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#### トピックス

#### ABO血液型遺伝子の5'上流域における多型とハプロタイプ

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#### 高血圧患者における頸動脈エコーの有用性

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#### 原著

#### 大腿骨頸部骨折患者における術前心機能評価

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愛媛医学 26(2):106-110,2007

Summary

The aim of this study is to evaluate the clinical prognosis associated with cardiac function in patients with hip fractures. We examined cardiac function using myocardial ultrasound in patients with hip fractures. Cardiac function was measured by two parameters: left ventricular hypertrophy (LVH) and left ventricular ejection fraction value (LVEF).

Subjects were 51 patients with hip fractures aged 65 years or older (n=51; 14 males and 37 females; mean age  $83.5 \pm 7.5$ , range 68-97 years) who underwent surgery by the same surgeon in our hospital between May 2001 and March 2003. We investigated cardiac function using myocardial ultrasound at the time of admission, and compared it to the Functional Independence Measure (FIM) of these patients before the injury and at the time of discharge. These patients were classified into the following 4 groups: LVH+ or LVH- and EF>=50% or EF< 50%. Both LVH+ and EF>50% patients showed no remarkable change after surgery with spinal anesthesia.

Also, in patients with LVH-, the FIM scores at the time of discharge were significantly lower than the preinjury FIM scores. In patients with EF>=50%, the cognitive function scores in FIM at the time of discharge were significantly lower than the pre-injury cognitive function scores.

Cardiac function is a valid measurement for assessing hip fracture patients and may be suitable as an objective procedure in determing risk for pre-surgery and Activities of Daily Living (ADL) for post-surgery.

Key Words: cardiac function, myocardial ultrasound, hip fracture

#### プロテオームの手法を用いて見出した新規口腔扁平上皮癌腫瘍マーカーの検討

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愛媛医学 26(2):111-120, 2007

Summary

Since advanced oral squamous cell carcinoma(OSCC) often has a poor outcome, early detection is an important issue in the field. However, no serum based test with sufficient sensitivity or specificity is available at present. Squamous cell carcinoma antigen(SCC antigen) used as a conventional tumor marker exhibits low sensitivity and specificity particularly in the early onset of the disease. Hence, there is great need for new biomarkers for early detection of OSCC. We have used a proteomic approach to identify the serum antibodies in OSCC patients as new tumor markers. Anti-Sideroflexin3 autoantibody(SFXN3-aAb) levels were higher in patients with OSCC and significantly showed 77% sensitivity and 89% specificity against control samples. Serum examination of SFXN3-aAb was more reliable than that of the serum SCC antigen when compared directly using the same samples. The serum SFXN3-aAb levels were also significantly higher in the early stage. In conclusion, the SFXN3-aAb can be used as a new tumor marker which is especially useful in the early diagnosis of OSCC.

Key Words: Proteomic approach, Autoantibody, Sideroflexin3

# 自己抗体を標的とした新規膵癌腫瘍マーカーの検討 一血清中の抗PGAM1自己抗体, 抗TPI1自己抗体の検出ー 今井 良典

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Summary

Pancreatic cancer is the fifth leading cause of cancer-related mortality in Japan. Early detection in pancreatic cancer is one of the most effective strategies to improve prognosis. Several tumor markers of pancreatic cancer have been identified; however, none of these markers are a true diagnostic marker. A proteomic approach was used to identify the serum antibodies in pancreatic cancer patients as a new tumor marker. Solubilized proteins from human pancreatic cancer cell lines (MIA PaCa-2) were separated using two-dimensional polyacrylamide gel electrophoresis, followed by Western blotting analysis in which the serum of the pancreatic cancer patient was tested for primary antibodies. Phosphoglycerate mutase 1 (PGAM1) and triosephosphate isomerase 1 (TPI1) were detected as cancer specific antigens using MALDITOF MS. Anti-PGAM1 autoantibody and anti-TPI1 autoantibody levels were elevated in the sera of pancreatic cancer patients significantly: 76.9–92.3% and 83.9–93.5% sensitivity. These values were better than those of the serum CA19–9 antigen levels when compared directly using the same samples. In conclusion, the detection of anti-PGAM1 autoantibody and anti-TPI1 autoantibody in serum may useful for the diagnosis of pancreatic cancer, and these autoantibodies may be new diagnostic markers for pancreatic cancer.

Key Words: Pancreatic cancer, Tumor marker, Autoantibody

#### アデノベクターによるマウス肝臓へのヒトBcl-xL遺伝子導入の虚血再灌流障害に対する肝保護効果

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愛媛医学 26(2):133-143, 2007

Summary

BACKGROUND: Hepatic ischemia / reperfusion injury can occur in various clinical situations including surgical resection, liver transplantation, and shock. It is well known that hepatic ischemia can lead to cell death such as

necrosis and apoptosis. Bcl-xL is a Bcl-2-related gene that regulates apoptosis by blocking the mitochondrial membrane potential transition. We examined the protective effect of a Bcl-xL gene transfer to a mouse liver in a partial ischemia/reperfusion model.

MATERIALS AND METHODS: We constructed adenoviral vector AxCAhBcl-xL and investigated its antiapoptotic effect RCN-H4 rat colon carcinoma cells in vitro. Adenoviral vector (AxCAhBcl-xL or AxCALacZ) was administered intravenously in a mouse model with 37% partial hepatic ischemia. The gene expression was evaluated by Western blotting and immunostaining. The serum AST and serum ALT levels were examined to evaluate the inhibitory effects of AxCAhBcl-xL on the hepatic ischemia / reperfusion injury and the hepatic histological damages were determined by using a point counting method and TUNEL staining.

RESULTS: The serum ALT level at 6 hours after reperfusion was 1,148  $\pm$  450 IU/I in the Bcl-xL group, 2,618  $\pm$  698 IU/I in the LacZ group, and 2,331  $\pm$  360 IU/I in the control group. The AST level was significantly lower in the Bcl-xL group than in the other groups (P<0.05).

Histological damage and the number of TUNEL positive cells were significantly lower in the Bcl-xL group than in the other groups (P < 0.05).

CONCLUSIONS: These findings suggest that Bcl-xL gene transfer by administration of the adenoviral vector reduces the severity of ischemia / reperfusion injury in a mouse liver.

Key Words: Bcl-xL, adenovirus vector, ischemia reperfusion injury

# Effects of c-kit receptor mutation on the maturation and the function of rat peritoneal mast cells in heterozygous Ws /+ rats

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#### 要旨

マスト細胞の分化・増殖にはマスト細胞の細胞膜に発現するc-kit 受容体にstem cell factor(SCF)が結合することにより生じる受容体のチロシン残基のリン酸化が重要な役割を果たしている。本研究においてc-kit 受容体遺伝子に12塩基の欠損をもつWs 遺伝子を有するヘテロ型ラット(Ws /+)と正常野生型ラット(+/+)のマスト細胞を比較することでc-kit 受容体がマスト細胞の増殖と機能に与える影響を検討した。

Ws /+ラットならびに+/+ラットから分離精製した腹腔マスト細胞を用いてIgE受容体凝集を介した免疫学的刺激およびcompound48/80による非免疫学的刺激を行い、マスト細胞のヒスタミン含量ならびにヒスタミン遊離率を測定した。Ws /+ラットの腹腔マスト細胞数は2.35 x 105個/ラット、ヒスタミン含量は0.181pmol/cellであり、+/+ラットの37.2%、89.1%であった。ジニトロフェニル化ウシ血清アルブミンによる抗原刺激ならびにcompound48/80刺激後に生じるヒスタミン遊離においてWs /+、+/+ラット腹腔マスト細胞両者間に有意差は認められなかった。

c-kit 受容体の変異によるKit シグナルの減少はラット腹腔マスト細胞の増殖に影響を及ぼすが、開口分泌機能には影響しないことが明らかとなった。

Key Words: mast cells, c-kit receptor, histamine

#### イトマキヒトデ胚初期発生における糖鎖の時空間的分布パターン

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#### Summary

The sea bat is a type of starfish. To gather basic information about sea bat embryogenesis, several stages of larvae were stained histochemically with 21 kinds of lectins. Three patterns of reaction were observed in the cytoplasm. 1 : Granular reactions were observed in the apical side of the cytoplasm. 2 : Reactions were observed in whole of the cytoplasm. 3 : Both reactions 1 and 2 were observed. Granular reactions were observed in mesendodermal cells with stability by DBA, SBA, BSL-\_, VVA, RCA-\_, Jacalin, and PNA staining. It seems that these reactive products have  $\alpha$ ,  $\beta$ -GalNAc, or  $\alpha$ ,  $\beta$ -Gal, or galactosyl- $\beta$ -GalNAc for their binding specificity, which shows that these lectins can be used as markers of mesendoderm. Though reactions shown by s-WGA, LEL, STL, DSL, BSL-\_, UEA-\_, Con A, PSA, LCA, PHA-E, and PHA-L staining were uniform in the whole of the cytoplasm from the swimming blastula stage until the mesenchyme differentiation stage, strong reactions were limited to the basal side in the cytoplasm of archenteron cells in early bipinnaria. It seems that the products made in cytoplasm were secreted through basement membranes to the extracellular matrix.

Key Words: starfish, lectin histochemistry, embryogenesis

#### イトマキヒトデ幼生における食道輪状筋線維数の経時的変化

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#### Summary

In echinoderms, esophageal circular muscles are differentiated by mesodermal cells. It has been reported that some molecules regulate myogenetic cells in sea urchins. In contrast, there are few reports of esophageal muscle in sea bat larvae. A sea bat is a type of asteroid. In this study, numerical changes of circum-esophageal muscle fibers were examined using TRITC-phalloidin during starfish embryogenesis. At 45-48 hours larvae, cell which had a strong signal was detected in the coelomic pouch and it was observed that processes were extended to the ventral or esophageal side. First, 11 bundles of esophageal muscle fibers were observed in the esophagus in 48 hour larvae. The fibers rapidly increased to about 28 bundles during the next 12 hours. In 72 hour larvae, 31 muscular bundles were seen. Then, those fibers did not increase for at least 24 hours. These results were independent of the batches, the breeding season, and the collected station. So, the number of circum-esophageal muscular bundles seems to be inherited. This method can be used to easily visualize the effects of some factors on myogenesis.

Key Words: starfish larva, circum-esophageal muscle, phalloidin

#### ヒト唾液腺癌細胞の浸潤増殖におけるHGF/c-Metシステムの役割

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愛媛医学 26(2):165-174,2007

Summary

HGF and c-Met expression have been associated with tumor progression in many human malignancies. In this study we have attempted to investigate the role of HGF/c-Met system in the invasive growth of human salivary gland cancer cells. We used two human salivary gland cancer cell lines, GFP-ACC2 and GFP-ACCM. We demonstrated that HGF enhanced the invasive growth of these two cells through the activation of Akt. Next, we examined the expression and function of Akt isoforms (Akt1, Akt2 and Akt3) in the HGF-induced invasive growth of human salivary gland cancer cells. Expression of all Akt isoforms was detected in both types of cells using Western blot analysis. To identify the predominant Akt active isoform, we used small interfering RNAs (siRNAs) specific for each isoform. The effect of these siRNAs on the HGFinduced invasive growth of cancer cells was evaluated by collagen gel culture system. Knockdown of only a single Akt isoform expression almost completely abrogated the invasive growth induced by HGF. These results suggest that all Akt isoforms are required for the HGF-stimulated invasive growth of human salivary gland cancer cells, and that targeting Akt isoforms is an effective approach for treatment of salivary gland cancer.

Key Words: Salivary gland cancer cell, HGF, Akt

#### 恒久的ペースメーカー・リード挿入時における"cut-down変法"の有用性

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愛媛医学 26(2):175-179, 2007

Summary

We reviewed our arranged technique for cephalic vein cutdown in 237 patients who underwent implantation of endocardial pacing leads from 1995 through 2005. The final successful implantation rate was 98.7% (234 patients). The puncture method was performed successfully on the other three patients. We had no major complications during implantation. Lead failure has occurred in three patients, but their leads were implanted by puncture method before our study, and we could not determine if the failure was associated with the arrange cutdown method. The conventional cutdown method seems to be complicated but significantly improves long-term performance of leads compared to the subclavian puncture method. Still, subclavian puncture method remains popular because of the ease of its technique, in spite of its short -term survival. Our arranged cutdown technique can transform the difficult conventional cutdown technique into an easy procedure without sacrificing the long-term performance of implanted pacing leads.

Key Words: pacemaker lead implantation, cutdown, arranged technique

#### 臨床経験録

dynamic splintによる早期運動療法を行った伸筋腱修復術後の成績

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愛媛医学 26(2):180-183, 2007

Summary

Repaired extensor tendons are traditionally immobilized with static palmar splints for 3 to 4 weeks before use, but this common practice has often been associated with a high incidence of tendon adhesion, tendon tightness,

intrinsic tightness and joint contracture. Our study consisted of a control group of 23 patients with extensor tendon divisions in zones 4 through 8. Patients had either complete or partial tears greater than 50%. Repaired tendons were mobilized in either one of two ways: by means of a passive extension and early controlled active flexion technique using dynamic splints (Group A); by means of a traditional early active extension regimen (Group B). We collected data from 10 patients in Group A and 13 patients in Group B over a period of six weeks. The results from our experiment did not indicate any ruptures in Group A or B, but Group A patients' conditions were generally better than those in Group B. Early controlled active flexion with passive rubber band extension can effectively prevent adhesion of the extensor tendons. These results suggest that dynamic splinting is more effective than static splinting for the prevention of extensor lag.

Key Words: dynamic splint, extensor tendon, early mobilization

# 2006年6~7月期に介護老人保健施設で多発したウィルス感染と考えられる発熱患者の考察 ーアルコール手指消毒の再検討ー

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愛媛医学 26(2):184-188, 2007

We observed an outbreak of high fever at our geriatric health service facility from June 15 to July 31, 2006. During this season, 97 persons were admitted to our facility. Thirty-one of the admitted users got a fever, and 10 of them suffered from pneumonia. Serological analysis suggested an infection with Adenovirus, Enterovirus or Coxsackievirus, which is epidemic around our facility during this season. Referring to reports showing that alcohol needs more exposure time and a higher concentration for virucidal effects, especially against non-enveloped ones, than for bactericidal effects, we substituted liquid soap (containing 3-Methy-4-isopropylphenol) with running water-hand wash method for alcohol-hand wash method. We also employed hydroxychloride environmental disinfection. After this modification of hand hygiene the outbreak subsided. Nevertheless, we could not exclude the possibility that the outbreak subsided spontaneously following the subsidence of the viral epidemic in surrounding areas. We need more information to determine an effective method for preventing viral transmission in geriatric health service facilities.

Key words: geriatric health service, hand hygiene, viral infection

#### 症例報告

#### 選択的低アルドステロン症の1例

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愛媛医学 26(2):189-192,2007

Summary

A 74-year-old man who complained of dyspnea and sore throat was admitted to our hospital. He was diagnosed with acute pneumonia upon examination and was hospitalized. After 8 days, he developed hyponatremia and hyperkalemia. Endocrinological examinations revealed selective hypoaldosteronisim. After he was medicated with 0.05 mg of fludrocortisone, serum levels of sodium and potassium normalized.

Selective hypoaldosteronism is a rare and critical illness, therefore we report this case.

Key words: selective hypoaldosteronism, critical illness, hyponatremia

#### 胸痛を契機に発見された皮下気腫、縦隔気腫を合併した糖尿病ケトアシドーシスの1例

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愛媛医学 26(2):193-196, 2007

Summary

A 33-year-old female exhibited loss of appetite and decreased body weight in early December, 2005. She visited the out-patient department of our university hospital due to abdominal and chest pain and was admitted in late December. Blood examination and arterial gas analysis revealed that she had been suffering from diabetic ketoacidosis. X-ray examination showed pneumomediastrium and subcutaneous emphysema, which was further confirmed by computed tomography. The patient recovered after 21 days due to rest and proper management. Her recovery was confirmed by computed tomography.

Ketoacidosis complicated by pneumomediastrium is rare and recovery can be spontaneous. However, as the patient was complaining of chest pain, a diagnosis of esophageal rupture and heart diseases should be investigated immediately.

Key Words: ketoacidosis, Pneumomediastium

#### 尿閉をきたした性器ヘルペスの2例

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愛媛医学 26(2):197-199, 2007

Summary

There are many causes of acute urinary retention. Two cases caused by herpes simplex infection, a rare cause, are reported here. A 42-year-old woman and a 24-year-old man exhibited urinary retention after a genital infection of herpes simplex virus (HSV). The virus may interrupt the detrusor reflux due to the involvement of the sacral dorsal root ganglia. Recovery from HSV-associated bladder emptying dysfunction can usually be achieved through conservative management, including intermittent self-catheterization or the insertion of an urethral balloon catheter. Fortunately, this process usually results in a full recovery of the detrusor.

Key Words: urinary retention, herpes simplex virus, Elsberg syndrome

#### 精神症状が先行したCushing症候群の1例

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愛媛医学 26(2):200-202,2007

Summary

A 34-year-old woman was admitted to our hospital with Cushing syndrome. She had had preceding psychiatric symptoms 3 years before the development of moon face, central obesity, hypertension, and muscle weakness. Her fasting serum cortisol concentration level was normal, and her plasma ACTH level was markedly low. No diurnal serum cortisol or plasma ACTH level fluctuations were recorded. Abdominal computed tomography and 131I-adosterol scintigraphy revealed a right functional adrenocortical tumor. She underwent a laparoscopic right adrenectomy, and her psychiatric symptoms improved. Patients who suffer mainly from psychiatric symptoms with hypertension and obesity should be investigated for Cushing syndrome.

Key Words: Cushing syndrome, psychiatric symptom, preceding

## 研究会抄録

## 第6回愛媛県摂食嚥下研究会

愛媛医学 26(2):203-204, 2007

第106回愛媛整形外科集談会

愛媛医学 26(2):205-209,2007

第92回愛媛脳神経外科懇話会

愛媛医学 26(2):210-213, 2007