

**\*Krpmotić A, Busch DH, Bubić I, Gebhardt F, Hengel H, Hasan M, et al. MCMV glycoprotein gp40 confers virus resistance to CD8+ T cells and NK cells in vivo. *Nat Immunol* 2002;3:529-35.**

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The susceptibility of certain inbred mouse strains to murine cytomegalovirus (MCMV) is related to their inability to generate a strong natural killer (NK) cell response. In this paper the authors addressed whether the MCMV susceptibility of the BALB/c strain is due to viral functions that control NK cell activation in a strain-specific manner. MCMV expresses two proteins, gp48 and gp40, that are encoded by the genes m06 and m152, respectively; they down-regulate major histocompatibility complex (MHC) class I expression at the plasma membrane. Using MCMV deletion mutants and revertants, the authors found that gp40 but not gp48 controls NK cell activation. Absence of gp40 improved antiviral NK cell control in BALB/c, but not C57BL/6, mice. Down-regulation of H-60, the high-affinity ligand for the NKG2D receptor, was the mechanism by which gp40 modulates NK cell activation. Thus, a single herpesvirus protein has a dual function in inhibiting both the adaptive as well as the innate immune response.

**\*Trobonjača Z, Kroger A, Stober D, Leithauser F, Moller P, Hauser H, et al. Activating immunity in the liver. II. IFN-beta attenuates NK cell-dependent liver injury triggered by liver NKT cell activation. *J Immunol* 2002;168:3763-70.**

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Dendritic cell (DC)-dependent activation of liver NKT cells triggered by a single i.v. injection of a low dose (10-100 ng/mouse) of alpha-galactosyl ceramide (alpha Gal-Cer) into mice induces liver injury. This response is particularly evident in HBs-tg B6 mice that express a transgene-encoded hepatitis B surface Ag in the liver. Liver injury following alpha Gal-Cer injection is suppressed in mice depleted of NK cells, indicating that NK cells play a role in NK T cell-initiated liver injury. In vitro, liver NKT cells provide a CD80/86-dependent signal to alpha Gal-Cer-pulsed liver DC to release IL-12 p70 that stimulates the IFN-gamma response of NKT and NK cells. Adoptive transfer of NKT cell-activated liver DC into the liver of nontreated, normal (immunocompetent), or immunodeficient (RAG(-/-) or HBs-tg/RAG(-/-)) hosts via the portal vein elicited IFN-gamma responses of liver NK cells in situ. IFN-beta down-regulates the pathogenic IL-12/IFN-gamma cytokine cascade triggered by NKT cell/DC/NK cell interactions in the liver. Pretreating liver DC in vitro with IFN-beta suppressed their IL-12 (but not IL-10) release in response to CD40 ligation or specific (alpha Gal-Cer-dependent) interaction with liver NKT cells and down-regulated the IFN-gamma response of the specifically activated liver NKT cells. In vivo, IFN-beta attenuated the NKT cell-triggered induction of liver immunopathology. This study identifies interacting subsets of the hepatic innate immune system (and cytokines that up- and down-regulate these interactions) activated early in immune-mediated liver pathology.

**\*Lipozenčić J, Skerlev M, Orofino-Costa R, Zaitz VC, Horvath A, Chouela E, et al. A randomized, double-blind, parallel-group, duration-finding study of oral terbinafine and open-label, high-dose griseofulvin in children with tinea capitis due to *Microsporum* species. *Br J Dermatol* 2002;146:816-23.**

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The objective of this study was (i) to establish the optimal duration for terbinafine treatment to bring about complete cure of tinea capitis due to *Microsporum* infection in a large paediatric population, and (ii) to obtain information on the maximum therapeutic effect of the existing therapy. This parallel-group, double-blind, multicentre study was conducted in Europe and South America. Patients were randomized to one of four oral terbinafine treatment arms (6, 8, 10 or 12 weeks treatment) or to an open label, 12-week, high-dose griseofulvin. All patients were followed up for 4 weeks after the end of the treatment phase. In the group of 134 intention-to-treat patients, effective treatment was observed at the end of study in 62% of patients treated with terbinafine for 6 weeks and in 63% treated for 8 weeks. Mycological cure was obtained in 59% and 57%, respectively, and clinical cure in 76% and 80%. In the griseofulvin group, effective treatment was 88%, mycological cure was 76% and clinical cure 96%. However, these high rates were believed to be due to the high dosage of this drug and the prolonged course of treatment. Complete cure was observed at the end of study in 62% patients treated with terbinafine for 6 weeks, in 60% treated for 8 weeks and in 84% patients treated with griseofulvin for 12 weeks. Although there was no statistical trend between the duration of terbinafine treatment within the groups for complete cure at the end of study, there was a positive correlation between the daily dose of terbinafine and complete cure. Terbinafine therapy for 6 weeks could represent an alternative to griseofulvin for the treatment of *Microsporum* tinea capitis. However, further clinical trials are required in order to optimize the dose regimen to allow higher cure rates to be reached.

**Kostović I, Judaš M, Radoš M, Hrabac P. Laminar organization of the human fetal cerebrum revealed by histochemical markers and magnetic resonance imaging. *Cereb Cortex* 2002;12:536-44.**

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The developing human cerebrum displays age-specific changes in its patterns of lamination. Among these, the subplate zone is the most prominent transient compartment because growing major afferent systems temporarily reside in this zone, establish synapses and take part in cellular interactions that are crucial for subsequent cortical development. The authors explored the potential of magnetic resonance imaging (MRI) for tracing the developmental history of the most prominent cortical layer (the subplate zone) and other laminar compartments of the fetal cerebral wall between 15 and 36 weeks post-ovulation. The main finding is that changes in the MRI lamination pattern of the human fetal cerebral wall are predominantly caused by changes

in the subplate zone. Histochemical staining of the extracellular matrix (ECM) enables selective visualization of the subplate zone and correlation with an increase in MRI signal intensity in the subplate zone and ingrowth and accumulation of thalamocortical and corticocortical afferents and their subsequent relocation to the cortical plate. Thus, dynamic changes in the MRI appearance of the subplate zone and histochemical staining of its ECM can be used as indirect parameters for an assessment of normal versus disturbed unfolding of crucial histogenetic events that are involved in prenatal shaping of the human cerebral cortex.

**Stanić P, Sonicki Z, Suchanek E. Effect of pentoxifylline on motility and membrane integrity of cryopreserved human spermatozoa. *Int J Androl* 2002;25:186-90.**

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The purpose of this study was to examine the effects of pentoxifylline used before and after semen cryopreservation-thawing on sperm motility and membrane integrity. Twenty-four semen samples were split into four equal aliquots. Aliquots were incubated at 37°C for 30 min, followed by cryopreservation with TEST-yolk freezing medium using slow programmable freezing protocol. After 2 weeks, the sperm samples were thawed, washed twice in Quinn's Sperm Washing Medium (modified HTF with 5.0 mg/mL Human Albumin) and incubated at 37°C for 30 min. Aliquots were treated by adding 3 mmol/L pentoxifylline to: (1) fresh sperm samples during incubation period prior to cryopreservation, (2) sperm samples as a supplement to the cryoprotectant prior to cryopreservation, and (3) thawed sperm samples during incubation period. One aliquot received no treatment (control group). The addition of 3 mmol/L pentoxifylline to fresh semen during incubation period prior to cryopreservation significantly decreased progressive and total motility compared with controls. However, the addition of 3 mmol/L pentoxifylline to cryopreserved semen after thawing significantly increased progressive and total motility compared with controls. After post-thaw, no differences in motion characteristics between sperm samples treated by adding 3 mmol/L pentoxifylline as a supplement to the cryoprotectant and control groups were observed. Post-thaw hypoosmotic swelling (HOS) test scores did not improve with the addition of pentoxifylline compared with the control group. It is concluded that pentoxifylline enhanced post-thaw motility of cryopreserved human spermatozoa when added after thawing. No improvement was found by freezing sperm with pentoxifylline.

**\*Valković T, Dobrila F, Melato M, Sasso F, Rizzardi C, Jonjić N. Correlation between vascular endothelial growth factor, angiogenesis, and tumor-associated macrophages in invasive ductal breast carcinoma. *Virchows Arch* 2002;440:583-8.**

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The aim of this study was to define, using immunohistochemical analysis, the microvessel density (MVD), VEGF expression, and TAMs level in 97 human invasive ductal breast carcinomas not otherwise specified (NOS), investigate a possible relationship between them and then correlate their values with tumor grade, mitotic activity index (MAI), tumor size and lymph-node status. Statistical analysis showed a strong positive relationship between MVD and VEGF expression ( $p < 0.001$ ). Furthermore, both MVD and VEGF expression were significantly correlated with tumor grade and lymph-node status, and TAMs infiltration with MAI. TAM level showed a significant positive connection

with VEGF expression and MVD. These in situ observations suggest that VEGF stimulates angiogenesis in human invasive ductal breast carcinoma NOS and attracts macrophages to the tumor locus, which then may be involved in angiogenesis promotion. The expression of this angiogenic molecule, and MVD and TAM level, can provide additional prognostic significance and help in the identification of patients who need postoperative adjuvant therapy.

**Vincelj J, Sokol I, Jakšić O. Prevalence and clinical significance of left atrial spontaneous echo contrast detected by transesophageal echocardiography. *Echocardiography* 2002;19:319-24.**

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The prevalence and clinical significance of left atrial spontaneous echo contrast (SEC) were studied in patients undergoing transesophageal echocardiography (TEE). The study group included 290 consecutive patients (186 male and 104 female, aged 17-86 years, mean age  $56.1 \pm 12.8$  years). Left atrial SEC was found in 50 (17.2%) patients, and was significantly associated with atrial fibrillation, mitral stenosis, absence of mitral regurgitation, and left atrial dimension. Atrial fibrillation was recorded in 44 (88%) patients, mitral stenosis or mitral valve replacement in 21 (42%) patients, and left atrial thrombus or previous embolism in 23 (46%) patients with SEC. Univariate analysis showed a significant association between the presence of SEC and atrial fibrillation, mitral stenosis or mitral valve replacement, and left atrial size. Multivariate analysis showed the presence of left atrial SEC and atrial fibrillation to be independent factors for thrombus formation and/or thromboembolism. Since left atrial SEC associated with atrial fibrillation, left atrial enlargement, mitral stenosis, or mitral valve prosthesis was found in 17.2% of patients undergoing TEE, it might be considered a marker of left atrial thrombus or previous thromboembolism.

**Bešenski N. Traumatic injuries: imaging of head injuries. *Eur Radiol* 2002;12:1237-52.**

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Computed tomography and MRI are the most common techniques in patients who have suffered brain injury. Computed tomography is currently the first imaging technique to be used after head injury, in those settings where CT is available. Using CT, scalp, bone, extra-axial hematomas, and parenchymal injury can be demonstrated. Computed tomography is rapid and easily performed also in monitored patients. It is the most relevant imaging procedure for surgical lesions. Computed tomography is a suitable method to follow the dynamics of lesion development giving an insight into the corresponding pathological development of the brain injury. Magnetic resonance imaging is more sensitive for all posttraumatic lesions except skull fractures and subarachnoidal hemorrhage, but scanning time is longer, and the problem with the monitoring of patients outside the MRI field is present. If CT does not demonstrate pathology as can adequately be explained to account for clinical state, MRI is warranted. Follow-up is best done with MRI as it is more sensitive to parenchymal changes. In routine MR protocol gradient-recalled-echo sequences should be included at any other time after a traumatic event since they are very sensitive in detection of hemosiderin as well as former hematoma without hemosiderin. The MR signal intensity varies depending on sequences and time scanning after trauma.