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Gagro A, Tominac M, Krstulović-Hresić V, Baće A, Matić M, Draženović V, et al. Increased Toll-like receptor 4 expression in infants with respiratory syncytial virus bronchiolitis. Clin Exp Immunol. 2004;135:267-72.

Institute of Immunology, Zagreb, Croatia

The fusion protein of the respiratory syncytial virus (RSV) binds to the pattern recognition receptors, TLR4 and CD14, and initiates innate immunity response to the virus. The aim of the study was to investigate the expression of TLR4 on peripheral blood lymphocytes and monocytes in peripheral blood of infants in both acute and convalescent phase of RSV bronchiolitis (n = 26). In addition, TNF-alpha expression in lipopolysaccharide-stimulated monocytes was also assessed. The results showed TLR4 to be expressed predominantly by monocytes in both sick infants and controls. During the acute phase of infection monocytes up-regulated TLR4 in eight infants, which returned to the levels recorded in controls 4-6 weeks from infection. There was no difference in the percentage of TNF-alpha secreting monocytes. Of the clinical parameters tested, minimal oxygen saturation was found to correlate negatively with this expression in the group of infants with increased TLR4. Additional studies are under way to correlate this finding with the outcome of the immune response to RSV.

Forčić D, Baričević M, Zgorelec R, Kružić V, Kaić B, Marina BM, et al. Detection and characterization of measles virus strains in cases of subacute sclerosing panencephalitis in Croatia. Virus Res. 2004;99:51-6.

Department of Molecular Biomedicine, Institute of Immunology Inc, Zagreb, Croatia

Two cases of subacute sclerosing panencephalitis (SSPE), diagnosed in Croatia in 2002, were investigated. The coding regions of the matrix (M), hemagglutinin (H) and nucleoprotein (N) genes of measles virus were sequenced following direct RT-PCR amplification of viral RNA extracted from brain tissue. Phylogenetic analysis of the sequences of H and N genes, showed that both strains belonged to genotype D6. No vaccine strain was detected although both patients had been previously immunized. The comparison of analyzed sequences of two SSPE causative viruses with corresponding sequences of D6 genotype and with each other revealed a number of mutations in N and H gene sequences. In comparison to the Edmonston reference strain, the M gene of the SSPE viruses showed the characteristic biased hypermutation and a premature termination codon in one of the patients.

Marušić-Vrsalović M, Dominis M, Jakšić B, Kušec R. Angiotensin I-converting enzyme is expressed by erythropoietic cells of normal and myeloproliferative bone marrow. Br J Haematol. 2003;123:539-41.

Division for Molecular Diagnostics, Institute of University Chemistry, Zagreb University Hospital, Zagreb, Croatia

It is proposed that a locally active, intrinsic renin-angiotensin system (RAS) exists in the bone marrow (BM) and plays a role in regulating haematopoiesis. Angiotensin II type I receptor has been detected on erythroid burst-forming unit-derived cells; its antagonist losartan and angiotensin I-converting enzyme (ACE) inhibitors can suppress erythropoiesis. The possible role of ACE/RAS in BM was investigated by evaluating ACE expression in normal BM, several myeloproliferative disorders and myelodysplasia. Immunohistochemical studies showed that erythroid elements expressed ACE protein in both normal and disturbed haematopoiesis. The presence of ACE in erythroid cells suggests another mechanism for direct ACE inhibitor activity in erythropoiesis.

Katavić V, Grčević D, Lukić IK, Vučenik V, Kovačić N, Kalajzić I, et al. Non-functional Fas ligand increases the formation of cartilage early in the endochondral bone induction by rhBMP-2. Life Sci. 2003;74:13-28.

Department of Anatomy, Croatian Institute for Brain Research, Zagreb University School of Medicine, Zagreb, Croatia

The authors investigated the expression of bone-related markers – alkaline phosphatase, collagen, bone sialoprotein, osteocalcin, osteopontin, and bone morphogenetic proteins (BMP) -2, -4, and -7; and cytokines interleukin-1alpha (IL-1), IL-1beta, and tumor necrosis factor-alpha (TNF-alpha) in ectopic new bone induced by recombinant human (rh) BMP-2 in mice without functional Fas-ligand (*gld* mice). At day 6 after rhBMP-2 implantation, *gld* mice formed more cartilage and mesenchyme compared with their wild type littermates. At later stages, *gld* mice did not differ from the control mice in the volume of newly formed tissue, expressing higher level of BMP genes and lower levels of genes involved in osteoblast maturation—bone sialoprotein and osteopontin. Differences in the levels of expression of IL-1alpha and TNF-alpha were observed only at day 12 after rhBMP-2 implantation. These results suggest that *gld* mice have an increased recruitment of cells of mesenchymal origin and an abnormal pattern of differentiation and maturation of the newly formed mesenchymal tissues.

Canki-Klain N, Milić A, Kovač B, Trlaja A, Grgičević D, Zurak N, et al. Prevalence of the 550delA mutation in calpainopathy (LGMD 2A) in Croatia. Am J Med Genet. 2004;125A:152-6.

Croatian Institute for Brain Research, Zagreb University Medical School, Croatia

Mutations in the calpain 3 (CAPN3) gene are responsible for limb-girdle muscular dystrophy (LGMD) type 2A. The authors report five causal mutations: 550delA, DeltaFWSAL, R541W, Y357X and R49H found on 45/50 of alleles studied in 25 unrelated families from Croatia. The 550delA mutation was present on 76% of CAPN3 chromosomes that led us to screen general population for this mutation; 532 random blood samples from three different regions were analyzed using allele-specific PCR. Four healthy 550delA heterozygous were found suggesting a frequency of 1 in 133. All four carriers detected originated from an island and mountain region close to the Adriatic Sea. These findings combined with haplotype analysis confirm that Croatian general population is rather "closed" with a probable founder effect in some parts of the country. In addition, the high frequency of 550delA mutation found in some neighboring European countries together with the easy detection of the 550delA mutation should streamline genetic analysis, especially bearing in mind the geographic and ethnic origin of the patients. These results, combined with published haplotype studies suggest that 550delA originated in the Eastern Mediterranean from which it has probably spread widely across Europe. The detection of patients relies on the direct detection of gene mutation and the findings described in this paper may be helpful in establishing diagnostic screening strategy.

Mareković Z, Mokoš I, Krhen I, Goreta NR, Rončević T. Long-term outcome after surgical kidney revascularization

for fibromuscular dysplasia and atherosclerotic renal artery stenosis. J Urol. 2004;171:1043-5.

Departments of Urology and Internal Medicine, Zagreb University Hospital Center, Zagreb, Croatia

The aim of this paper was to review surgical kidney revascularization and the long-term clinical outcome of fibromuscular dysplasia (FMD) and atherosclerotic renal artery stenosis. The study group comprised 140 patients with renovascular hypertension, 72 with FMD and 68 with atherosclerotic renal artery disease, who underwent surgical revascularization between 1982 and 1999. The indications for surgical revascularization were the treatment of hypertension and the preservation of renal function in 17 patients with renal artery occlusion, 55 with ostial stenosis, 52 with branch stenosis, 6 with bilateral artery stenosis, 7 with solitary kidney renal artery stenosis and 3 with solitary kidney renal artery occlusion. Postoperative blood pressure and renal function were monitored for 1 to 17 years (mean, 11.3). Long-term blood pressure control was observed in 93% of patients with FMD and in 71% of those with atherosclerosis. Improvement or stabilization of renal function was observed in 92% of patients with FMD and in 68% of those with atherosclerosis. The preoperative estimated glomerular filtration rate compared to postoperative was significantly increased in both groups. In conclusion, surgical kidney revascularization is effective in secondary hypertension with a high long-term efficacy in the normalization of blood pressure and in the preservation of renal function, especially in patients with a solitary or one functional kidney.

Žnidarčić Z. Ethical problems in cytology. Cytopathology. 2004;15:49-52.

Zagreb University School of Medicine, Zagreb, Croatia

Great advances in medical science have raised a number of ethical issues, many of which affect cytopathology. Some of the main issues addressed in this paper relate to the organization of a cytology laboratory: internal and external quality control, adequate staffing levels and staff education, cytopathology reporting format and contents, confidentiality issues, relationship with the clinicians and involvement of cytopathologists in clinical management teams. Quality control has to be provided within cytology departments but external quality assurance is also essential, with national monitoring. New technologies should be used according to the best scientific methods, following cytological analysis. Scientific work in cytology has to respect the general principles of scientific ethics. The patient's interest has to be the main reason for such work.

Brajač I, Tkalčić M, Dragojević DM, Gruber F. Roles of stress, stress perception and trait-anxiety in the onset and course of alopecia areata. J Dermatol. 2003;30:871-8.

Department of Dermatovenerology, Rijeka University Hospital Centre and Rijeka University School of Medicine, Rijeka, Croatia

The aim of this study was to determine whether stressful life events, stress perception, and trait-anxiety are risk factors in the onset and course of alopecia areata (AA). A group of 45 patients diagnosed with AA and a group of 45 healthy controls were participants in the study. The patients with AA were divided into two subgroups: patients with a first episode of AA and patients with recidivism of the disease. The frequency and types of stressful life events experienced over the previous six months were recorded. Lemyre and Tessier's Mesure de Stress Psychologique was used to measure emotional, cognitive, behavioral, and physiological aspects of distress. Anxiety was evaluated by the Spielberg's Trait Anxiety Inventory. The number of patients with four stressful life events over the previous 6 months was significantly higher in the group of AA patients with recidivism of disease compared to the control group ($p=0.004$). There were no differences among the other groups with respect to the frequency of life events. A significantly higher degree of trait-anxiety and perceived distress were observed among patients in both AA subgroups than in the healthy control group. The highest scores for anxiety and stress perception among examined groups were obtained in the group with recidivism of AA (33.42±12.71 and 90.32±50.74, respectively). Trait-anxiety and stress perception constitutes risk factors that may influence the onset and exacerbation of AA. The present study does not provide evidence of a significant role of stress in the onset of AA. Life events may play an important role in triggering of some episodes.

Marić S, Bulić-Jakuš F, Ježek D, Jurić-Lekić G, Kos M, Vlahović M. Expression of the proliferating cell nuclear antigen and protein products of tumour suppressor genes in the human foetal testis. Andrologia. 2004;36:24-30.

Department of Biology, Osijek University School of Medicine, Osijek, Department of Histology and Embryology, and Department of Obstetrics and Gynaecology, Zagreb University School of Medicine, Zagreb, Croatia

Tumour suppressor genes retinoblastoma (Rb1) and adenomatous polyposis coli (Apc) as well as the proliferating cell nuclear antigen (PCNA) are involved in embryonic development. The purpose of the present study was to investigate the expression of Rb1 protein, APC protein and PCNA during development of the human foetal testis. Qualitative analysis of their expression at the single-cell level was performed using immunohistochemistry on archive samples of the foetal testis (18-37 gestation week). Stereological parameters (volume density, absolute volume, numerical density, absolute number) were calculated for quantification of the overall expression of those proteins that were expressed frequently enough for such an analysis. PCNA was frequently expressed in nuclei of immature Sertoli cells and prospermatogonia and less frequently in surrounding peritubular (myoid) and interstitial cells. The pRb1 protein was present in nuclei of prospermatogonia and Sertoli cells but was absent from the interstitial tissue. APC protein was expressed in the cytoplasm of a very small number of prospermatogonia and interstitial (Leydig) cells. The overall expression of PCNA in all stages of development was higher than pRb1 expression.

Kolaček S, Jadrešin O, Petković I, Mišak Z, Sonicki Z, Booth IW. Gluten-free diet has a beneficial effect on chromosome instability in lymphocytes of children with coeliac disease. J Pediatr Gastroenterol Nutr. 2004;38:177-80.

Referral Center for Paediatric Gastroenterology & Nutrition, Children's Hospital Zagreb, Zagreb University School of Medicine, Zagreb, Croatia

Children with coeliac disease (CD) have an increased number of chromosome aberrations in peripheral blood lymphocytes. The aim of the study was to follow a group of children with CD in whom the initial frequency of chromosome aberrations at diagnosis was known and to measure the same variable after a minimum of 2 years on a gluten-free diet. Chromosome aberrations in peripheral blood lymphocytes were determined in 17 patients with CD, before and after at least 24 months of a gluten free diet (mean, 33 months), and in 15 healthy children. Twelve patients adhered to the diet and had a significantly lower frequency of chromosome aberrations than did 5 patients not following the diet (0.16% vs. 1.2%; $p=0.03$), whereas at presentation there had been no difference (1.54% vs. 1.2%; $p=0.09$). The frequency of aberrations at follow-up in patients who were diet adherent was significantly lower than at presentation (1.54% vs. 0.16%; $p=0.02$) and remained unchanged in patients who were not diet adherent (1.2% vs. 1.2%; $p=1$). After at least 24 months of a gluten-free diet, children with CD did not differ from healthy control subjects (0.16% vs. 0.27%; $p=0.54$), whereas children not following the diet had an increased frequency of aberrations (1.2% vs. 0.27%; $p=0.05$). In conclusion, the frequency of chromosome aberrations in peripheral blood lymphocytes of patients with CD decreased significantly on a gluten-free diet. Therefore, the genomic instability is a secondary phenomenon, possibly caused by chronic intestinal inflammation