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トピックス

がん治療における熱エネルギー利用の新しい展開

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愛媛大学大学院臓器再生外科学分野

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原 著

糖尿病患者の健康食品摂取状況に関する実態調査(愛媛県糖尿病臨床研究グループ多施設共同研究)

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Summary

Dietary supplements are one of complementary and alternative medicines(CAM)that are used in clinics. Different dietary supplements are increasingly used by diabetic patients in Japan. Although, these supplements may have some beneficial effects, there may be serious adverse effects including liver injuries due to use of dietary supplementary in these patients. Another potential important point is that many patients discontinued conventional medicine after starting CAM.

To assess the effect of CAM, we conducted a survey using questionnaire among diabetic patients in nine hospitals of Ehime prefecture, Japan. Dietary supplements were used by 304 of 699 patients. Most of them have been using dietary supplements without discussing with their physicians. This was mostly prevalent in elderly female patients. Something about adverse effects.

All medical staff must be aware dietary supplements among diabetic populations and we must educate patients about risk of CAM. People with diabetes should tell their health care provider about any dietary supplements or medications that they are using or considering for future use.

Key Words : Diabetes Mellitus, dietary supplements, complementary and alternative medicine

顔面神経麻痺モデルを用いたbFGF徐放による神経再生促進効果

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Summary

Basic fibroblast growth factor(bFGF)promotes regeneration of injured nerves. This study examined the efficacy of a bFGF-impregnated biodegradable hydrogel as a drug-delivery medium for the treatment of facial nerve palsy. Facial nerve paralysis was induced in guinea pigs by compressing the intratemporal portion of the nerve. The animals were then subjected to one of the following three procedures : Group A : no further treatment ; Group B : application of aqueous bFGF solution to the nerve ; and Group C : application of bFGF-impregnated gelatin hydrogel. The regeneration of the facial nerve was evaluated 6 weeks later by observing facial movements, electrophysiological testing, and histological examination. The results for Groups A and B were similar in the three tests, indicating that the application of bFGF alone did not benefit facial nerve recovery. By contrast, Group C

achieved better results in all three indices : the total facial movements score, nerve conduction velocity, and number of nerve fibers. Our results suggest that bFGF-impregnated biodegradable hydrogel facilitates regeneration of facial nerves due to the sustained release of bFGF. Clinically, this therapeutic regimen may be useful for facial nerve decompression, which is indicated for severe facial nerve paralysis.

Key Words : basic fibroblast growth factor, biodegradable hydrogel, facial nerve regeneration

前立腺癌におけるAkt isoformsの発現と機能

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Summary

The Akt family of serine/threonine kinases is found in mammals and is comprised of three highly homologous members known as Akt 1, Akt 2, and Akt 3. Recent studies indicate that Akt is frequently constitutively active in many types of human cancer. In this study, we aimed to clarify the expression and function of Akt isoforms in human prostatic carcinoma cells. First, we examined the expression of Akt isoforms in prostate cancer tissues and four human prostate cancer cell lines using immunohistochemical staining and western blotting, respectively. Next, we designed and constructed 5 small interfering RNAs (siRNAs) specific for each Akt isoform, and evaluated their anti-tumor effect in vitro and in vivo . Expression of Akt 1 and Akt 2 was detected in all cells tested. However, Akt 3 was expressed only in cancer cells which do not express androgen receptor. All synthetic siRNAs suppressed the expression of each Akt isoform even at the concentration of 1 nM, and markedly inhibited the growth of cancer cells. Furthermore, atelocollagen-mediated systemic administration of siRNAs significantly reduced the growth of tumors, which had been subcutaneously xenografted. These results suggest that targeting Akt isoforms may be a novel approach for the treatment of prostate cancer.

Key Words : Akt, Prostate cancer, Synthetic siRNA

IV型痔瘻症例の治療経験

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Summary

There have been many difficulties with the diagnosis and treatment of type IV fistula (pelvicorectal fistula). However, recent advances of diagnostic modalities, especially in MRIs, has enabled us to make precise preoperative diagnoses. The treatments include an anal protecting operation and the seton method. In the seton method, there were slightly fewer postoperative complaints in comparison with the anal protecting operation. However, neither procedure causes a disruption in daily life. As for postoperative anal functional examinations, the anal resting pressure was decreased in both procedures, but slightly less in the seton method. These results show that the seton method may be an efficient treatment in type IV fistula as much as the anal protecting operation, although the long term effects of rubber band installation are unknown.

Key Words : type IV fistula, anal protecting operation, seton

乳房外Paget病における間質変化 —血管・リンパ管新生に基づいた87症例の考察—

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Summary

Extramammary Paget's disease, a form of carcinoma in the skin, is known to develop from apocrine glands. Although Paget cells, the tumor cells of the disease, are well documented in their pathologic features, their tumor microenvironment has not been clearly elucidated so far even though red patchy appearance of the disease strongly suggests underlying angiogenesis. In order to identify the potential role of microenvironment of the tumors, I examined angiogenesis and lymphangiogenesis using computer-assisted morphometric analysis. Furthermore, cancer-associated fibroblasts were identified using their specific marker alpha smooth muscle actin (α SMA). Tumor angiogenesis and lymphangiogenesis were dramatically induced already in carcinoma in situ of extramammary Paget's disease although angiogenesis was further enhanced in invasive carcinomas. Importantly, α SMA stains among tumor stroma were observed in advanced cases of the disease. Moreover, stromal α SMA expression was significantly correlated with tumor invasion compared to α SMA-negative cases in extramammary Paget's disease. Taken together, tumor microenvironment of extramammary Paget's disease plays a key role in promoting tumor progression and metastatic spread of the disease. Therefore, tumor angiogenesis and lymphangiogenesis may be a therapeutic target for the prevention of metastatic spread in extramammary Paget's disease.

Key Words : (lymph)angiogenesis, α SMA, prognosis

ヒト大腸癌細胞の細胞運動とLeucine-rich PPR motif-containing proteinとの関連

—機能的モノクローナル抗体による解析—

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Summary

Background and purpose : The mechanism of cell motility is comprised of very complicated molecular systems, and it is an important factor for tumor progression. The purpose of this study is to identify the cell molecule associated with the advancement of colon cancer by analyzing a key protein, which controls the cell motility mechanism of human colon cancer cells.

Material and methods : SW480 cells, originated from human colon carcinoma primary lesion, and SW 620 cells, originated from lymph node metastatic lesion of the same human colon cancer, were used in this study. Hybridomas were developed with SW480 cells to produce mouse monoclonal antibodies (mAbs). mAbs which inhibited cell motility were selected by membrane penetration analysis. The specificity was confirmed by Western Blotting and the band from the SDS-PAGE gel was subjected to protein analysis to identify the epitope determined by the mAb. Flow cytometry, cell fluorescence staining, immunostaining and Real Time PCR were performed to analyze the identified protein using the developed mAb..

Results : The newly developed mAb significantly inhibited the motility of SW480 cells, but SW620 cells were not affected. In Western Blotting with proteins from SW480 cell line, a single band of about 160 kDa was shown by the mAb, and protein analysis identified the band as Leucine-rich PPR motif-containing protein (Homo sapiens)

(following, LRPPRC). Flow cytometry showed a larger amount of LRPPRC antigen on the cell surface of SW480 than SW620. However, Real Time PCR revealed that the total amount of LRPPRC-mRNA in SW620 cells were larger than SW480. In cell fluorescence staining, LRPPRC was chiefly present on the cell membrane with SW480, while it was mostly located inside the cells with SW620. In immunostaining of clinical specimens, the cancer portion was strongly stained and non-cancer areas were not dyed or weakly stained.

Conclusions : The results of this study suggest that LRPPRC is involved in the control mechanism of cell motility of human colon cancer SW480 cells. In addition, it was suggested that the expression of LRPPRC is different at each stage of carcinogenesis and tumor development, because LRPPRC distribution was different at each normal and carcinoma tissue, or primary and metastatic lesion.

Key Words : LRPPRC, Monoclonal antibodies, Human colon cancer cell line

生後発生におけるラット中枢神経系プロサポシン免疫反応の変化

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Summary

Prosaposin is the precursor protein of four glycoproteins called saposins A, B, C and D, which activate sphingolipid hydrolases in lysosomes. Besides this role, intact prosaposin is also known as a potent neurotrophic factor in preventing neuronal cell death. It also stimulates neurite outgrowth in in vivo and in vitro experiments. In the present study, we examined the chronological changes of prosaposin immunoreactivity in the rat central nervous system using DAB immunohistochemistry and triple immunofluorescence staining. The strongest staining of prosaposin was observed on postnatal day 1 in hippocampal CA1, CA3 and dentate gyrus. After that the prosaposin immunoreactivity decreased gradually until it reached the level of adult on postnatal day 28. The immunoreactive particles observed in these immature neurons were much bigger than those observed in the mature neurons. These results indicate that prosaposin may play an important role in the development of the central nervous system.

Key Words : Prosaposin, Hippocampus, Neurotrophic factor

カイニン酸神経細胞障害によるプロサポシン動態

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Summary

Four sphingolipid activator proteins, saposin A, B, C and D, are synthesized from a single precursor protein, prosaposin. In addition to its role as a precursor of saposin in lysosome, intact prosaposin has neurotrophic effects in vivo or in vitro when supplied exogenously. In our previous study, prosaposin immunoreactivity was enhanced in the hippocampal neurons after kainic acid injection. In the present study, we performed an in situ hybridization of the hippocampus. Prosaposin mRNA expression was increased in the kainic acid-treated hippocampal neurons at the 1st day after the injection, and maintained high levels even at 3 weeks. Some neurons in/out of the stratum pyramidale showed more intense prosaposin mRNA expression than the other pyramidal neurons. Double immunofluorescent staining of prosaposin and GABA showed their overlap. This

study suggested that the stimulated hippocampal neurons synthesized prosaposin for their survival, and inhibitory interneurons are strongly activated to prevent CA 1 neurons from death.

Key Words : prosaposin, hippocampus, kainic acid

臨床経験録

髄内釘による上腕骨近位部骨折の治療成績

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Summary

The purpose of this study was to investigate the clinical results of the intramedullary fixation procedure on proximal humeral fractures. Twenty-seven shoulders of 26 patients (5 males, 21 females) underwent the intramedullary fixation procedure from April 2001 to December 2007. The mean age was 56.6 years old (range 16 to 94 years old). Fracture types were A2 (8 shoulders), A3 (14 shoulders), B1 (2 shoulders), B2 (2 shoulders), and B3 (1 shoulder) as classified by the AO classifications. All the patients who underwent osteosynthesis obtained a bony union. The mean postoperative pain score was 25.2 points (range 20 to 30 points) evaluated according to the Japanese Orthopaedic Association. The mean range of motion of the shoulder joint was 138.7 degrees in elevation. The positive functional results indicate that the intramedullary humeral nail was an effective method for the treatment of proximal humeral fractures.

Key Words : Proximal humeral fractures, Intramedullary nailing, Open reduction

症例報告

救命しえた腸腰筋血腫を合併したアルコール性肝硬変の1例

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Summary

In this report, we treated a case of iliopsoas muscle hematoma caused by alcoholic liver cirrhosis. A 60-year-old man with a past history of hospitalization for alcoholism was referred to our hospital for transient consciousness loss in January 2007. He complained of back pain and coxalgia, also extreme anemia was found on the first hospital day. We diagnosed the patient with an iliopsoas muscle hematoma. Our diagnosis was based on abdominal computed tomography and magnetic resonance imaging. No bleeding of the gastrointestinal tract was observed in the gastroscopy findings. On the nineteenth hospital day, We performed a blood transfusion and administered fresh frozen plasma to the patient, which enabled the start of the rehabilitation process.

Key Words : alcoholic liver cirrhosis, iliopsoas muscle hematoma

GAD抗体およびIA-2抗体ともに高力価で診断された高齢Slowly progressive IDDMの1例

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Summary

A 67-year-old woman was diagnosed with type2 diabetes mellitus (DM) at 63 years of age. One year after diagnosis, she was prescribed sulfonylurea-based therapy, but her blood sugar levels were poorly controlled. At the age of 67, she tested positive for anti-GAD antibody (23,000 U/ml) and anti-IA-2 antibody (39.5 U/ml). She was diagnosed with slowly progressive type1 DM (SPIDDM).

She had undergone surgery for Basedow disease at 49 years of age and has been maintained on thyroid hormone (Levothyroxine Sodium) until now. She was diagnosed with polyglandular autoimmune syndrome type III. The anti-IA-2 antibody is usually positive in young onset insulin-dependent DM patients, but not in adult onset SPIDDM patients with thyroid diseases.

We should pay attention regarding the development of SPIDDM as a cause of hyperglycemia during the follow-up for autoimmune thyroid diseases.

Key Words : SPIDDM, anti-IA-2 antibody, polyglandular autoimmune syndrome

研究会抄録

第109回愛媛整形外科集談会

愛媛医学 27(2): 139-142, 2008

第6回愛媛 NST(栄養サポートチーム)研究会

愛媛医学 27(2): 143-145, 2008

第41回愛媛県血管外科研究会

愛媛医学 27(2): 146-147, 2008

第95回愛媛脳神経外科懇話会

愛媛医学 27(2): 148-150, 2008

第96回愛媛脳神経外科懇話会

愛媛医学 27(2): 151-154, 2008