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List of Abstracts

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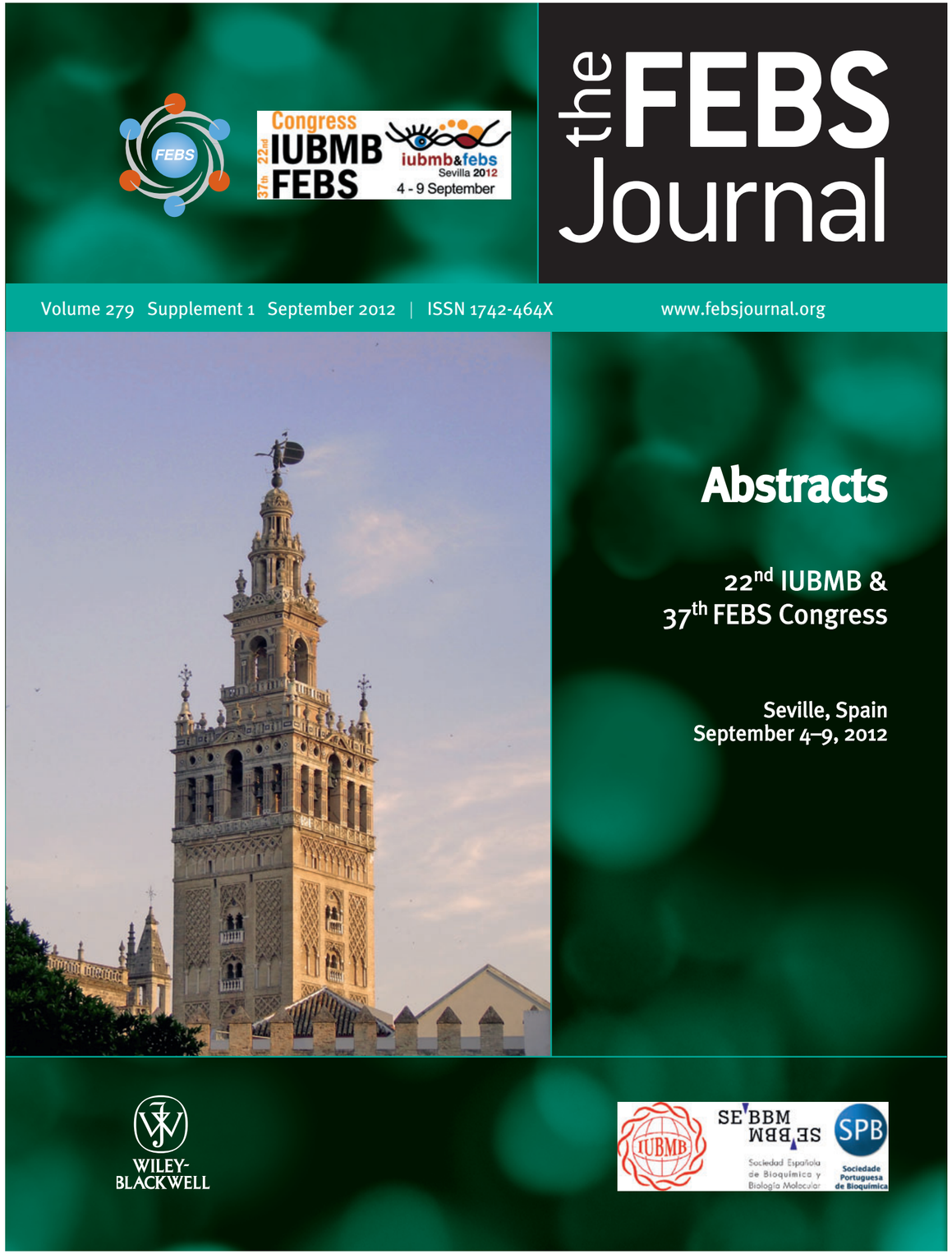

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P13-105
The polyQ protein ataxin-3 protects against stress conditions

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Spinocerebellar ataxia type 3 (SCA3) is a neurodegenerative disorder caused by the expansion beyond a certain threshold of a polyQ tract in the protein ataxin-3 (AT3). AT3 consists of a globular N-terminal Josephin domain and of a flexible C-terminal tail containing the poly-Q tract. The pathology results from protein misfolding and intracellular accumulation of fibrillar amyloid-like aggregates. The loss of function resulting from misfolding might also be involved in the mechanisms of pathogenesis. AT3 is a conserved and ubiquitous protein known to bind polyubiquitin chains and to function as a deubiquitinating enzyme. It seems to be involved in different cellular pathways, i.e. aggresome formation and ubiquitin-proteasome pathway, but the physiological role is still poorly understood. To investigate possible functions of AT3 in cellular pathways that respond to altered protein homeostasis, we constitutively expressed several AT3 variants in *Pichia pastoris*, a methylotrophic yeast lacking proteins homologous to AT3. Growth assays showed that expression of wild type AT3 or the sole Josephin domain allows yeast growth even under stress conditions, such as heat-shock or ER stresses (dithiothreitol, tunicamycin). The expression of a catalytically inactive variant could not restore yeast viability, which suggests that the deubiquitinating activity of AT3 is required for the protective effect. We also created a transgenic *C. elegans* strain over-expressing wild type AT3 in neurons under the control of a pan-neuronal promoter *unc-119*. Based on body bends counting, preliminary studies suggest that under stress condition *C. elegans* over-expressing wild-type AT3 shows an increased motility compared with wild type. Our data suggest that AT3, thanks to its deubiquitinating activity, displays a protective effect against stress conditions.

P13-106
Allelic frequency of single nucleotide polymorphisms involved in cancer related bioprocesses

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Chronic and complex diseases stem mainly from the complex interactions of genes with the environment. Numerous genetic polymorphisms have been identified, directly or indirectly contribute to susceptibility to complex diseases. Cancer is one of the complex diseases and second causes of deaths in the worldwide. In this study we aim to assess allelic frequency of cancer-related single nucleotide polymorphisms in Turkish participants.

Genotyping was performed using MALDI_TOF based mass spectrometry. The genetic variations predisposing to cancer etiology were analyzed according to manufacturer's protocol of Sequenom hME platform. Results were statistically analyzed for SNPs; MnSOD rs1799725, GSTP1 rs1695, GSTP1 rs1138272, CYP1A1 rs4646903, CYP1B1 rs1800440, CYP1B1 rs1056836, COMT rs4680, CYP17A1 rs743572, ELAC2 rs34152967, CYP19A1 rs10046, SRD5A2 rs523349, SRD5A2 rs9282858.

Genotype and allele frequencies were calculated and compared with European, Asian and African populations and allelic distributions mainly were close to the European community Genotyping results for five SNPs were inconsistent with the Hardy-Weinberg equation. Some genotypes, causing susceptibility to cancer, were found to be frequent in heterozygote state.

Rapid changes in genetics/genomics knowledge are affecting the content of health services, leading to personalized health care. Preventive health care models which also include genetic testing, allows developing individualized nutritional, pharmacological and medical follow-up advice to reduce risk for chronic diseases. The information on the allelic frequencies of genes in a given population is important for research, development and implementation of personalized health care models which may bring targeted preventative healthcare strategies.

Keywords: genetics of complex diseases, cancer predisposition, SNP genotyping

P13-107
Toxicogenomics in the mitochondrial diseases

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Mitochondrial DNA contains 37 genes, all of which are essential for normal mitochondrial function: two rRNA genes, 22 tRNA genes, and 13 structural genes encoding subunits of the oxidative phosphorilation system, which is the 'business end' of oxidative metabolism, where ATP is generated. Therefore, mutations in these genes can cause an energy deficit and cause mitochondrial diseases. The effects of mitochondrial disease can be quite varied and the severity of the specific defect may also be great or small. The pathogenic mutations are usually heteroplasmic whereas neutral polymorphisms are homoplasmic. However, there are many exceptions and an increasing awareness of the possible or documented pathogenicity of homoplasmic mutations. In fact, mutations causing LHON are homoplasmic (11778/ND4, 3460/ND1, and 14484/ND6). Similarly, most nonsyndromic forms of deafness are due to homoplasmic mutations, including A1555G in the 12S-rRNA gene. One possible explanation is that these mutations are modulated by other nuclear or mitochondrial variants and/or the adverse effect of environmental causes. We used transmitochondrial cell line models (cybrids) to analyze whether the combination of mtDNA mutations and xenobiotics (environment factors) may trigger the patient's pathology. We built cybrids with pathological mtDNA mutations in osteosarcoma (143B) and another cell line that shares many characteristics of neuronal progenitor cells, teratocarcinoma (NT2). We analyzed their mitochondrial function and their interactions with different xenobiotics (pesticides, antibiotics and organotin compounds).

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