

トピックス

サーモグラフィによるトラベクレクトミー術後の濾過胞の機能評価

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原著

S100A11蛋白の発現と大腸癌細胞株SW480細胞の浸潤能との関連

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Summary

S100A11 is reported to be highly expressed in colorectal cancer, and while its expression is correlated with cancer progression, its actual role is not clear. We investigated the involvement of S100A11 in the migration and invasion of human colon cancer cells in vitro. Expression levels of S100A11 in 35 colorectal cancer samples were estimated using real-time PCR and compared to those of normal tissues. Twelve tissue samples were stained with anti-human S100A11 antibody. The cDNA of S100A11 was transfected into SW480 human colon cancer cells, which express high levels of S100A11, and into LoVo cells, which express it at a low level.

S100A11-specific shRNA was transfected into SW480 cells. Migration was assessed using BD Falcon™ Cell Culture Inserts with 8 μm pores, and invasion was assessed using BD BioCoat™ Matrigel™ Invasion Chambers. The mean value of the tumor to normal tissue ratios of S100A11 expression in 35 samples was 4.86. S100A11 was expressed in both the nuclei and cytoplasm in the cancer cells, but staining was faint in the cytoplasm of normal cells. Overexpression of S100A11 did not affect the migration of LoVo or SW480 cells. The migration of SW480 cells was also unaffected by downregulation of S100A11. However, overexpression of S100A11 increased the invasion of SW480 cells, and downregulation of S100A11 decreased the number of invasive cells. The expression of S100A11 protein is higher in colorectal cancer than in normal tissues. Our results suggest that S100A11 is involved in the process of cell invasion.

Key Words : colorectal cancer, invasion assay, S100A11

アデノベクターによるヒトBcl-xL遺伝子導入マウス

部分肝切除モデルにおける肝再生に対する効果

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Summary

Liver regeneration is an important factor which decides the prognosis of the patients in liver surgery, as well as in management of various liver diseases. The human Bcl-xL gene was introduced into the mouse liver using a newly developed adenovector to investigate the role of anti-apoptotic Bcl-xL protein in liver regeneration. C57BL mice (n

=6) received intravenous injections of AxCAhBcl-xL (Bcl-xL group), Null adenovector (Null group), or PBS (PBS). Three days after injection, the mice underwent 70% hepatectomy. The residual liver and blood samples were collected 1, 3, 5, and 7 days after hepatectomy. The liver weight was measured and the restituted liver mass was calculated. PCNA index, serum TNF- α , serum TGF- β , and liver tissue HGF were estimated. Changes of the expression of aurora kinase A, TPX2, PRC1, and aurora kinase B, which were selected by expression profiling using a RNA microarray, were determined by real time PCR. The restituted liver mass of the Bcl-xL group was larger than the PBS group and the Null group at day 5 and day 7. The expression of PRC1 was extremely elevated at day 1 and gradually decreased, while aurora kinase A, TPX2, and aurora kinase B tended to increase in the Bcl-xL group. The overexpression of Bcl-xL in the mouse liver enhanced the restitution after 70% hepatectomy. Different from the 3 other genes, PRC1 was excessively expressed at day 1 after hepatectomy.

Key Words : adenovector, Bcl-xL gene, liver restitution

ヒトヘルペスウイルス6型感染樹状細胞におけるToll-like receptorの発現と機能解析

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Summary

Human herpesvirus 6 (HHV-6) exhibits tropism for immunocompetent cells including T lymphocytes, monocytes/macrophages, and dendritic cells (DCs), suggesting that HHV-6 infections affect the immunosurveillance system. The Toll-like receptor (TLR) system plays an important role in innate immunity against various pathogens. In the present study, I investigated the effect of HHV-6 infection on the expression and intracellular signaling of TLRs in DCs. Although expression levels of TLRs were slightly elevated or not lower following HHV-6 infection, the amount of cytokines produced upon stimulation with ligands for TLRs appeared to be dramatically lower in HHV-6-infected DCs as compared with mock-infected DCs. Similarly, phosphorylation levels of TAK-1, I κ B kinase and I κ B- α following stimulation of HHV-6-infected DCs with lipopolysaccharide, which is the ligand for TLR4, appeared to be lower as compared with those in mock-infected DCs. This data shows that HHV-6 impairs intracellular signaling through TLRs, suggesting a novel HHV-6-mediated immunomodulation mechanism.

Key Words : human herpesvirus 6, dendritic cell, Toll-like receptor

GRIP1b欠損によるFraser症候群様表現型の発現

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Summary

Glutamate Receptor Interacting Protein1 (GRIP1) is an adaptor protein that interacts with α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor subunits and also binds to the intracellular C-termini of Fras1 and Fras1-related extracellular matrix (ECM) gene2 (Frem2). We have accidentally generated a transgenic mouse, which is expressed in Fraser syndrome-like phenotypes exhibiting fused eyelids, syndactyly and renal defect. Analysis of the mice revealed that multiple copies of the transgene were inserted between exon1a and exon1b of Grip1 gene. RT-PCR and immunoblot analysis showed that expression of GRIP1b mRNA and protein but not GRIP1a was undetectable in limb skin, lung and kidney of

the newborn mice, indicating that defect of GRIP1b gene expression was caused by the insertion of the transgene. The immunohistochemical analysis on limb skin sections from newborn mice also showed remarkable reduction of Fras1 and Frem2 immunoreactivities at the basement membrane of epidermis. Immunofluorescence staining of cells expressing GRIP1a or GRIP1b exhibited that GRIP1b localizes to plasma membrane and GRIP1a is in the cytosol. The stability of Fras1 was markedly enhanced by coexpression of either GRIP1a or GRIP1b. These results suggested that GRIP1b regulates the stability of Fras1 and Frem2 protein on the basal plasma membrane of epidermal basal cells through direct interaction. Key Words : GRIP1, Fraser syndrome, ECM

Development of simultaneous measurement method of histamine and N τ -methylhistamine using HPLC-amperometry and its application for study of histamine function

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要旨

高速液体クロマトグラフィー(HPLC)ー電気化学検出法を用いてヒスタミン(HA)ならびにその代謝物であるN τ -メチルヒスタミン(N τ -MHA)の高感度かつ高選択的な同時測定法を開発した。

HA, N τ -MHAを0.25 mMオルソフタルアルデハイド, 1.25 mM亜硫酸ナトリウムとpH9.65にて反応させ, N-アルキルイソインドールスルフォネート誘導体化した。固定相には逆相ODSカラムを, 移動相には20%メタノールを含む50 mMリン酸カリウム緩衝液(pH6.80)を用いて流速200 μ /minにてアミン誘導体を溶出し, 電気化学法(+0.75 V)にて酸化時に流れる電流を測定することにより, 両アミンの計測を行った。HA, N τ -MHA誘導体の保持時間はそれぞれ14.2分, 23.3分であり, 検出感度は両者ともに0.125 pmolであった。

本法を用いて測定したdd Y系マウスの全脳, 皮膚, 腺胃のHA含量はそれぞれ0.27 \pm 0.03, 65.9 \pm 4.3, 124.9 \pm 14.7 nmol/g湿重量, N τ -MHA含量は0.25 \pm 0.08, 2.01 \pm 0.05, 6.96 \pm 1.92 nmol/g湿重量であった。本法をヒスタミンN-メチル基転移酵素活性の測定に応用し, ラット腎臓において0.138 \pm 0.047 nmol/min/mg蛋白質の比活性値を得た。さらにマスト細胞欠損ラット(Ws/Ws)にレセルピン5mg/kgを腹腔内投与した結果, 視床下部におけるノルアドレナリン含量は非投与群に比べ約10%に減少したが, HAならびにN τ -MHA含量の有意な減少が認められなかったことより脳内ヒスタミン神経がレセルピンに対し感受性が低いことが明らかとなった。

本法は脳におけるヒスタミンニューロンの活動性の評価や胃, 皮膚などの末梢組織におけるヒスタミンの代謝回転の解析に有効である。

Key Words : histamine, N τ -methylhistamine, HPLC-amperometry

Wntシグナル伝達経路を制御する新規E3ユビキチンリガーゼの機能解析

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Summary

The Wnt signaling pathway is essential in normal differentiation and development, while it leads to tumor formation when aberrantly activated. A genetic screening of *Drosophila* was conducted to find a new component of this pathway or a new partner of adenomatous polyposis coli (APC). Goliath was selected as a candidate from the results of the screening using Flybase, a *Drosophila* genome database. The activity of the Wnt signaling

pathway was inhibited by h-Goliath, a human homologue of Goliath, in 293T culture cells expressing Wnt3A, which activates this pathway. When a mutation was introduced in its RING-H2 domain, which has E3 ubiquitin activity, the mutated h-Goliath didn't inhibit the pathway. It is suggested that h-Goliath works as an E3 ubiquitin ligase. Wild-type h-Goliath inhibited, and mutated h-Goliath didn't, the pathway in the cells cotransfected with either mutated β -TrCP or mutated β -catenin in place of Wnt3A, suggesting that h-Goliath works in the downstream of the pathway. The results of immunohistochemistry showed that h-Goliath exists in the cytoplasm, therefore it's not thought to ubiquitinate β -catenin. The substrate of h-Goliath is still unknown, and its discovery will clarify the functional significance of h-Goliath.

Key Words : Wnt signaling pathway, E3 ubiquitin ligase, RING-H2

臨床経験録

当院における腹部緊急手術5年間の推移

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Summary

We studied 764 cases of patients who received abdominal emergency operations at Matsuyama Shimin Hospital from 2004 to 2008. The rate of appendicitis and other diseases increased in 2008. The average age of patients increased from 44.6 to 53.2 years old. The annual percentage of male patients was 52.7%, 56.5%, 53.3%, 56.0%, and 49.7%, respectively. The percentage of patients operated on duty day was 23.0%, 26.1%, 24.4%, 24.8%, and 33.5%. Except for patients with appendicitis, most of the patients lived in Matsuyama city and neighboring districts, but other medical service areas have been added since 2006. Therefore, these facts show an advancing aging society and the population of woman is increasing. Also, they signify the migration from surgical operations at small and medium sized hospitals, decreases of emergency hospitals, and malfunctions of the third emergency medical care system. We should train young surgeons and change the medical policy in order to keep away the emergency medical breakdown.

Key Words : abdominal emergency operation, medical breakdown, medical policy

Direct Anterior Approach(DAA)による大・骨人工骨頭置換術の経験—30例の検討—

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Summary

The direct anterior approach(DAA) enables bipolar hip arthroplasty(BHA) to be performed in a minimally invasive manner that requires no muscle dissection. This report presents the clinical results of BHA by DAA. Between September 2008 and October 2009, DAA was used to treat 30 patients in our hospital. Seven cases were male and twenty three cases were female. All cases exhibited femoral neck fractures. Mean age at the time of operation was 78.0 years(60 to 95 years). Mean operation time was 77.0 minutes(42 to 169 minutes) and mean intraoperative blood loss was 200 ml(50 to 400 ml). These numbers decreased to 54.1 minutes and 158.2 ml in the most recent ten cases. Stem setting alignment was in good position, valgus and varus inclined angles were less than 3 degrees in all. There were no major complications during the operation, except in one patient who

sustained a femoral greater trochanter partial avulsion fracture. Mean post operative period before free gait enabling was 17.9 days. BHA by DAA has the advantage of shortening the recovery period to gait.

Key Words : femoral neck fracture, Direct Anterior Approach, bipolar hip arthroplasty

症例報告

直視下アルゴンプラズマ凝固療法が有用であった難治性放射線直腸炎の4例

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Summary

We reported 4 cases of intractable radiation-induced hemorrhagic proctitis successfully treated by endoscopic and direct APC (Argon plasma coagulation) using an operative kit. Two patients had been diagnosed with cancer of the cervix uteri, one with cancer of the anal canal, and one with cancer of the prostate. Radiation dosage was 45 to 70 Gy, time after radiation exposure was 2~70 months. Electric power was set from 30 to 70W, argon gas flow from 1.2 to 2.0 L/min, and two to three second coagulations were repeated. We used a PPH anoscope, and TEM rectoscope for the direct APC. Bleeding ceased immediately with one session for all patients, with no recurrences of bleeding or complications. This therapy can be used as an effective option for severe radiation proctitis because of its safe and precise hemostasis.

Key Words : Radiation proctitis, Argon plasma coagulation (APC), direct APC

化膿性筋炎を合併した糖尿病の2症例

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Summary

Case 1 : A 46-year-old man visited our hospital with left thigh pain and swelling. MRI demonstrated a high signal lesion in the left femoris muscle. Red pus was found by needle aspiration of the muscle, and a pus culture revealed staphylococcus aureus. A clinical diagnosis of pyomyositis was made. We performed open surgical drainage and antibiotic therapy. Laboratory data and clinical symptoms improved after the operation.

Case 2 : A 66-year-old woman visited our hospital with pain in her lower back and left lower leg. MRI demonstrated a high signal lesion around the psoas muscles, indicating a psoas abscess and pyogenic spondylitis of the lumbar spine at L2/3. However, when we performed drainage, the patient's back and leg pain worsened. We performed drainage under general anesthesia and the pain resolved. Pyomyositis should be taken into account as one of the differential diagnosis when a diabetic patient exhibits swelling, pain and hotness of muscles. MRI scans are useful for a diagnosis of pyomyositis.

Key Words : Pyomyositis, Diabetes mellitus, Magnetic resonance image (MRI)

研究会抄録

第10回愛媛NST(栄養サポートチーム)研究会

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第11回愛媛肛門疾患懇話会

愛媛医学 29(2):134-136, 2010

第 119 回愛媛整形外科集談会

愛媛医学 29(2):137-140, 2010

第 20 回愛媛県耳鼻咽喉科内視鏡研究会

愛媛医学 29(2):141-142, 2010