
Ivančić-Jelečki J, Šantak M, Forčić D. Variability of hemagglutinin-neuraminidase and nucleocapsid protein of vaccine and wild-type mumps virus strains. *Infect Genet Evol.* 2008;8:603-13.

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The mumps virus (MuV) molecular evolution is characterized by the co-circulation of numerous distinct strains. Standardized phylogenetic analyses based on the nucleotide sequences of the SH gene are important for mumps surveillance, but lack the information regarding antigenic properties. So far, the location of antigenic epitopes has been determined for two MuV proteins, the hemagglutinin-neuraminidase (HN) and the nucleocapsid (N) protein. The authors performed multiple sequence comparisons of putative HN and N protein sequences in order to describe their diversity and plasticity, and to determine the level of similarity between vaccine and wild-type strains. The results of full-length HN or N protein phylogeny showed that MuV strains form a number of differing clades which are in concordance with grouping obtained by standard MuV genotyping. When vaccine strains are compared to all wild-type strains, the highest mean percentage of amino acid differences in both HN and N protein analysis was found for Jeryl Lynn 5 and Jeryl Lynn 2 strains while the lowest value was obtained for Leningrad-3 and L-Zagreb strains. When only 3 antigenic regions of the HN protein, comprising 45 amino acids in total, were investigated, the diversity is considerably diminished: 51.5% of all putative HN proteins show identical sequences (including those of vaccine strains L-Zagreb, Leningrad-3, Hoshino and Urabe). Another 26.5% proteins (including Miyahara vaccine strain) differ in only one amino acid, while the others differ in two to five amino acids from the most common sequence. Jeryl Lynn 2 and Jeryl Lynn 5 strains differ in four amino acids each. N protein antigenic sites have been mapped within its hyper-

variable C-terminus. These results indicate that there might be genotype-specific amino acids residing in this antigenic region. The results of our study present the background information for investigations of MuV heterogeneity and antigenic diversity.

Delimar D, Bičanić G, Koržinek K. Femoral shortening during hip arthroplasty through a modified lateral approach. *Clin Orthop Relat Res.* 2008;466:1954-8.

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The authors describe a modification of the direct lateral approach to the hip that provides excellent femoral and acetabular exposure and an easy way to shorten the proximal femur and equalize leg length. The approach also is useful for lower extremity elongation while preserving muscle continuity and minimizing postoperative complications. The exact amount of shortening can be calculated and planned preoperatively and measured and corrected intraoperatively if necessary. It avoids the necessity for osteotomies of the trochanter and transverse cuts or detachment of abductor muscles. LEVEL OF EVIDENCE: Level IV, therapeutic study.

Rudan I, Boschi-Pinto C, Biloglav Z, Mulholland K, Campbell H. Epidemiology and etiology of childhood pneumonia. *Bull World Health Organ.* 2008;86:408-16.

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Childhood pneumonia is the leading single cause of mortality in children aged less than 5 years. The incidence in this

age group is estimated to be 0.29 episodes per child-year in developing and 0.05 episodes per child-year in developed countries. This translates into about 156 million new episodes each year worldwide, of which 151 million episodes are in the developing world. Most cases occur in India (43 million), China (21 million) and Pakistan (10 million), with additional high numbers in Bangladesh, Indonesia and Nigeria (6 million each). Of all community cases, 7-13% are severe enough to be life-threatening and require hospitalization. Substantial evidence revealed that the leading risk factors contributing to pneumonia incidence are lack of exclusive breastfeeding, undernutrition, indoor air pollution, low birth weight, crowding and lack of measles immunization. Pneumonia is responsible for about 19% of all deaths in children aged less than 5 years, of which more than 70% take place in sub-Saharan Africa and south-east Asia. Although based on limited available evidence, recent studies have identified *Streptococcus pneumoniae*, *Haemophilus influenzae* and respiratory syncytial virus as the main pathogens associated with childhood pneumonia.

Pavelić SK, Čačev T, Kralj M. A dual role of p21waf1/cip1 gene in apoptosis of HEP-2 treated with cisplatin or methotrexate. *Cancer Gene Ther.* 2008;15:576-90.

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The authors investigated the effects of p21(waf1/cip1) gene overexpression in human laryngeal squamous carcinoma cells HEP-2 lacking p53 protein expression on apoptosis induction upon the treatment with two commonly used chemotherapeutic agents, cisplatin and methotrexate. For that purpose, they employed cDNA arrays and qPCR to monitor gene expression upon treatment with AdCMV-p21 alone or in combination with the chemotherapeutic compounds. It has been found that p21(waf1/cip1) gene overexpression provoked apoptosis of HEP-2 through the induction of the TNFRSF9 gene and activation of caspase 7. In addition, the authors have proved that p21(waf1/cip1) can assume a dual role in apoptosis in the same cell system depending on the chemotherapeutic agent: its overexpression enhances apoptosis in cisplatin-treated cells and attenuates apoptotic signals in methotrexate-treated cells. The observed dual role of p21(waf1/cip1) was in direct correlation with the modulation of caspases 3 and 7 activation and changes in the expression of GADD45a gene. The results presented herein encourage future use of targeted p21(waf1/cip1) gene therapy in cancer treatment in a well-defined therapeutic and genetic context.

Harjaček M, Margetić T, Kerhin-Brkljačić V, Martinez N, Grubić Z. HLA-B*27/HLA-B*07 in combination with D6S273-134 allele is associated with increased susceptibility to juvenile spondyloarthropathies. *Clin Exp Rheumatol.* 2008;26:498-504.

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Juvenile spondylarthropathies (jSpA) are polygenic and the clustering of disease in families is caused mainly by genetic factors. The aim of this study was to look for possible associations of other HLA-A and B specificities, MICA and D6S273 microsatellite polymorphisms that might play a role in determining the susceptibility to jSpA. Juvenile SpA were diagnosed in 74 Croatian children, and 169 healthy unrelated individuals served as the control group. HLA class I (A, B) typing of all individuals was performed, and HLA-B7 and HLA-B27 positive subjects were subtyped by PCR-SSP method. MICA and D6S273 microsatellites alleles were analyzed by electrophoresis in an automated sequencer. The authors identified 26 HLA-B*07 and 31 HLA-B*27 positive patients with jSpA. DNA subtyping of HLA-B*27 specificity demonstrated only two subtypes, B*2702 (19.35%) and B*2705 (80.65%), among jSpA patients. Subtyping analysis of HLA-B*07 gene showed presence of only one subtype, B*0702. The OR for HLA-B*07 was 2.61, while the highest OR for a single HLA specificity was found for HLA-B*27 (OR=5.60). The HLA-B*07/B*27 combination found in six children showed higher risk (OR=14.82), but the combination of specificities: HLA-B*07/HLA-B*27, and D6S273-134 allele demonstrated the highest risk (OR=26.83). The association with D6S273-134 allele was not a result of the linkage disequilibrium with HLA-B*27 specificity (LD=-0.5). In conclusion, these findings provide evidence that HLA-B*27/HLA-B*07 in combination with D6S273-134 allele is associated with increased susceptibility to jSpA in Croatian children.

Ljubin-Šternak S, Šantak M, Čepin-Bogović J, Baće A, Vojnović G, Mlinarić-Galinović G, et al. Detection of genetic lineages of human metapneumovirus in Croatia during the winter season 2005/2006. *J Med Virol.* 2008;80:1282-7.

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The genetic characteristics of human metapneumovirus (HMPV) circulating in Croatia have not been studied so

far. The aim of this study was to determine the incidence of HMPV infection in hospitalized children with acute respiratory tract infection (ARTI) in the season 2005/2006 in Croatia, as well as to perform the genotypic analysis of detected HMPV strains. From December 1 to March 31 nasopharyngeal secretions (NPSs) were collected from 402 inpatients up to 5 years of age with ARTI. NPSs were tested by real-time RT-PCR assay targeting the nucleoprotein (N) gene of HMPV. HMPV infection was detected in 33 patients (8.2%). To perform the phylogenetic study, partial nucleotide sequences were obtained for HMPV fusion (F) gene of 30 HMPV positive samples. Phylogenetic analysis showed the circulation of two main genetic lineages (A and B), with B lineages being prevalent. It also showed the existence of two sublineages within the group B (B1 and B2) and three subclusters within lineage A (A1, A2a and A2b). Further molecular analysis revealed point mutations in HMPV strains of sublineage B1.

Liščić RM, Grinberg LT, Zidar J, Gitcho MA, Cairns NJ. ALS and FTLN: two faces of TDP-43 proteinopathy. Eur J Neurol. 2008;15:772-80.

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Major discoveries have been made in the recent past in the genetics, biochemistry and neuropathology of frontotemporal lobar degeneration (FTLD). TAR DNA-binding protein 43 (TDP-43), encoded by the TARDBP gene, has been identified as the major pathological protein of FTLN with ubiquitin-immunoreactive (ub-ir) inclusions (FTLN-U) with or without amyotrophic lateral sclerosis (ALS) and sporadic ALS. Recently, mutations in the TARDBP gene in familial and sporadic ALS have been reported which demonstrate that abnormal TDP-43 alone is sufficient to cause neurodegeneration. Several familial cases of FTLN-U, however, are now known to have mutations in the progranulin (GRN) gene, but granulin is not a component of the TDP-43- and ub-ir inclusions. Further, TDP-43 is found to be a component of the inclusions of an increasing number of neurodegenerative diseases. Other FTLN-U entities with TDP-43 proteinopathy include: FTLN-U with valosin-containing protein (VCP) gene mutation and FTLN with ALS linked to chromosome 9p. In contrast, chromosome 3-linked dementia, FTLN-U with chromatin modifying protein 2B (CHMP2B) mutation, has ub-ir, TDP-43-negative inclusions. In summary, recent discoveries have generated new insights into the pathogenesis of a spectrum of disorders

called TDP-43 proteinopathies including: FTLN-U, FTLN-U with ALS, ALS, and a broadening spectrum of other disorders. It is anticipated that these discoveries and a revised nosology of FTLN will contribute toward an accurate diagnosis, and facilitate the development of new diagnostic tests and therapeutics.

Jadrešin O, Mišak Z, Sanja K, Sonicki Z, Žižić V. Compliance with gluten-free diet in children with coeliac disease. J Pediatr Gastroenterol Nutr. 2008;47:344-8.

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Coeliac disease (CD) is a lifelong disorder with gluten-induced manifestations in different organs. Gluten-free diet (GFD) is required to achieve remission and prevent complications; however, study reports on GFD growth effect are not consistent. Compliance with GFD was estimated according to current body mass and height; presence of anaemia and other signs and symptoms; and attitude toward GFD. Seventy-one patients with CD (mean age = 12 years; mean age after CD diagnosis = 9 years) were examined and their blood sampled for determination of endomysial antibodies (EMA), haemoglobin, and red blood cell count. Questionnaire analysis revealed 42 (59.1%; 4 EMA positive) patients to be on strict GFD, 19 (26.8%; 5 EMA positive) were taking small amounts of gluten, and 10 (14.1%; all EMA positive) were not on a diet at all. The patients on strict GFD had greatest body height, yet the difference was not significant. These patients also had a higher mean body mass ($P=0.05$) and significantly higher mean haemoglobin and mean cell haemoglobin levels ($P=0.05$ and $P<0.05$, respectively). Apart from chronic fatigue in patients on partial diet ($P=0.05$), patient groups did not differ significantly in the frequency of symptoms. Anaemia and delayed puberty were recorded only in noncompliers ($P<0.01$ and $P<0.05$, respectively). Noncompliers often found the specific diet to pose a major life burden ($P < 0.01$) and did not visit a gastroenterologist on a regular basis ($P<0.01$). In conclusion, almost half of the coeliac patients were likely to abandon GFD without experiencing major symptoms, thus increasing the risk for developing complications later in life. An active attitude is required in the follow-up of patients with CD.