.
Results: The massive weight gain in HFD mice was dose-dependently delayed, the moderate weight gain in aging ND mice was abolished by coffee consumption. In both cases this was due to a lower feeding efficiency. Water or coffee consumption depended on the type of diet but not on the type of fluid. HFD mice had a 50% lower intake. At week 21 intraperitoneal glucose tolerance tests (IPGTT) showed a dose-dependent significantly faster decline of elevated glucose levels in coffee-consuming HFD mice, but not in ND mice. At week 39 the IPGTT showed diminished peak levels in coffee-consuming HFD mice, but also an improved glucose tolerance in all treatment groups vs. week 21. This spontaneous improvement was also visible as a decrease of the non-fasting glycaemia between week 21 and week 30, both in HFD and ND mice. Coffee-consuming ND mice and control ND mice had closely similar values for total cholesterol, triglycerides, HDL cholesterol and also blood glucose. The coffee-consuming HFD mice, in contrast, differed significantly from the corresponding ND mice in each single parameter. Irrespective of coffee consumption HFD mice were hyperinsulinaemic at week 21, grossly hyperinsulinaemic at week 39 and had significantly enlarged islets at week 45. Coffee consumption did not affect islet size or parameters of beta cell apoptosis, proliferation and insulin granule content.
Conclusion: The chronic consumption of regular coffee diminishes weight gain both in HFD and ND mice and favourably affects glucose tolerance in HFD mice. Thus, this model seems appropriate to explore which of the coffee constituents is responsible for the diabetes-preventive effect of coffee consumption in humans.
Supported by: Institute for Scientific Information on Coffee

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Dietary intake of carbohydrates and risk of type 2 diabetes: European Prospective Investigation into Cancer in Norfolk study

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Background and aims: To better understand the role of dietary patterns in development of type 2 diabetes we investigated the association of dietary intake of carbohydrates and risk of type-2 diabetes in a large prospective study.
Materials and methods: A total of 25,639 men and women aged 40-79 were recruited in the European Prospective investigation into Cancer in Norfolk study. Incident cases of diabetes (N=749) were identified and compared with a randomly selected sub-cohort of 3496 participants. Seven-day food diary administered at baseline was used for dietary assessment. We performed modified Cox-proportional hazards regression analyses and compared results from the different methods of adjustment for total energy intake.
Results: Dietary intakes of sucrose, starch, lactose, maltose, or total carbohydrates were not significantly related to diabetes risk after adjustment for con-