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トピックス

ケモカインおよびそのレセプターを分子標的にした自己免疫疾患の治療

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コムギ胚芽無細胞タンパク質合成法:マラリアワクチン研究への応用

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原 著

Genome microarray (アレイCGH法) を用いた口腔癌抑制遺伝子のスクリーニング法の検討

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Summary

Mapping copy number alterations in the cancer genome has contributed to the subsequent identification of tumor suppressor genes and oncogenes. Array comparative genomic hybridization(aCGH) technologies such as bacterial artificial chromosome(BAC), single nucleotide polymorphism(SNP), cDNA, and spotted oligonucleotide arrays provide high-resolution detection of copy number changes. To develop a more effective genome-wide screening method for oral cancer, we employed an aCGH SNP array and a BAC array in oral cancer cell line HSC3 and compared the results. The SNP array showed a higher density than the BAC array. Therefore, it detected high resolution deleted regions, but it was inferior to BAC array in accuracy. It is important to note these features when using a genome microarray.

Key Words : genome microarray, tumor suppressor gene, oral cancer

手術的二分脊椎ニワトリ胚モデルにおけるIslet-1陽性運動神経細胞の経時的変化

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Summary

Spina bifida aperta(SBA) is a congenital malformation of spinal cord with complications such as spinal ataxia and bowel and bladder dysfunctions. Our group has developed a post-hatching chick model with surgical-induced SBA showing spinal ataxia. In this model motor neurons in the neural tube were observed by immunohistochemical staining with the monoclonal antibody against Islet-1 as a marker of motor neurons. In this study the delay in migration and maturation of motor neurons were observed in SBA. Although the final numbers

of Islet-1 positive neurons in these two groups were not different, the defect in the production and elimination of excess motor neurons in these early developmental stages may be due to the pathological mechanism of the motor complications in this disease.

Key Words : spina bifida aperta, chick, motor neuron

アルツハイマー病の危険な自動車運転者をスクリーニングする基準について

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Summary

Background:There are no evidence-based standardized methods or criteria to screen for high risk drivers with Alzheimer's disease(AD).

Aim:To establish simple, data-based criteria to screen for high risk drivers in patients with Alzheimer's disease.

Method:Forty-nine consecutive AD patients who drove at the initial assessment were divided into two groups : patients with driving problems in the past and patients with no driving problems in the past. The patients' profiles and scores on the Clinical Dementia Rating(CDR)and subtests of the Mini-Mental State Examination(MMSE)of the two groups were compared and examined carefully to classify them correctly.

Results:Twenty-six patients had some driving problems in the past and twenty-three patients had no driving problems in the past. All patients who fulfilled the criteria of CDR2 or CDR3 had had driving problems in the past. The criteria of classification as CDR1, failing both on the orientations and serial 7s of MMSE correctly classified 90.9% of the patients with driving problems in the past and 100% of the patients without driving problems in the past. Some patients with very mild dementia had had driving problems.

Conclusion:Our criteria of using the CDR and MMSE score was a simple and useful way to identify unsafe drivers with AD. Therefore this criteria is feasible for implementation and assessment at the primary care level.

Key Words : criteria, unsafe driver, Alzheimer's disease

口腔扁平上皮癌細胞株における膜型増殖因子 amphiregulinの発現とshedding反応の亢進

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臓器機能再生・再建学講座口腔顎顔面外科学分野

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Summary

Amphiregulin(AR)is a member of the EGF family and is synthesized in membrane-anchored precursor form (proAR). In response to various extracellular stimuli, proAR is shed by a disintegrin and metalloprotease 17 (ADAM17)on cell surfaces to become a soluble EGFR ligand and activates cell growth signaling pathways. We found the over-expression of AR mRNA in oral squamous cell carcinoma(OSCC) cell lines, Ca9-22, HSC3 and HSC4. We also found constitutive over-production of the proAR-carboxy terminal fragment(AR-CTF). ADAM17 knock-down by siRNA markedly reduced ADAM17 protein levels, resulting in the reduction of AR-CTF production in HSC3 and HSC4 cells. Combination analyses with cell surface biotinylation, immunoprecipitation and immunostaining of ADAM17 in Ca9-22, HSC3 and HSC4 cells suggested the intracellular shedding of proAR in

HSC3 and HSC4 cells.

Key Words : Amphiregulin, Oral squamous cell carcinoma, ADAM17

2003年から2005年の新生児搬送症例の検討

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Summary

We examined the number of neonatal transportations to our hospital from 2003 to 2005 by, analyzing the neonatal information from patient records. We have found that the prognosis for the neonatal transportation cases is very poor. It is vital to study techniques for neonatal resuscitation through the Neonatal Resuscitation Program (N-RP). The maintenance of the local perinatal center and the system of neonatal transportation are also important. The preparation of four systems-childbirth, resuscitation, transportation and intensive care is essential. It is important that both sending and receiving hospitals have a mutual understanding and keep in touch closely.

Key Words : Neonatal transportation, Neonatal Resuscitation Program(NRP), Perinatal Medical Center

メシル酸ナファモスタットのラット大腸癌肝転移抑制効果

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Summary

Nafamostat mesilate (NM), a synthetic protease inhibitor, is widely used in Japan for the treatment of acute pancreatitis and disseminated intravascular coagulation. In this study we investigated the inhibitory effect of NM on the migration and invasion of RCN-H4 cells in vitro and in vivo to evaluate the anti-cancer potential of NM.

NM had no cytotoxic effect on RCN-H4 cells and did not affect the migration of RCN-H4 cells in BD Falcon™ Cell Culture Insert Chamber (Becton Dickinson) at any concentration. However, NM inhibited the invasion of RCN-H4 cells in BD BioCoat™ Matrigel™ Invasion Chamber (Becton Dickinson) at a concentration of 10–6M or more in vitro ($p < 0.05$ and $p < 0.01$). RCN-H4 cells were injected intrasplenically into F344 male rats to produce a liver metastasis model. NM was infused continuously into the jugular vein (50 $\mu\text{g/hr}$) with an ALZET osmotic pump for 7 days in the NM group, while a 5% glucose solution was given to the control group. The number of liver metastasis in the NM group was significantly smaller than in the control group ($p = 0.0016$).

In this study NM inhibited the invasion of tumor cells in vitro and decreased the number of liver metastasis in the rat model.

Key Words : Nafamostat mesilate, liver metastasis, rat

局所脳虚血に対するSignal transducer and activator of transcription3(Stat3)の役割についての検討

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Summary

To examine the effects of the signal transducer and activator of transcription3(Stat3) gene expression on

ischemic brain injury, a replication-defective adenoviral vector containing wild-type Stat3 (Ad-Stat3WT), dominant negative Stat3 (Ad-Stat3F), or a suppressor of the cytokine signaling3 (Ad-SOCS3) gene was directly injected into the striatum of rats one day before a 90-minute transient middle cerebral artery occlusion (MCAO). Stat3 protein in the ipsilateral cortex was markedly expressed in the Ad-Stat3WT and Ad-Stat3F treated groups. However, strong expression of the phosphorylated Stat3 (pStat3) protein was observed only in the Ad-Stat3WT treated group. The infarct areas of two coronal sections (4 and 6 mm caudal from the frontal pole) of the Ad-Stat3WT treated group were significantly smaller than those of all the other groups 24 hours after the transient MCAO as shown by 2, 3, 5-Tripheniltetrazolium chloride staining. And neurological symptoms were also significantly improved in the Ad-Stat3WT treated group 24 hours after reperfusion, compared to all other groups. Western blot analysis of the vascular endothelial growth factor (VEGF) expression 24 hours after adenoviral inoculation showed that VEGF protein in the ipsilateral cortex was significantly higher in Ad-Stat3WT treated animals, compared to all other groups. These results suggest that the successful exogenous Stat3 gene transfer ameliorates ischemic brain injury after transient MCAO due to the upregulation of VEGF.

Key Words : Stat3, VEGF, cerebral ischemia

臨床経験録

小児特発性ネフローゼ症候群における短期プレドニゾン治療の骨代謝調節ホルモンへの影響

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愛媛医学 26(1):62-65, 2007

Summary

Bone metabolism in children is different from bone metabolism in adults, particularly with respect to growth and mineralization with high bone turnover rate. It is well known that excess glucocorticoid disturbs bone metabolism both directly and indirectly in adults by decreasing the hormone levels that regulate bone metabolism. But there have been few reports on disturbed hormone levels in children induced by glucocorticoid.

We measured serum levels of bone-metabolism regulating hormones and bone turnover markers in 11 boys aged 5 to 12 years old with nephrotic syndrome and no proteinuria. The first test was done four weeks after the initiation of prednisolone therapy, and the second test was done two months after ceasing the prednisolone therapy. Through provocative testing, we found that the growth hormone, luteinizing hormone, follicle stimulating hormone levels, and free triiodothyronine, 1,25-dihydroxyvitamin D, calcium, phosphorus levels were significantly lower in the first test than those in the second test. The levels of the bone turnover markers, alkaline phosphatase, osteocalcin and urine-deoxypyridinoline were significantly lower in the first test than in the second test.

These data indicate that prednisolone suppresses bone metabolism regulating hormone levels and decreases bone turnover rate in children with nephrotic syndrome. A hormone replacement therapy may be important for children with disturbed bone metabolism due to excess glucocorticoid.

Key Words : bone metabolism, prednisolone, nephrotic syndrome

症例報告

流産を契機に診断に至った先天性胆道拡張症の1例

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愛媛医学 26(1):66-69, 2007

Summary

We treated a case of Congenital Biliary Dilatation (CBD) that was diagnosed while treating a spontaneous abortion. A 30's-year-old primiparous woman in her 21st week of pregnancy was referred to the Department of Gynecology and Internal Medicine of Ehime Prefecture Central hospital for a threatened spontaneous abortion on October, 2005, immediately after showing marked icterus, a high fever, and continuous epigastralgia. An abdominal ultra-sonography examination found a large cystic lesion near the liver that was greater than 15 cm in size, and dilatation of the intrahepatic bile duct was detected in the epigastrium. She was diagnosed with a hepatic cyst infection which threatened the pregnancy. We planned a percutaneous drainage of the cystic lesion, but the pregnancy was lost on the same day. Epigastralgia remained, so we performed percutaneous transhepatic drainage from the cystic lesion the next day, which led to the remission of abdominal pain and high fever. She then underwent an endoscopic retrograde cholangio-pancreatography (ERCP) examination, which revealed a stricture of the lower common bile duct, and malformations of the main pancreatic duct and common bile duct were suspected. On November, we performed a porta hepatis choledochojejunostomy, and the cystic lesion was diagnosed as a CBD from the operative findings, while malignancy was pathologically absent.

Key Words : malformations of the main pancreas duct and common bile duct, congenital biliary dilatation, abortion

糖尿病にガス産生を伴うFournier's gangreneを合併した1例

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Summary

A 79-year-old woman was admitted with general fatigue and anorexia. A few days later when she consulted the department of neurosurgery in our hospital, she was found to have severe hyperglycemia (769 mg/dL), a high level of HbA1c at 15.0%, and cloudy consciousness. She was admitted to the department of internal medicine. Because she had no ketone bodies in her urine, she was diagnosed with a nonketotic hyperglycemic coma. After adequate fluid therapy, her plasma glucose concentration improved. But on 8th day of hospitalization, swelling appeared in her perineal area and spread rapidly. The next day a snow-ball crepitation was found upon examination, and an abdominal X-ray image showed gas in tissue. On the basis of these findings she was diagnosed with Fournier's gangrene with gas in tissue. Thus, surgical intervention was performed. During surgery, debridement of necrotic tissue was performed. The predominant isolates were E.coli .

Nonclostridial anaerobic cellulitis is a mortal complication, usually occurring more often in diabetic patients. Therefore, a timely diagnosis is important.

Key Words : diabetes mellitus, necrotizing infections, Fournier's gangrene

一過性脳虚血症状にて発症し同一内頸動脈に多発性脳動脈瘤を認めた1例

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愛媛医学 26(1):74-77, 2007

Summary

We report an unusual case of multiple aneurysms on the same internal carotid artery.

A 59-year-old female was transferred to our hospital because of transient left hemiparesis and dysarthria. An MRI revealed no ischemic change, but an MRI showed two neighboring aneurysms that originated in the right internal carotid-posterior communicating artery (ICPCA) and the ipsilateral internal carotid-anterior choroidal artery (ICAChA). After close investigation by 3D/CTA and an angiogram, the patient was surgically treated by the right pterional approach. Adhesion between the two aneurysms was not observed. Neck clipping was performed on each aneurysm successfully, and the anterior choroidal artery (AchA) could be secured under the use of a microscope. Postoperative angiograms revealed no aneurysm and the preservation of the AchA. The patient left hospital with no neurological deficits. We believe that a close preoperative examination, careful observation during operation, and cautious clipping lead to healthy and timely recovery when treating neighboring aneurysms.

Key Words : multiple aneurysms, same internal carotid artery, neck clipping

研究会抄録

第2回愛媛 NST(栄養サポートチーム)研究会

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第3回愛媛 NST(栄養サポートチーム)研究会

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第91回愛媛脳神経外科懇話会

愛媛医学 26(1):84-87, 2007

第105回愛媛整形外科集談会

愛媛医学 26(1):88-92, 2007

第37回愛媛臨床血液懇話会

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