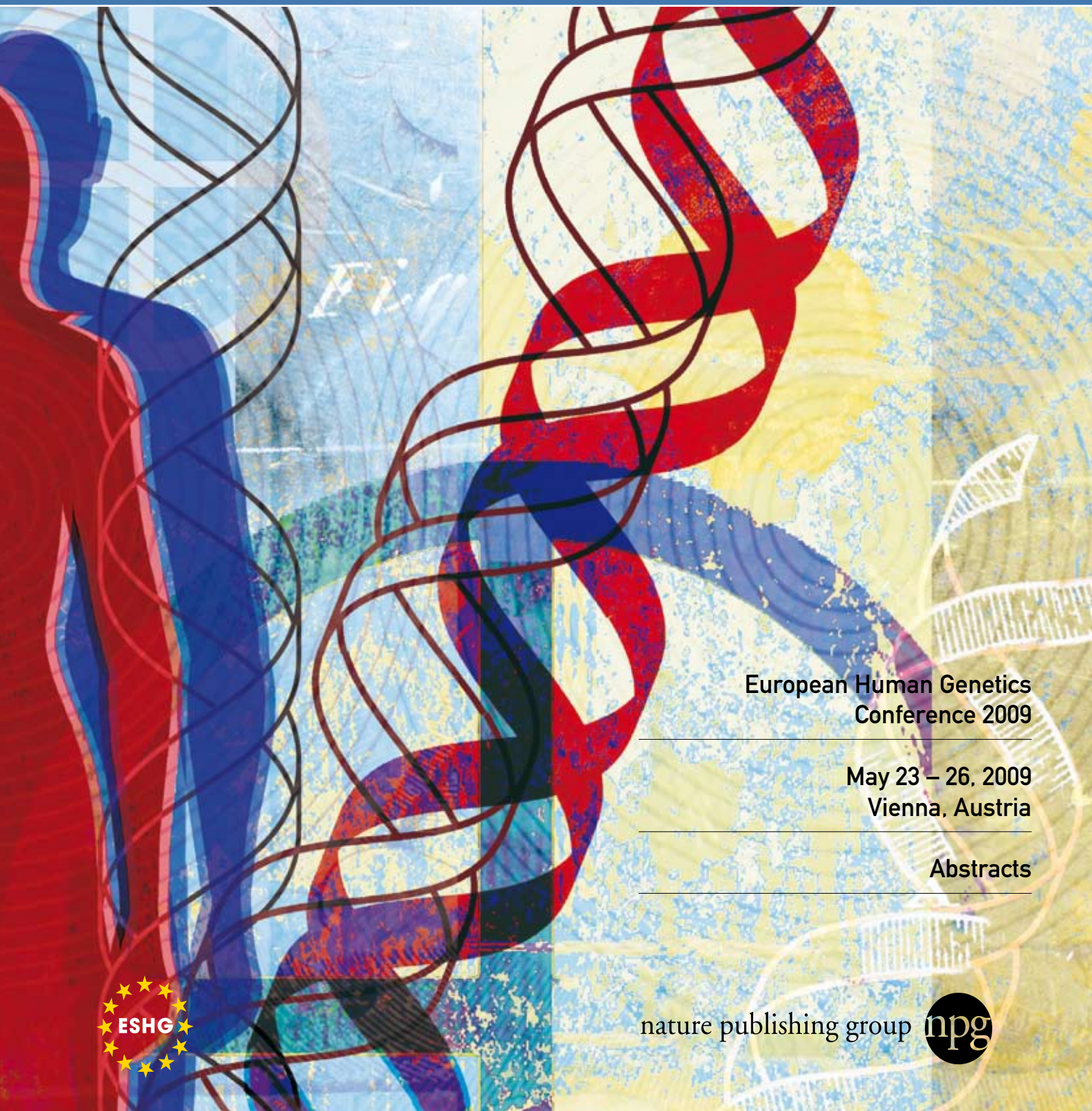
European Journal of Human Genetics

Volume 17 Supplement 2 May 2009 www.nature.com/ejhg



European Human Genetics Conference 2009

May 23 – 26, 2009
Vienna, Austria

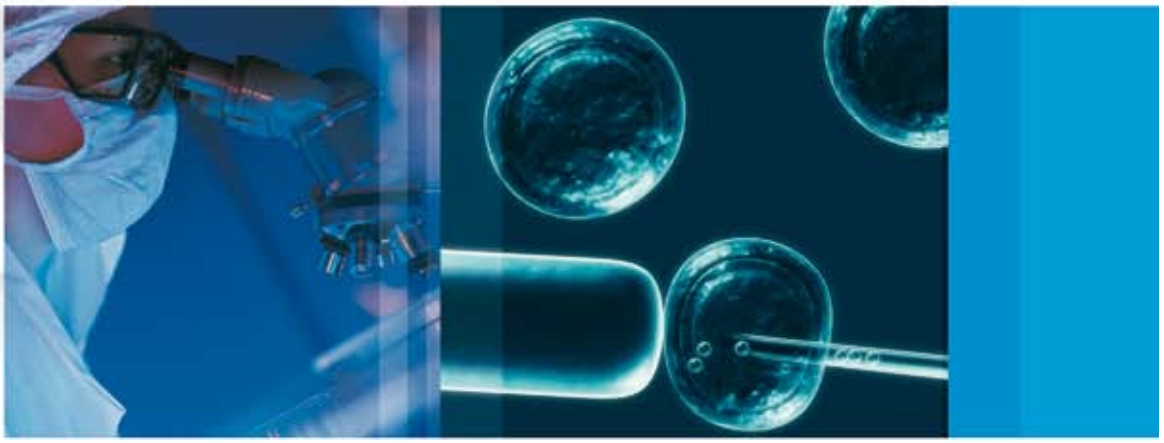
Abstracts

ESHG

nature publishing group npg

sistemas genómicos® BIOMÉDICA

Leading company in DNA analysis



Integrated genetic services applied to human health

- Experience and technological capability to approach genetic diagnosis of any genetic known disease
- International reference centre for the diagnosis of genetic diseases

MEDICAL GENETICS

New diagnosis tools to improve your clinical practice

GENETIC COUNSELLING

GENETIC DIAGNOSIS

PRENATAL GENETIC DIAGNOSIS

RARE DISEASES

HEREDITARY CANCER

GENETICS IN ONCOHEMATOLOGY

PERSONALIZED GENETIC STUDIES

REPRODUCTIVE GENETICS

An easy way to offer PGD to your patient

PREIMPLANTATION GENETIC DIAGNOSIS SERVICE (PGD)
Detection of aneuploidies
Embryo sex determination
Structural chromosome anomalies
Monogenic diseases
HLA Typing

GENETIC INFERTILITY

GENETIC STUDIES FOR GAMETE AND EMBRYO DONORS

REPRODUCTIVE GENETIC COUNSELLING

Parque Tecnológico de Valencia
Ronda G. Marconi, 6
46980 PATERNA (Valencia)
Tel. 902 364 669 · Fax 902 364 670
info@sistemasgenomicos.com
www.sistemasgenomicos.com

Request our brochure
902 364 669

European Society of Human Genetics

EUROPEAN HUMAN GENETICS CONFERENCE 2009

Austria Center Vienna

Vienna, Austria

Saturday, May 23 – Tuesday, May 26, 2009

Abstracts

www.eshg.org

Committees – Board – Organisation

European Society of Human Genetics

ESHG Office

European Society of Human Genetics
Ms. Karin Knob
c/o Vienna Medical Academy
Alserstrasse 4
1090 Vienna
Austria
Tel: +43 1 405 13 83 20
Fax: +43 1 405 13 83 23
Email: office@eshg.org
Website: www.eshg.org

Executive Board 2008-2009

President
Jean-Jacques Cassiman, BE

Vice-President
PierFranco Pignatti, IT

President-Elect
Dian Donnai, UK

Secretary-general
Helena Kääriäinen, FI

Secretary-general-elect
Gunnar Houge, NO

Treasurer
Andrew Read, UK

Scientific Programme Committee

Chair
Han Brunner, NL

Members
Hans-Christoph Duba (Local Host), AT
Thierry Frébourg, FR
Peter Heutink, NL
Helena Kääriäinen, FI
Batsheva Kerem, IL
Florian Kronenberg, AT
Inge Libaers, BE
Mark McCarthy, UK
Olaf Riess, DE
Mariano Rocchi, IT
Pete Scambler, UK
Raquel Seruca, PT
Michael Speicher, AT
Eduardo Tizzano, ES
Draga Toncheva, BG
Mikka Vikkula, BE
Ciska Wijmenga, NL
Andrew Wilkie , UK
Brunhilde Wirth; DE

Board Members

Nurten Akarsu, TR
Karen B. Avraham, IL
Jacques Beckmann, CH
Agnes Bloch-Zuppan, FR
John Burn, UK
Francoise Clerget-Darpoux , FR
Anne Cambon-Thomsen, FR
Gerry Evers-Kiebooms, BE
Peter Heutink, NL
Klaus W. Kjaer, DK
Vaidutis Kučinskas, LI
Jan Lubinski, PL
Andres Metspalu, EE
Giuseppe Novelli, IT
Tayfun Ozcelik, TR
Alessandra Renieri, IT
Alexandre Reymond, CH
Jorge Sequeiros, PT
Maria Soller, SE
Silke Sperling, DE

Liaison Members

Segolène Aymé, FR
Jacques Beckmann, CH
Han Brunner , NL
Martina Cornel, NL
Domenico Coviello, IT
Ros Hastings, UK
Ulf Kristoffersson, SE
Heather Skirton, UK

Further information on structure and organisation can be found on the website **www.eshg.org**

Future European Human Genetics Conferences

European Human Genetics Conference 2010
June 12 – 15, 2010
Gothenburg, Sweden

European Human Genetics Conference 2011
May 28 - 31, 2011
Amsterdam, The Netherlands

Spoken Presentations

Posters

P17.16
Genetic markers of essential hypertension, located on chromosome 1q

Y. R. Timasheva[1], *T. R. Nasibullin*[1], *A. N. Zakirova*[2], *O. E. Mustafina*[1];
[1]*Institute of Biochemistry and Genetics, Ufa, Russian Federation,* [2]*Bashkir State Medical Academy, Ufa, Russian Federation.*

Elevated blood pressure is a complex trait regulated by multiple factors. Genetic predisposition, along with lifestyle changes, plays the crucial role in the development of essential hypertension (EH). Twin studies have demonstrated that almost 50 percent of the inter-individual variability in blood pressure level is heritable. Genome-wide linkage studies have associated the incidence of hypertension with some genomic regions (chromosome 1q, 2p, 2q, 3p, 6q, 16q, 15q, 18q, 19p).

We performed screening of genetic markers located on chromosome 1q. DNA samples, used in the study, were obtained from 1095 individuals (355 Tatars, 362 Bashkirs and 378 Russians residing in Bashkortostan, Russia). SNP-genotyping of 1q candidate loci was performed using polymerase chain reaction followed by restriction enzyme digestion. Data were analyzed using Arlequine 2.0.

We found that haplotypes of polymorphic variants in E-selectine (*SELE,* rs2076059), P-selectine (*SELP,* rs6131), L-selectine (*SELL,* rs3177980), beta 1 polypeptide of Na+/K+ transporting ATPase (*ATP1B1,* rs12731646) and regulator of G-protein signaling 5 (*RGS5,* rs2255642) genes are associated with essential hypertension. *TSLCG* haplotype was associated with increased risk of EH in ethnic Russians (OR=2.88, CI_{OR} 1.45-5.72, P=0.002), while *TALCA* (OR=0.01, CI_{OR} 0.01-0.82, P=0.042), *TSFCA* (OR=0.34, CI_{OR} 0.12-0.93, P=0.033) and *TSFCG* (OR=0.44, CI_{OR} 0.21-0.90, P=0.022) haplotypes were found to be protective against EH. Increased risk of EH in Tatar ethnic group was associated with *CAFTA* haplotype (OR=29.64, CI_{OR} 3.92-224.30, P=0.000), decreased - with *TSFTA* (OR=0.04, CI_{OR} 0.01-0.31, P=0.001) and *TSLCA* (OR=0.06, CI_{OR} 0.01-0.49, P=0.033) haplotypes. Our data confirm the association between genetic markers on chromosome 1q and human hypertension.

P17.17
Haplotypic effect of three functional promoter polymorphisms of MMP1 confers higher risk of myocardial infarction

P. Román-García, *E. Coto, J. R. Reguero, I. Lozano, P. Avanzas, C. Morís, J. B. Cannata-Andía, I. Rodríguez;*
Servicio de Salud del Principado de Asturias, Oviedo, Spain.

Purpose

Inherited and acquired risk factors contribute to the development of the atherosclerotic lesion and its most serious clinical manifestation, myocardial infarction (MI). Studies with human tissues and animal models have suggested a role for matrix metalloproteases (MMPs) in atherosclerosis, and several functional polymorphisms in the *MMP-1* gene have been linked to the risk for MI. The aim of this study was to evaluate the association between three promoter polymorphisms and early MI in a Spanish cohort.

Methods

We performed a case-control study with 261 unrelated male patients who had suffered an early MI and 194 healthy matched controls. All participants were smokers and younger than 60 years. The genotypes for the three *MMP-1* promoter polymorphisms (-1607 1G/2G; -519 A/G; -340 T/C) were determined through restriction enzyme digestion of a PCR fragment (PCR-RFLP). Comparison of allele and genotype frequencies of individual polymorphisms and haplotypes was carried out using the chi-square test (SHEsis software).

Results

Allelic and genotypic frequencies of individual polymorphisms did not differ between patients and controls. Statistical analysis of the haplotypes showed that the combination $-1607_{2G}/-519_{G}/-340_{T}$, present in 3.4 % of controls, had a higher frequency among patients (p=0.005; OR=2.4; CI=[1.27-4.55]). Moreover, the haplotype $-1607_{1G}/-519_{G}/-340_{T}$ showed higher frequency in controls (p=0.02; OR=0.68; 95 % CI=[0.49-0.94]). This haplotype is the combination of alleles with a described less transcriptional activity.

Conclusion

Our results confirmed and extended the previously reported association between *MMP-1* promoter polymorphisms and MI, proving that its action could be through the instability and rupture of the plaque.

P17.18
Relationship of the APOE polymorphism and lipid profile: a population-based study in the Azores Islands (Portugal)

M. Raposo[1], *Y. Dahmani*[1], *F. Silva*[1], *M. Tavares*[1], *T. Cymbron*[1], *C. Santos*[1,2], *C. Bettencourt*[1], *R. Ferin*[1], *C. Correia*[1], *M. L. Pavão*[1], *M. Lima*[1];
[1]*Center of Research in Natural Resources (CIRN), University of the Azores, Ponta Delgada, Portugal,* [2]*Unitat Antropologia Biològica, Universitat Autònoma de Barcelona, Barcelona, Spain.*

The factors leading to a two-fold mortality rate from coronary artery disease (CAD) in the Azores, as compared to Mainland Portugal, have not been elucidated. Previous studies reported a population tendency for hypercholesterolemia, one of the main factors contributing to the development of atherosclerosis (AT), considered the primary cause of CAD. Apolipoprotein E has a key role in plasma lipid metabolism, given its function as a ligand for cell-surface receptor mediated uptake of lipoproteins. Polymorphism in the apolipoprotein gene (*APOE*) results in three major isoforms encoded by three codominant alleles (E2, E3 and E4). With the purpose of establishing the pattern of variation at the *APOE* locus and determining its association with lipid profile, we studied a random sample of 298 unrelated, apparently healthy individuals of Azorean origin. In nearly 50% of the sample total cholesterol (TC) was above 200mg/dl; in 25% of the individuals LDL-cholesterol (LDL-C) was higher than 130 mg/dl. Allele frequencies were 0.0833, 0.8317 and 0.0850 for E2, E3 and E4, respectively. Genotype frequencies were higher for E3*E3 genotype (66.1%); genotype distribution displayed conformity with Hardy-Weinberg expectations. No differences in allelic frequencies were found in comparison with other Caucasian populations, namely with mainland Portugal. E3*E4 individuals presented the highest cholesterol levels. Analysis of variance performed with the most represented genotypes (E2*E3, E3*E3 and E3*E4) revealed a clear association between the genotypic composition and TC, as well as LDL-C, thus confirming in this population, the role of *APOE* as one of the genetic determinants of AT.

P17.19
Genetic risk factors for arterial ischemic stroke in children: a possible MTHFR and eNOS gene-gene interplay?

V. Djordjevic[1], *M. Stankovic*[1], *V. Brankovic-Sreckovic*[2], *L. Rakicevic*[1], ***D. Radojkovic***[1];
[1]*Institute of Molecular Genetics and Genetic Engineering, Belgrade, Serbia,* [2]*Clinic for Child Neurology and Psychiatry, Belgrade, Serbia.*

Pediatric stroke has become increasingly recognized as an important cause of morbidity and mortality. The etiological heterogenity of this disease implicates careful consideration of the complex interactions between genetic and acquired risk factors. In order to investigate the influence of genetic factors in childhood stroke, we compared the distributions of mutations/polymorphisms affecting haemostasis and/or endothelial function (FVLeiden, FIIG20210A, MTHFRC677T, ACE ID and eNOSG894T) among children with stroke and controls. A total number of 26 children with arterial ischemic stroke, and a control group of 50 healthy children were included in the study. No statistically significant differences in allelic and genotypic distribution were detected in comparisons between groups. However, when combined genotypes were analyzed, statistical significance was observed for the association of MTHFR CT and eNOS TT gene variants. The results of our study suggest that this genotype combination represents a risk factor of 7.2 (p=0.017) for stroke in children.

P17.20
HMOX1 polymorphism in patients with Atherosclerosis

A. Aleyasin, *Z. Mohammad;*
NIGEB, Tehran, Islamic Republic of Iran.

Introduction: Heme oxygenase (HO) is important in the defense against oxidative stress and as a factor in an antiatherogenic mechanism. Heme oxygenase (HO) leads to the generation of free iron, carbon monoxide, and bilirubin. A length polymorphism of GT repeats in the promoter of human HO-1 gene shows difference transcriptional activity which modulate the transcription of the gene in vascular cells. The aim of this study was to assess the association of the length of (GT)(n) repeats in the development of coronary artery disease (CAD).

METHODS:We screened the allelic frequencies of (GT)(n) repeats in the HO-1 gene promoter in 59 patients who underwent coronary angiography. Because the distribution of numbers of (GT)(n) repeats