Croat Med J 2005;46(6):1020-1022

**Ugarković D. Functional elements residing within satellite DNAs. EMBO Rep. 2005;6:1035-9.**

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Satellite DNAs represent a fast-evolving portion of the eukaryotic genome whose evolution is proposed to be driven by the stochastic process of molecular drive. Recent results indicate that satellite DNAs are subject to certain structural constraints, which are probably related to their interaction with proteins involved in the establishment of specific chromatin structures. The evolutionary persistence and high sequence conservation of some satellites, as well as the presence of stage- or tissue-specific, differentially expressed transcripts in several species, are consistent with the hypothesis that satellite DNA could have a regulatory role in eukaryotic organisms. Although the role of most transcripts is not known, some act as precursors of small interfering RNAs, which are now recognized as having an important role in chromatin modulation and the control of gene expression. Furthermore, some transcripts are involved in the cellular response to stress.

**Cvetko L, Markotić A, Plyusnina A, Margaletić J, Miletić-Medved M, Turk N, et al. Puumala virus in Croatia in the 2002 HFRS outbreak. J Med Virol. 2005;77:290-4.**

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HFRS is an endemic disease throughout Croatia. The incidence of HFRS varies in a cyclic fashion, with peaks occurring every couple of years, coinciding with peaks in vole populations. PUUV was shown to be dominant pathogen during the last HFRS outbreak in Croatia in 2002. The authors focused the research on two newly discovered localities (Okucani and Nova Gradiska) with a high number of reported HFRS cases and a significant increase in rodent population. PUUV infection was verified in 84.2% of patients at this region during the 2002 outbreak. Genetic analysis of wild-type (wt) PUUV strains was performed. Fifty seven bank voles lethrionomys glareolus originating from PUUV-associated HFRS areas were screened for the presence of PUUV N antigen and 15 (26%) were found positive. Total RNA isolated from rodent lung tissues was reverse transcribed followed by PCR amplification with primers specific for PUUV medium (M) or small (S) genome segments. Partial PUUV M segment sequences (approximately 450 bp long) were recovered from five bank voles and partial S segment sequences (app. 250 nt long)-from two bank voles. Genetic analysis of Croatian wt-PUUV strains revealed their close relatedness suggesting that the two localities belong to the same natural focus of infection. On phylogenetic trees, Croatian PUUV strains clustered together with the strains from Slovenia and Austria forming distinct Alpe-Adrian genetic lineage.

**Lisak M, Trkanjec Z, Mikula I, Demarin V. Mean blood flow velocities in posterior cerebral arteries during visual stimulation. Mt Sinai J Med. 2005;72:346-50.**

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Changes of mean blood flow velocities (MBFV) in the posterior cerebral arteries (PCA) recorded during visual stimulation in a group of 51 healthy, right-handed volunteers are presented. There were 27 (52.9%) males and 24 (47.1%) females, aged 20-59 years (mean age: 36.98 years). Measurements were performed with a hand-held 2 MHz transcranial Doppler (TCD) probe through the temporal window, with the subjects' eyes open and closed, and while they were looking at constant and at flashing white light. In half of the subjects, first the right PCA was insonated and then the left PCA, while in the other half the reverse procedure was used. Statistical analysis was done using Wilcoxon's matched-pair signed-rank test. Mean MBFV value in the left PCA was $41.2 \pm 8.6$ cm/s (mean $\pm$ SD) with eyes open, $27.8 \pm 8.5$ cm/s with eyes closed, $42.3 \pm 9.1$ cm/s while looking at constant white light, and $43.0 \pm 9.6$ cm/s while looking at flashing white light. Mean MBFV value in the right PCA was $41.7 \pm 8.9$ cm/s with eyes open, $28.2 \pm 9.1$ cm/s with eyes closed, $42.4 \pm 8.8$ cm/s while looking at constant white light, and $43.4 \pm 9.2$ while looking at flashing white light. Value differences for the left PCA, between eyes open and closed and between looking at constant white light and looking at flashing white light were statistically significant ($p < 0.001$, $z = -6.2146$, and $p < 0.001$, $z = -3.4836$, respectively). For the right PCA, a value difference between eyes open and closed, and between looking at constant and flashing white light was statistically significant ($p < 0.001$, $z = -6.2146$ and $p < 0.001$, $z = -3.6928$), but there was no significant difference between eyes open and constant white light ($p = 0.03$, $z = -2.1693$). The results showed that simple visual stimulation had an effect on blood flow velocities in PCA and that it could be measured with TCD.

**Zemunik T, Škrabić V, Boraska V, Diklić D, Terzić IM, Capkun V, et al. FokI polymorphism, vitamin D receptor, and interleukin-1 receptor haplotypes are associated with type 1 diabetes in the Dalmatian population. J Mol Diagn. 2005;7:600-4.**

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Vitamin D and interleukin (IL)-1 have been suggested to function in the pathogenesis of type 1 diabetes mellitus (T1DM). Therefore, the authors examined the influence of gene polymorphisms in vitamin D receptor (VDR) and interleukin-1 receptor type I (IL-1-R1) on susceptibility to T1DM in the Dalmatian population of South Croatia. A total of 134 children with T1DM and 132 controls were genotyped. For FokI polymorphism studies, they extended the control group to an additional 102 patients. The VDR gene polymorphism FokI displayed unequal distribution ($p=0.0049$) between T1DM and control groups, with the ff genotype occurring more frequently in T1DM individuals whereas the VDR gene polymorphism Tru9I did not differ in frequency between studied groups. All tested polymorphisms of the IL-1-R1 gene [PstI, HinfI, and AluI (promoter region) and PstI-e (exon 1B region)] displayed no differences between cases and controls. Haplotype analysis of the VDR gene (FokI, BsmI, ApaI, TaqI, Tru9I) and of the IL-1-R1 gene (PstI, HinfI, AluI, PstI-e) found haplotypes VDR FbATu ($p=0.0388$) and IL-1-R1 phap'($p=0.0419$) to be more frequent in T1DM patients whereas the BatU haplotype occurred more often in controls ($p=0.0064$). These findings indicate that the VDR FokI polymorphism and several VDR and IL-1-R1 haplotypes are associated with susceptibility to T1DM in the Dalmatian population.

**Tedeschi-Reiner E, Strozzi M, Škorić B, Reiner Ž. Relation of atherosclerotic changes in retinal arteries to the extent of coronary artery disease. Am J Cardiol. 2005;96:1107-9.**

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The aim of this study was to explore the relation between atherosclerosis of the retinal arteries and the extent and severity of coronary artery disease (CAD). In 109 patients, aged 40 to 80 years, who underwent coronary angiography for suspected CAD, the degree of retinal arterial atherosclerosis (stages 1 to 4 according to Scheie) was determined. The fundus examination was done using direct ophthalmoscopy by an ophthalmologist blinded to the extent of the CAD. The CAD extent was evaluated by Gensini score, and coronary angiograms were analyzed by 2 expert observers who had no knowledge of the patients' retinal artery status. The extent and severity of retinal vessel atherosclerosis correlated strongly with the extent and severity of CAD. Thus, atherosclerotic changes in the retinal arteries may be a predictor of the extent of CAD.

**Bogović Crncić T, Laškarin G, Juretić K, Štrbo N, Dupor J, Sršen S, et al. Perforin and Fas/FasL cytolytic pathways at the maternal-fetal interface. Am J Reprod Immunol. 2005;54:241-8.**

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The immunogenetic enigma of maternal acceptance of the fetal semiallograft has been termed an immunological paradox. The first trimester decidua is heavily infiltrated with CD56(bright) CD16- uterine natural killer (uNK) cells which must be prepared to respond to potential pathogen challenges and still be able to control immune responses that allow the development of the fetus. The significant presence of cytolytic mediators, perforin and Fas/Fas ligand (FasL), at the maternal-fetal interface raises a question of their role(s) in the immunological interrelations between maternal tissues and trophoblast cells. As uNK cells in vitro lyse target cell lines (K562, P815 and P815Fas) using these effector molecules, it seems that, although immunocompetent, their cytotoxicity is not directed against trophoblast during normal pregnancy. Therefore, it is generally believed that the hormonal and Th1/Th2 cytokine balance plays an important role in the tolerance and maintenance of pregnancy. This paper gives an overview of the recent findings on the complex immunological events that occur at the maternal-fetal interface.

**Brčić-Kostić K. Neutral mutation as the source of genetic variation in life history traits. Genet Res. 2005;86:53-63.**

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The mechanism underlying the maintenance of adaptive genetic variation is a long-standing question in evolutionary genetics. There are two concepts (mutation-selection balance and balancing selection) which are based on the phenotypic differences between alleles. Mutation -selection balance and balancing selection cannot properly explain the process of gene substitution, i.e. the molecular evolution of quantitative trait loci affecting fitness. The author assumes that such loci have non-essential functions (small effects on fitness), and that they have the potential to evolve into new functions and acquire new adaptations. Here the author shows that a high amount of neutral polymorphism at these loci can exist in real populations. Consistent with this, the author proposes a hypothesis for the maintenance of genetic variation in life history traits which can be efficient for the fixation of alleles with very small selective advantage. The hypothesis is based on neutral polymorphism at quantitative trait loci and both neutral and adaptive gene substitutions. The model of neutral – adaptive conversion (*nac*) assumes that neutral alleles are not neutral indefinitely, and that in specific and very rare situations phenotypic (relative fitness) differences between them can appear. In this paper the author focuses on *nac* due to phenotypic plasticity of neutral alleles. The important evolutionary consequence of *nac*

could be the increased adaptive potential of a population. Loci responsible for adaptation should be fast evolving genes with minimally discernible phenotypic effects, and the recent discovery of genes with such characteristics implicates them as suitable candidates for loci involved in adaptation.

**Kučić N, Mahmutefendić H, Lučin P. Inhibition of protein kinases C prevents murine cytomegalovirus replication. J Gen Virol. 2005;86(Pt 8):2153-61.**

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For successful establishment of infection and initiation of the replication cycle, murine cytomegalovirus (MCMV) utilizes cellular structures and functions, including cell-membrane penetration, capsid dismantling and cytosolic transport of viral DNA into the nucleus. These early events of MCMV infections are dependent on cellular regulatory mechanisms, primarily protein phosphorylation. In the present study, protein kinase inhibitors were used to explore the role of protein phosphorylation mediated by protein kinases C (PKCs) in the very early events of MCMV infection. Inhibitory effects were determined by immunofluorescence and Western blot analysis of MCMV IE1 and E1 protein expression and by production of infectious virions in cell culture. It was found that H-7, a broadly specific inhibitor of cellular protein kinases, prevented virus replication in a dose-dependent and reversible manner, and that the block in replication occurred very early in infection. More specific PKC inhibitors (sangivamycin, calphostin C and bisindolylmaleimide II), $Ca^{2+}$/calmodulin inhibitors (EDTA and W7) and phorbol esters (PMA) were used to dissect PKC-subclass contribution in the very early events of MCMV replication. The results indicate that the role of diacylglycerol/phorbol ester-dependent but calcium-independent PKCs is essential for establishment of MCMV infection in the host cell, starting at a very early stage of infection.

**Tonkić M, Goić-Barišić I, Punda-Polić V. Prevalence and antimicrobial resistance of extended-spectrum beta-lactamases-producing Escherichia coli and Klebsiella pneumoniae strains isolated in a University hospital in Split, Croatia. Int Microbiol. 2005;8:119-24.**

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The prevalence of Escherichia coli and Klebsiella pneumoniae that produce extended-spectrum b-lactamases (ESBL) was investigated in patients of a university hospital in Split, Croatia. Patients were grouped according to age (pediatric vs. adult), antibiotic type, and hospital ward. From Jan. 2001 to Dec. 2002, the susceptibility of E. coli and K. pneumoniae isolates to antimicrobials was tested. ESBL production was assayed using the double-disk synergy test. ESBL-producing E. coli and K. pneumoniae were detected in all sites of infection sampled. The percentages of ESBL-positive isolates were higher in the pediatric wards than in the adult wards. The antibiotics most commonly prescribed to patients in all hospital wards belonged to the third-generation cephalosporin group. Among ESBL producers, E. coli isolates were more resistant to aminoglycosides, but less resistant to ciprofloxacin and cotrimoxazole. Resistance of E. coli and K. pneumoniae to ciprofloxacin was exclusively found in isolates from adult patients. None of the isolates, regardless of ESBL production, was resistant to carbapenemes. In addition, the prevalence and antimicrobial resistance of ESBL-producing E. coli and K. pneumoniae isolates differed between pediatric and adult patients.

**Mladina R, Clement P, Lopatin A, Mann W, Passali D. International consensus on nasal polyposis 2002-2004. Eur Arch Otorhinolaryngol. 2005;262:519-21.**

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Seventeen well-known experts in rhinosinusology from various countries tried to achieve consensus on the etiology, conservative approach and surgical approach to nasal polyposis. A Digi-Vote electronic system was used for an immediate computer analysis of expert answers to 23 questions related to the problem of nasal polyposis.

**Dimanovski J, Anticevic D, Stimac G, Kraus O, Tripkovic B. Radical prostatectomy in a patient with osteogenesis imperfecta: a possible surgical trap. Scand J Urol Nephrol. 2005;39:334-6.**

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An exceedingly rare case of a patient with osteogenesis imperfecta and prostate cancer is reported. The patient underwent radical prostatectomy, which had to be stopped due to the extremely narrow space for surgical manipulation. The clinical, diagnostic and operative peculiarities of the case are presented and the relevant literature reviewed.