

**Katavić V, Lukić IK, Kovačić N, Grčević D, Lorenzo JA, Marušić A. Increased bone mass is a part of the generalized lymphoproliferative disorder phenotype in the mouse. J Immunol 2003;170:1540-7.**

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The authors investigated the bone phenotype of mice with generalized lymphoproliferative disorder (*gld*) due to a defect in the Fas-ligand-mediated apoptotic pathway. C57BL/6-*gld* mice had greater whole body bone mineral density and greater trabecular bone volume than their wild-type controls. *Gld* mice lost 5-fold less trabecular bone and had less osteoclasts on bone surfaces after ovariectomy-induced bone resorption. They also formed more bone in a model of osteogenic regeneration after bone marrow ablation, had less osteoclasts on bone surfaces and less apoptotic osteoblasts. *Gld* and wild-type mice had similar numbers of osteoclasts in bone marrow cultures, but marrow stromal fibroblasts from *gld* mice formed more alkaline phosphatase-positive colonies. Bone diaphyseal shafts and bone marrow stromal fibroblasts produced more osteoprotegerin mRNA and protein than wild-type mice. These findings provide evidence that the disturbance of the bone system is a part of generalized lymphoproliferative syndrome and indicates the possible role of osteoprotegerin as a regulatory link between the bone and immune system.

**Judaš M, Rasin MR, Krušlin B, Kostović K, Jukić D, Petanjek Z, et al. Dendritic overgrowth and alterations in laminar phenotypes of neocortical neurons in the newborn with semilobar holoprosencephaly. Brain Dev 2003;25:32-9.**

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The authors analyzed neuronal phenotypes and dendritic growth in the newborn with semilobar holoprosencephaly and 18p deletion. They found that the holoprosencephalic neocortex retained its basic six-layered lamination but displayed a number of intralaminar and modular architectonic alterations and contained a mixture of normal and aberrant neuronal phenotypes. The most conspicuous finding was the presence of the pronounced increase in soma size and total basal dendritic length of holoprosencephalic layer III pyramidal neurons in comparison to age-matched control brains. The dramatic (5-fold) dendritic overgrowth observed in associative cortico-cortical pyramidal neurons is probably related to the pronounced diminution of the cortical afferent input.

**Barišić K, Karuzić O, Petrik J, Grubišić TZ. Regulation of Na<sup>+</sup>/H<sup>+</sup> exchanger by urogastrone, a potent activator of cell proliferation. Physiol Res 2002;51:483-91.**

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The authors tested the effects of epidermal growth factor (EGF) on Na<sup>+</sup>/H<sup>+</sup> exchanger (NHE) activity using urogastrone for treatment of Wistar rats and rat kidney tissue slices. NHE activity was monitored in isolated kidney brush border membrane vesicles by following fluorescence quenching of acridine orange. A significant increase of NHE activity was detected as early as 5 min after addition of urogastrone to rat kidney slices

in vitro. In Wistar rats treated with urogastrone the authors also found increased NHE activity (by about 12 %). Both changes of NHE activity were the result of a significant rise of V<sub>(max)</sub> value and an apparent decrease in K<sub>(m)</sub> value in in vitro experiments. The rise of NHE activity caused by urogastrone was sensitive to the inhibitors of transcription and translation. The presence of phosphatase inhibitor, NaF, elevated NHE activity of non-stimulated as well as of urogastrone-stimulated exchanger, suggesting that phosphorylation plays an important role in Na<sup>+</sup>/H<sup>+</sup> exchange. Osmolarity of the medium seems to regulate NHE activity in such a manner that both hyper- and hypoosmolar conditions inhibited NHE activity. The absence of Ca<sup>2+</sup> ions produced a 60 % decrease of NHE activity. The chemical modification of histidine residues with diethyl pyrocarbonate or SH groups with N-ethylmaleimide inhibited NHE activity.

**Kanceljak-Macan B, Macan J, Plavec D, Klepac T, Milković-Kraus S. The 3 mm skin prick test (SPT) threshold criterion is not reliable for *Tyrophagus putrescentiae*: the re-evaluation of SPT criterion to dust mites. Allergy 2002;57:1187-90.**

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The mean wheal diameter 3 mm is the usual criterion for positive skin prick test (SPT) reaction to dust mites. The study assessed the accuracy of this SPT criterion with respect to specific IgE values of above 0.35 kUAl ( + sIgE). Specific IgE (ImmunoCAP, Pharmacia AB Diagnostics, Uppsala, Sweden) and standard SPT to *Dermatophagoides pteronyssinus* (DP) and *farinae* (DF), *Lepidoglyphus destructor* (LD) and *Tyrophagus putrescentiae* (TP) (ALK, Horsholm, Denmark) were performed in a random sample of 457 subjects, of whom 273 men (mean age 35.3 ± 11.0 years) and 184 women (mean age 37.9 ± 9.5 years). Statistical analysis was performed using the chi-square test, regression analysis and discriminant analysis. When the mean wheal diameter of 3 mm was considered positive (+ SPT), the correlation between + SPT and + sIgE was 0.47 for DP (p < 0.001), 0.43 for DF (p = 0.004), 0.35 for LD (p = 0.03) and 0.37 for TP (p = 0.014). Regarding + sIgE, this SPT criterion has a specificity of 92.2% for DP, 82.3% for DF, 80.8% for LD and 70.1% for TP. When the value 4.5 mm was taken as the threshold for the positive SPT reaction to TP, specificity increased significantly from 70.1% to 86.4% (chi-square = 32.04, p < 0.001). In conclusion, the 3 mm SPT threshold criterion is not reliable in evaluating sensitization to TP due to an insufficient specificity of the allergen extract to this mite. It is advisable either to re-evaluate the TP allergen extract or change the threshold criterion for positive SPT reaction to TP.

**Fieschi C, Dupuis S, Catherinot E, Feinberg J, Bustamante J, Breiman A, Altare F, Baretto R, Le Deist F, Kayal S, Koch H, \*Richter D, Brezina M, et al. Low penetrance, broad resistance, and favorable outcome of interleukin 12 receptor beta1 deficiency: medical and immunological implications. J Exp Med 2003;197:527-35.**

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The authors report 41 patients with complete IL-12Rbeta1 deficiency from 17 countries. The only opportunistic infections ob-

served, in 34 patients, were of childhood onset and caused by weakly virulent *Salmonella* or *Mycobacteria* (*Bacille Calmette-Guerin* -BCG- and environmental *Mycobacteria*). Three patients had clinical tuberculosis, one of whom also had salmonellosis. Unlike salmonellosis, mycobacterial infections did not recur. BCG inoculation and BCG disease were both effective against subsequent environmental mycobacteriosis, but not against salmonellosis. Excluding the probands, seven of the 12 affected siblings have remained free of case-definition opportunistic infection. Finally, only five deaths occurred in childhood, and the remaining 36 patients are alive and well. Thus, a diagnosis of IL-12Rbeta1 deficiency should be considered in children with opportunistic mycobacteriosis or salmonellosis; healthy siblings of probands and selected cases of tuberculosis should also be investigated. The overall prognosis is good due to broad resistance to infection and the low penetrance and favorable outcome of infections. Unexpectedly, human IL-12 is redundant in protective immunity against most microorganisms other than *Mycobacteria* and *Salmonella*: moreover, IL-12 is redundant for primary immunity to *Mycobacteria* and *Salmonella* in many individuals and for secondary immunity to *Mycobacteria* but not to *Salmonella* in most.

**Kušec V, Jelić M, Borovečki F, Kos J, Vukičević S, Koržinek K. Distraction osteogenesis by Ilizarov and unilateral external fixators in a canine model. *Int Orthop* 2003;27:47-52.**

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The authors studied distraction osteogenesis in canine experimental model using two types of external fixators, Ilizarov (n=6) or AO unilateral (n=9) external fixator. Distraction started 1 week after surgery (2x0.5 mm/day) and lasted for 3 weeks. Specimens were harvested from weeks 7 through 12. The outcome was assessed by X-ray, histology, histomorphometry and microradiography. Bone regeneration as observed by X-rays was satisfactory and similar in both groups. Both endochondral ossification and intramembranous ossification were found simultaneously in both groups. In both groups, bone formation parameters were significantly higher in the area of consolidating bone. No differences in histomorphometric parameters existed between the groups. In the study period, the bone formation was enhanced and prevailed in the distraction area. This study demonstrated the utility of the canine experimental model for the study of distraction osteogenesis.

**\*Juretić A, Spagnoli GC, Schultz-Thater E, Šarčević B. Cancer/testis tumour-associated antigens: immunohistochemical detection with monoclonal antibodies. *Lancet Oncol* 2003;4:104-9.**

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Cancer/testis tumour-associated antigens (C/T TAA) were the first human tumour-associated antigens to be characterised at the molecular level. Specific genes are expressed in the testis and in tumours of varying histological origin. The tissue expression pattern supports the notion that these antigens could be targets for active specific immunotherapy. Specific serological reagents have been developed and have helped to clarify biochemical characteristics of C/T TAA and to assess their distribution within clinical tumour samples. The authors review immunohistochemical evidence of the expression of C/T TAA known to be recognised by specific cytotoxic T lymphocytes. The emerging picture is consistent with a mostly heterogeneous expression in human cancers. These findings support the concept

of multiantigenic tumour vaccine preparations. Moreover, the wide range of tumours in which C/T TAA have been detected urges further efforts to develop effective specific immunotherapeutic procedures.

**Brnić Z, Hebrang A. Usefulness of Doppler waveform analysis in differential diagnosis of cervical lymphadenopathy. *Eur Radiol* 2003;13:175-80.**

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The authors compared Doppler spectral parameters in acute inflammatory, reactive, lymphomatous, and metastatic lymph nodes, and evaluated pulsed Doppler sonography as a method for distinguishing between different causes of cervical lymphadenopathy. Spectral Doppler analysis with measurements of resistance index (RI), pulsatility index (PI), peak systolic velocity (PSV), and end-diastolic velocity (EDV) was performed in 197 patients with cervical lymphadenopathy. Results of Doppler analysis were compared with findings of cytology and histology or with clinical presentation and follow-up. Student's t-test was used to assess statistical significance of differences in Doppler parameters between groups of patients. Significant differences for RI and PI were shown between all groups of patients except between lymphomatous and reactive nodes. Specificity of 100% for metastatic nodal involvement was shown for cut-off values RI > 0.80 and PI > 1.80. A positive predictive value (PPV) of 100% for acute lymphadenitis was shown for cutoff values RI < 0.50 and PI < 0.60. An EDV > 9 cm/s has 100% negative predictive value for nodal metastasis, and EDV < 1 cm/s has 100% specificity and PPV for metastasis. Although there exist differences in RI, PI, PSV, and EDV between different nodal diseases, none of these parameters offer both good sensitivity and good specificity, and only extreme cutoff values may occasionally be helpful in differential diagnosis. Doppler spectral analysis is a valuable noninvasive adjunct which can help in differentiation between metastatic, lymphomatous, acute inflammatory, and reactive lymphadenopathy, but cannot obviate biopsy in the majority of cases.

**Šalković-Petrišić M, Lacković Z. Intracerebroventricular administration of betacytotoxics alters expression of brain monoamine transporter genes. *J Neural Transm* 2003;110:15-29.**

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Intracerebroventricular (icv) administration of betacytotoxics alters brain monoamine neurotransmission, without producing hyperglycemia. By means of *in situ* hybridization, the authors have investigated the expression of dopamine, noradrenaline and serotonin transporter (DAT, NAT, 5-HTT, respectively) mRNAs, in the brain of alloxan- and streptozotocin-icv treated rats. DAT1 mRNA expression is increased in 1-week alloxan-icv treated rats in arcuate nucleus (+51%) and ventral medial bundle (VMB) (+32%), and decrease in VMB of 4-week alloxan- (-53%) and streptozotocin- (-9%) icv treated rats, respectively. NAT1 mRNA expression in locus coeruleus is decreased in 4-week alloxan-icv treated rats (-35%) and increased in A1 cell group of 1- (+19%) and 4- (+14%) week streptozotocin-icv treated rats. 5-HTT mRNA expression in dorsal raphe nucleus is increased in 1- (+13%) and 4- (+21%) week alloxan-icv treated rats. Observed changes may suggest altered response to antidepressants in streptozotocin-icv treated rats, used as an animal model of sporadic Alzheimer's disease.