

Čačev T, Radošević S, Križanac S, Kapitanović S. Influence of interleukin-8 and interleukin-10 on sporadic colon cancer development and progression. *Carcinogenesis*. 2008;29:1572-80.

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The aim of this study was to investigate the influence of interleukin (IL)-8 and IL-10 on sporadic colon cancer development and progression. In this study, a statistically significant increase in IL-8 messenger RNA (mRNA) expression and decrease in IL-10 mRNA expression in tumour tissue compared with normal mucous tissue was observed ($P = 0.003$; $P = 1.3 \times 10^{-9}$). No association was found between IL-8 -251 A/T genotypes and IL-8 mRNA expression in tumour and corresponding normal mucous tissue, as well as susceptibility to sporadic colon cancer. Positive immunohistochemical IL-8 staining was more frequent in moderately and poorly differentiated tumours compared with well-differentiated tumours ($P = 0.024$). Finally, IL-8 significantly stimulated invasion of HT-29 cells in vitro ($P = 0.000172$). Significant association of IL-10 -1082 A/G, -819 T/C and -592 A/C genotypes and IL-10 mRNA expression in tumour tissue was observed ($P = 0.022$; $P = 0.013$; $P = 0.02$). Significant association of -819 T/C and -592 A/C genotypes and IL-10 mRNA expression in corresponding normal mucous tissue was observed ($P = 0.01$; $P = 0.04$) as well. IL-10 single-nucleotide polymorphism (SNP) promoter genotypes associated with low IL-10 mRNA expression (-819 TT; -592 AA) were also associated with increased risk of sporadic colon cancer compared with high-expression genotypes [odds ratio, 5.53; 95% confidence interval (CI), 1.53-20.1; odds ratio, 4.07; 95% CI, 1.28-12.96]. Positive IL-10 immunohistochemical reaction was more frequent in well-differentiated and moderately differentiated tumours compared with poorly differentiated tumours ($P = 0.036$). In Dukes' C tumours, positive IL-10 immunohistochemical reaction was less frequent compared with Dukes' A and B tumours ($P = 0.023$). Taken together, these results point to possible tumour promoting role of IL-8 and potential protective role of IL-10 in sporadic colon cancer.

Mihaljević Peleš A, Božina N, Šagud M, Rojnić Kuzman M, Lovrić M. MDR1 gene polymorphism: therapeutic response to paroxetine among patients with major depression. *Prog Neuropsychopharmacol Biol Psychiatry*. 2008;32:1439-44.

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MDR1 gene belongs to the best understood mediators of drug resistance. Different polymorphisms in MDR1 have been found to be connected with P-gp expression and function. The aims of the study were to investigate the potential influence of MDR1 polymorphisms, exon 26 C3435T and exon 21 G2677T/A, on treatment response to paroxetine (20 mg/day) in patients with major depression. To assess and evaluate therapeutic response to paroxetine, all patients were rated weekly using the HAMD-17 scale. Responders were defined as subjects with a decrease in HAMD scale by $\geq 50\%$ at week 6 of treatment. The study population included 127 patients with major depression (diagnosed by Structured Clinical Interview for DSM-IV disorders). The results of this study indicate that MDR1 variants G2677T and C3435T are not associated with therapeutic response to paroxetine in patients with major depressive disorder. The associations between paroxetine and P-glycoprotein still need to be clarified.

Šimić G. Pathogenesis of proximal autosomal recessive spinal muscular atrophy. *Acta Neuropathol*. 2008;116:223-34.

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Although it is known that deletions or mutations of the SMN1 gene on chromosome 5 cause decreased levels of the SMN protein in subjects with proximal autosomal recessive spinal muscular atrophy (SMA), the exact sequence of pathological events leading to selective motoneuron cell death is not

fully understood yet. In this article, new findings regarding the dual cellular role of the SMN protein (translocation of beta-actin to axonal growth cones and snRNP biogenesis/pre-mRNA splicing) were integrated with recent data obtained by detailed neuropathological examination of SMA and control subjects. A presumptive series of 10 pathogenetic events for SMA is proposed as follows: (1) deletions or mutations of the SMN1 gene, (2) increased SMN mRNA decay and reduction in full-length functional SMN protein, (3) impaired motoneuron axono- and dendrogenesis, (4) failure of motoneurons to form synapses with corticospinal fibers from upper motoneurons, (5) abnormal motoneuron migration towards ventral spinal roots, (6) inappropriate persistence of motoneuron apoptosis due to impaired differentiation and motoneuron displacement, (7) substantial numbers of motoneurons continuing to migrate abnormally ("heterotopic motoneurons") and entering into the ventral roots, (8) attracted glial cells following these heterotopic motoneurons, which form the glial bundles of ventral roots, (9) impaired axonal transport of actin, causing remaining motoneurons to become chromatolytic, and (10) eventual death of all apoptotic, heterotopic and chromatolytic neurons, with apoptosis being more rapid and predominating in the earlier stages, with death of heterotopic and chromatolytic neurons occurring more slowly by necrosis during the later stages of SMA. According to this model, the motoneuron axonopathy is more important for pathogenesis than the ubiquitous nuclear splicing deficit. It is also supposed that individually variable levels of SMN protein, together with influences of other phenotype modifier genes and their products, cause the clinical SMA spectrum through differential degree of motoneuron functional loss.

Bura M, Musani V, Cretnik M, Botica I, Levanat S. Hedgehog-Patched pathway aberrations in a malignant triton tumor case study. *Oncol Rep.* 2008;20:347-52.

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Transition from malignant schwannoma to malignant triton tumor is analyzed in a case report on a patient with recurring cancers and suspected familial predisposition. It is hypothesized that rhabdomyoblastic differentiation, which distinguishes triton from schwannoma, might be attributable to Hedgehog-Patched pathway malfunctioning. Loss of one Patched gene allele was found in the tissue of advanced triton, but the retained allele had no exon or promoter mutations. Protein levels at early cancer stag-

es indicated possible Patched response to the pathway activation in the first occurrence of triton tumor. Later, in the recurring triton, Patched expression was several times lower than in the control tissue, suggesting that haploinsufficiency was aided by silencing of the remaining allele, although its promoter was not hypermethylated. These findings may justify further investigation of the Hedgehog-Patched pathway role in triton malignancies, especially because of the recent research on the therapeutic potential of the pathway.

Bedenić B, Vraneš J, Sviben M, Beader N, Kalenić S. Postantibiotic and post-beta-lactamase inhibitor effect of carbapenems combined with EDTA against *Pseudomonas aeruginosa* strains producing VIM-metallo beta-lactamases. *Chemotherapy.* 2008;54:188-93.

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Postantibiotic effect (PAE) is a delay of bacterial growth after short exposure to antibiotics. The phenomenon of continuing suppression of bacterial growth after removal of beta-lactamase inhibitors is termed post-beta-lactamase inhibitor effect (PLIE). Recently, *Pseudomonas aeruginosa* strains producing metallo-beta-lactamases were described in many countries of the world. The aim of the study was to investigate the PLIE of carbapenems in combinations with EDTA against VIM-MBL-positive strains of *P. aeruginosa*. The experiments were performed on two *Pseudomonas aeruginosa* isolates, one producing VIM-1 and the other producing VIM-2 metallo-beta-lactamase. Minimum inhibitory concentrations (MICs) and minimum bactericidal concentrations (MBC) of imipenem and meropenem alone and combined with EDTA, time-kill curves, PAE and PLIE were performed as described previously. The duration of PAE with meropenem combined with EDTA at 8 x MIC was longer against both VIM-1 and VIM-2 producer than that of imipenem with EDTA on VIM-1- and VIM-2-positive strains. The duration of PLIE was similar on both strains of *P. aeruginosa* regardless of the sort of carbapenem. At lower concentrations, meropenem with EDTA induced slightly longer PAE and PLIE than imipenem with EDTA. In conclusion, this study has shown that EDTA combined with carbapenems produced a significant PLIE on VIM-MBL-positive *P. aeruginosa* strains. The results do not have any clinical relevance so far since metal chelators such as EDTA are not used as therapeutic agents due to their toxicity.

Metelko Z, Pavlič-Renar I, Poljicanin T, Szivovitz L, Turek S. Prevalence of diabetes mellitus in Croatia. *Diabetes Res Clin Pract.* 2008;81:263-7.

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The aim of this study was to obtain an accurate estimate of diabetes prevalence in Croatia and additional estimates of impaired fasting glucose (IFG), undiagnosed diabetes, and insulin resistance. The study was part of the First Croatian Health Project. Field work included a questionnaire, anthropological measurements, and blood sampling. A nationally representative sample of 1653 subjects aged 18-65 years was analyzed. A total of 100 participants with diabetes were detected, among them 42 with previously unknown diabetes. The prevalence was 6.1% (95% CI: 4.59-7.64), with a significant difference by age. IFG prevalence (WHO-criteria) was 11.3%. The ratio of undiagnosed/diagnosed diabetes was 72/100, unevenly distributed by the regions. HOMA-IR was >1 in 40.4% of the subjects. This survey revealed a higher prevalence of diabetes than previously estimated, whereas that of IFG was as expected. A significant difference in the proportion of undiagnosed diabetes among the regions warrants attention.

Šetić M, Domijan D. Modeling the top-down influences on the lateral interactions in the visual cortex. *Brain Res.* 2008;1225:86-101.

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Attention modulates the amount of excitatory and inhibitory lateral interactions in the visual cortex. A recurrent neural network is proposed to account for modulatory influence of top-down signals. In the model, two types of inhibitions are distinguished: dendritic and lateral inhibitions. Dendritic inhibition regulates the amount of impact that surrounding cells may exert on a target cell via the dendrites of excitatory neurons and the dendrites of subpopulation of inhibitory neurons mediating lateral inhibition. Attention increases the amount of dendritic inhibition and prevents contextual interactions, while it has no effect on the target cell when there is no surround input. Computer simulations showed that the proposed model is able to exhibit properties of attentional gating. In the condition of focused attention, neural activity in the presence of surrounding stimuli is restored to the level as when the target stimulus is presented alone. Moreover, the model is able to show contrast gain and response gain on the contrast sensitivity function depending on the strength of the dendritic inhibition.

Begovac J, Gedike K, Lukas D, Lepej SZ. Late presentation to care for HIV infection in Croatia and the effect of interventions during the Croatian Global Fund Project. *AIDS Behav.* 2008;12(4 Suppl):S48-53.

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There are limited data on how HIV prevention interventions affect individuals presenting to care in settings with a low-level HIV epidemic. We examined whether interventions undertaken during the Croatian Global Fund Project in 2004-2006 had an influence on patients entering care. The number of men who have sex with men (MSM) presenting in 2004-2006 ($n = 86$) was 59% higher than in 2001-2003 ($n = 54$); in heterosexual patients the increase was 14% ($n = 51$ in 2001-2003; $n = 58$ in 2004-2006). MSM presented at a younger age (median 32 years) in 2004-2006 than in 2001-2003 (median 36 years). Late presentation to care was found in 28% of MSM and in 59% of heterosexual patients in 2004-2006. MSM were less frequently late presenters in 2004-2006 compared with 2001-2003 (odds ratio, 0.48; 95% confidence interval, 0.24 to 0.99; $P = 0.046$). Additional strategies for earlier initiation of care must be developed for MSM and particularly for heterosexual patients.

Sorić M, Mišigoj-Duraković M, Pedišić Z. Dietary intake and body composition of prepubescent female aesthetic athletes. *Int J Sport Nutr Exerc Metab.* 2008;18:343-54.

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The purpose of this study was to assess dietary intake and body composition of prepubescent girls competing in 3 aesthetic sports (artistic and rhythmic gymnastics and ballet). Because physiological demands of ballet training are similar to those in other aesthetic sports, ballet dancers were, for the purpose of this study, regarded as athletes. The sample consisted of 39 athletes (median age, 11 years, range 9-13) and 15 controls (median age, 11 years, range 10-12). Dietary intake was assessed using a quantitative food frequency questionnaire, and body composition, by means of anthropometry. There was no significant difference in total energy intake between groups, but there was a significant difference in energy substrate distribution. Artistic gymnasts reported significantly higher carbohydrate and lower fat contribution to total energy ($57\% \pm 6\%$ and $29\% \pm 5\%$, respectively) than rhythmic gymnasts ($48\% \pm 6\%$ and $36\% \pm 5\%$), ballet dancers ($51\% \pm 4\%$ and

34% ± 3%), or controls (51% ± 5% and 34% ± 4%). Relative to body weight, artistic gymnasts reported higher intake of carbohydrates (9.1 ± 4.2 g/kg) than rhythmic gymnasts (5.6 ± 3.1 g/kg), ballet dancers (6.6 ± 2.5 g/kg), or controls (5.4 ± 1.9 g/kg). Artistic gymnasts also had the lowest body-fat percentage among the groups. In all the

groups mean reported daily intakes of most nutrients were higher than the current daily recommended intakes. The exceptions were dietary fiber and calcium. The proportion of athletes with an inadequate reported intake was highest for phosphorus (33%), followed by vitamin A and niacin (18%) and zinc (13%).