

## 愛媛医学 第32巻2号

### トピックス

#### 生理活性物質によるヒト制御性T細胞および免疫寛容樹状細胞の誘導

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愛媛医学 32(2):91-96, 2013

#### 重症心不全患者に対するの補助人工心臓治療—体外式から植込型, 在宅療養へ—

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### エディトリアル

#### bFGF 徐放薬を用いた末梢神経性嗅覚障害の治療

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#### Dystroglycan 糖鎖研究の現状と展望

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#### 副作用のない口腔癌治療を目指して

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### 原 著

#### bFGF-ゼラチンハイドロゲル局所投与による神経性嗅覚障害の治療

##### —実験的嗅覚障害モデルマウスを用いた研究—

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#### Summary

The aim of this study was to investigate the effects of bFGF-gelatin hydrogel on recovery of neural anosmia that was induced in mice by intraperitoneal injection of 3-methylindole (3-MI, 200 mg/kg). After administration of 3-MI for one week, the animals were subjected to one of the following three procedures bilaterally: 1) group A: single-shot intranasal drip infusion of PBS, 2) group B: single-shot intranasal drip infusion of 10 µg bFGF, and 3) group C: placement of bFGF (10 µg)-hydrogel in the nasal cavity. The olfactory function of the animals was

evaluated by the odor-detection test (ODT) 2 and 4 weeks later. Following the testing, the animals were sacrificed, the thickness of the olfactory epithelium was measured, and the number of olfactory marker protein (OMP)-positive cells was counted. ODT proved that neural anosmia recovered in group C but not in groups A and B. Histologically, the olfactory epithelium became thicker and the number of OMP-positive cells increased in group C while such functional and histological recovery was poor in groups A and B. These findings suggested that placement of bFGF-hydrogel in the nasal cavity is an efficient way to facilitate recovery of neural anosmia.

Key Words : Neural anosmia, bFGF, 3-methylindole

### **口腔癌における dystroglycan の発現と機能解析**

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#### Summary

Metastasis is one of the most important prognostic factors in oral cancer. Recently, it is reported that a loss of protein glycosylation lead to cancer invasion and metastasis. Dystroglycan (DG) is known as the key molecule of the muscle dystrophy.  $\alpha$ -DG, one of DG subtype, have a laminin anchoring glycosylation which contributes to connect actin cytoskeleton and extracellular matrix (ECM). The defects in  $\alpha$ -DG glycosylation cause the malignant phenotype of several types of cancer, but the expression and function of DG in oral cancer remain unclear. We analysed DAG1 (dystrophin-associated glycoprotein 1) mRNA expression by real-time quantitative reverse transcription-polymerase chain reaction (RT-PCR) and DG protein expression by Western blots of oral cancer tissues and cell lines. Moreover, we investigated whether some glycosyltransferases affect to  $\alpha$ -DG glycosylation exist. As the result,  $\alpha$ -DG glycosylation was reduced significantly, although  $\alpha$ -DG core protein expression was maintained. The mRNA expression level of like-glycosyltransferase (LARGE), known as one of  $\alpha$ -DG glycosyltransferases, was decreased in all oral cancer cell line. Transduction of LARGE expression vector restored  $\alpha$ -DG glycosylation. Our results suggest that the loss of  $\alpha$ -DG glycosylation and LARGE might cause malignant phenotype in oral cancer.

Key Words : dystroglycan, oral cancer, like-glycosyltransferase (LARGE)

### **Src の発現抑制は口腔癌細胞の増殖を抑制し TRAIL によるアポトーシス抵抗性を解除する**

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#### Summary

A radical operation for advanced oral cancer results in malfunction of chewing, swallowing, and pronouncing etc. Desirable treatment is less-invasive and effective against primary lesion, metastatic sites and cells with metastatic potential. Since resistance to anoikis and apoptosis is essential to successfully metastasize, we focused on the apoptotic signaling pathways mediated by natural death ligands.

In this study, we have used oral squamous cell carcinoma cell lines with distinct metastatic potential and have analyzed their apoptosis sensitivity. SAS cells established from human tongue squamous cell carcinoma showed modest sensitivity to tumor necrosis factor-related apoptosis-inducing ligand (TRAIL), whereas SAS-T5 and SAS-L1 cells, subclones with high metastatic potential, showed robust resistance. One of mechanisms underlying

the differences in TRAIL-resistance among the cell lines was pSrc (Tyr 416) activation by Src kinase. Src kinase inhibitor PP2 suppressed cell proliferation in all three cell clones. Knockdown of Src with siRNA dissolved the resistance to TRAIL-induced apoptosis in SAS-L1 cells. These results suggest that combination therapy with TRAIL plus Src kinase inhibitor may be an efficient strategy for oral squamous cell carcinoma.

Key Words : Oral squamous cell carcinoma, TRAIL, Src

## 症例報告

### 悪性リンパ腫に対して Rituximab を使用し HBV 再増殖による重症肝炎を来した3例

#### —免疫抑制・化学療法にともなう B 型肝炎対策ガイドラインの検証—

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愛媛医学 32(2):133-137, 2013

#### Summary

We had experienced three cases of serious hepatitis due to the enhancement of hepatitis B virus (HBV) replication induced by rituximab treatment (anti-CD20 monoclonal antibody) for malignant lymphoma. Two cases were HBV reactivation from patients with HBs antigen negative (de novo HBV hepatitis), and one case was the enhancement of HBV from a patient with HBs antigen positive. Among them, two cases were died. However, all of the patients were treated with nucleotide analogues. In 2009, the Japanese guideline for prevention of immunosuppressive therapy or chemotherapy-induced reactivation of hepatitis B virus infection was presented. Two of our cases were treated in conformity to the guideline, however, we could not prevent serious hepatitis with HBV enhancement. The guideline should be discussed in a timely manner to establish a safer treatment for patients taking rituximab who are infected with HBV.

Key Words : hepatitis B virus, de novo HBV hepatitis, rituximab

### アルコール多飲者に発症した ACTH 単独欠損症の1例

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愛媛医学 32(2):138-140, 2013

#### Summary

A 73-year-old man was admitted to our emergency room with loss of consciousness and fainting. His blood glucose level was 25 mg/dL, and he became conscious immediately after a glucose injection. He was feeling general fatigue, headache, and had lost 10 kg in the last 6 months. He had been taking about 100 g of ethanol per day. There was no history that he took oral hypoglycemic agents or anything else to cause hypoglycemia. During hospitalization, he always presented hypoglycemia at fasting time. When he presented hypoglycemia, prasma IRI and C-peptide levels were not detectable. A hormone examination found that ACTH and cortisol showed no reaction for CRH, and other pituitary hormones were normal for the TRH, LHRH and GHRP loading test consistent with isolated ACTH deficiency (IAD). After starting administration of 15 mg of hydrocortisone per day, hypoglycemia disappeared, and the patient presented a remarkable improvement of clinical condition.

The clinical features of IAD such as hypoglycemia, hyponatremia, dehydration are very similar to other

effects of chronic alcohol abuse. Thus, IAD could be considered as one of the differential diagnoses for any chronic alcoholisms presenting these symptoms.

Key Words : isolated ACTH deficiency (IAD) , alcoholism, hypoglycemia

### **妊娠34週に発症した腎動脈瘤破裂の1例**

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愛媛医学 32(2):141-145, 2013

#### Summary

Rupture of renal arterial aneurysms during pregnancy are a rare but well-documented complication associated with a high incidence of maternal and fetal morbidity and mortality. We experienced a case in which a rupture of a renal arterial aneurysm caused fetal asphyxia.

A 30-year-old nullipara received prenatal care in a nearby clinic without any significant medical events. At 34 weeks of gestation, she suddenly suffered from severe right flank pain and, since hydronephrosis was suspected, was taken to our hospital. She underwent a cesarean section for non-reassuring fetal status, and a retroperitoneal hemorrhage was found. Computed tomography and angiography showed a rupture of the right renal arterial aneurysm. An arterial embolization was successfully performed and she was admitted to the intensive care unit. She then suffered disseminated intravascular coagulation, pulmonary edema, bacterial sepsis, hemorrhagic shock, and right renal failure ; however, she was discharged on the 34th hospital day. It is thought that a precipitous delivery, including cesarean section, and an arterial embolization after the delivery may be an ideal choice for treating the rupture of renal arterial aneurysms due to fears of maternal hemorrhagic shock and fetal asphyxia.

Key Words : arterial embolization, pregnancy, renal arterial aneurysm

#### **研究会抄録**

##### **第 49 回愛媛臨床血液懇話会**

愛媛医学 32(2):146-147, 2013

##### **第 14 回愛媛肛門疾患懇話会**

愛媛医学 32(2):148-150, 2013

##### **第 46 回愛媛県血管外科研究会**

愛媛医学 32(2):151, 2013

##### **第 6 回愛媛脊椎脊髄病セミナー**

愛媛医学 32(2):152-155, 2013

##### **第 16 回愛媛 NST(栄養サポートチーム)研究会**

愛媛医学 32(2):156-158, 2013

##### **第 131 回愛媛整形外科集談会**

愛媛医学 32(2):159-162, 2013