

Henry Ford Health System Publication List October 2006

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You can access this page at http://www.henryford.com/body_nologin.cfm?id=46638.

Adams, B. (2006). "Managing access clotting through online surveillance." *Nephrology News & Issues*. **20**(5): 44, 47. **Full-text Not Available / [Click for Article Request Form](#)**

Anton, T., J. Gutierrez and J. Rock (2006). "Tentorial schwannoma: a case report and review of the literature." *J Neurooncol* **76**(3): 307-11. **[PDF Full-Text](#)**

INTRODUCTION: Schwannomas are most often found in association with the eighth cranial nerve, but may also arise from any other cranial nerve. They are rarely found in an intra-parenchymal location. Unusual locations for intracranial schwannomas have also been reported in association with neurofibromatosis. CLINICAL PRESENTATION: A 23-year-old male without von Recklinghausen's disease presented with intermittent dizziness and difficulty swallowing. Past medical history was significant for a motor vehicle accident (MVA) without loss of consciousness 6 months prior. Magnetic resonance imaging revealed a large tentorial-based tumor. At surgery the origin of the tumor was clearly the tentorium, and while the trigeminal nerve was displaced, it easily separated from the mass. There was no attachment to any other cranial nerve in the immediate vicinity and postoperative cranial nerve examination was unremarkable. Pathological review was consistent with schwannoma. CONCLUSION: While there are few reported cases of tentorial-based schwannoma, these tumors have been noted in unusual locations within the intracranial vault, and clinicians should be aware of this diversity of origin.

Benninger, M., I. Brook and D. J. Farrell (2006). "Disease severity in acute bacterial rhinosinusitis is greater in patients infected with *Streptococcus pneumoniae* than in those infected with *Haemophilus influenzae*." *Otolaryngol Head Neck Surg* **135**(4): 523-8. **[PDF Full-Text](#)**

BACKGROUND: *Streptococcus pneumoniae* and *Haemophilus influenzae* are the most common causative pathogens in acute bacterial rhinosinusitis. A post hoc pooled analysis of four multinational Phase III clinical trials was conducted to compare disease severity in acute bacterial rhinosinusitis caused by *S. pneumoniae* or *H. influenzae*. METHODS: Patients were evaluated for acute bacterial rhinosinusitis clinician-assessed symptom severity and radiologic findings (total opacity, mucosal thickening, and air-fluid levels on maxillary sinus x-rays). Specimens for bacteriologic identification were collected by maxillary sinus tap, or by selective middle meatal cultures (sinus aspirates or swabs). RESULTS: Compared with patients infected with *H. influenzae* (n = 106), patients infected with *S. pneumoniae* (n = 143) showed a statistically significant higher incidence of severe disease (39.2% vs 23.6%, P = 0.0097) and total opacity (46.2% vs 29.2%, P = 0.0085). Mucosal thickening (47.6% vs 56.6%, P = 0.1616) and air-fluid levels (49% vs 56.6%, P = 0.2500) were comparable between the two groups. CONCLUSIONS: In acute bacterial rhinosinusitis, infection with *S. pneumoniae* is associated with more severe clinical symptoms and radiographic total opacification findings than infection with *H. influenzae*.

Chen, J. and M. Chopp (2006). "Neurorestorative treatment of stroke: cell and pharmacological approaches." *NeuroRx* 3(4): 466-73. **Full-text Not Available** / [Click for Article Request Form](#)

There is a compelling need to develop cell and pharmacological therapeutic approaches to be administered beyond the hyperacute phase of stroke. These therapies capitalize on the capacity of the brain for neuroregeneration and neuroplasticity and are designed to reduce neurological deficits after stroke. This review provides an update of bone marrow-derived mesenchymal stem cells (MSCs) and select pharmacological agents in clinical use for other indications that promote the recovery process in the subacute and chronic phases after stroke. Among these agents are 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors (statins), erythropoietin (EPO), and phosphodiesterase type 5 (PDE-5) inhibitors and nitric oxide (NO) donors. Both the MSCs and the pharmacologic agents potentiate brain plasticity and neurobehavioral recovery after stroke.

Chen, J., A. Zacharek, Y. Li, A. Li, L. Wang, M. Katakowski, C. Roberts, M. Lu and M. Chopp (2006). "N-cadherin mediates nitric oxide-induced neurogenesis in young and retired breeder neurospheres." *Neuroscience* 140(2): 377-88. [PDF Full-Text](#)

Neurogenesis may contribute to functional recovery after neural injury. Nitric oxide donors such as DETA-NONOate promote functional recovery after stroke. However, the mechanisms underlying functional improvement have not been ascertained. We therefore investigated the effects of DETA-NONOate on neural progenitor/stem cell neurospheres derived from the subventricular zone from young and retired breeder rat brain. Subventricular zone cells were dissociated from normal young adult male Wistar rats (2-3 months old) and retired breeder rats (14 months old), treated with or without DETA-NONOate. Subventricular zone neurosphere formation, proliferation, telomerase activity, and Neurogenin 1 mRNA expression were significantly decreased and glial fibrillary acidic protein expression was significantly increased in subventricular zone neurospheres from retired breeder rats compared with young rats. Treatment of neurospheres with DETA-NONOate significantly decreased neurosphere formation and telomerase activity, and promoted neuronal differentiation and neurite outgrowth concomitantly with increased N-cadherin and beta-catenin mRNA expression in both young and old neurospheres. DETA-NONOate selectively increased Neurogenin 1 and decreased glial fibrillary acidic protein mRNA expression in retired breeder neurospheres. N-cadherin significantly increased Neurogenin 1 mRNA expression in young and old neurospheres. Anti-N-cadherin reversed DETA-NONOate-induced neurosphere adhesion, neuronal differentiation, neurite outgrowth, and beta-catenin mRNA expression. Our data indicate that age has a potent effect on the characteristics of subventricular zone neurospheres; neurospheres from young rats show significantly higher formation, proliferation and telomerase activity than older neurospheres. In contrast, older neurospheres exhibit significantly increased glial differentiation than young neurospheres. DETA-NONOate promotes neuronal differentiation and neurite outgrowth in both young and older neurospheres. The molecular mechanisms associated with the DETA-NONOate modulation of neurospheres from young and older animals as well as age dependent effects of neurospheres appear to be controlled by N-cadherin and beta-catenin gene expression, which subsequently regulates the neuronal differentiating factor Neurogenin expression in both young and old neural progenitor cells.

Coffey, C. E. (2006). "Pursuing perfect depression care." *Psychiatr Serv* 57(10): 1524-6. [PDF Full-Text](#)

Cohen, A., C. Brodie and R. Sarid (2006). "An essential role of ERK signalling in TPA-induced reactivation of Kaposi's sarcoma-associated herpesvirus." *J Gen Virol* 87(Pt 4): 795-802. [PDF Full-Text](#)

Kaposi's sarcoma-associated herpesvirus (KSHV) is implicated causally in the development of several human malignancies, including primary effusion lymphoma (PEL). PEL cells serve as tools for KSHV research, as most of them are latently infected and allow lytic virus replication in response to various stimuli. 12-O-Tetradecanoyl-phorbol-13-acetate (TPA) is the most potent inducer of lytic KSHV reactivation; nevertheless, the exact mechanism by which it induces reactivation remains unknown. It has previously been reported by our group that the protein kinase C (PKC) delta isoform plays a crucial role in TPA-mediated KSHV reactivation. Here, the activation pathway was dissected and it was demonstrated that TPA induces KSHV reactivation via stimulation of the mitogen-activated protein kinase (MAPK)/extracellular signal-regulated kinase (ERK) pathway. Western blot analysis revealed a rapid phosphorylation of ERK1/2. Cells treated with MAPK/ERK inhibitors before TPA addition

demonstrated repression of ERK1/2 phosphorylation, which was associated with a block of KSHV lytic-gene expression. This inhibition prevented c-Fos accumulation, yet increased c-Jun phosphorylation. Similar results were obtained in response to rottlerin, a selective PKCdelta inhibitor. Notably, the PKC inhibitor GF 109203X reduced ERK1/2 phosphorylation, c-Fos accumulation, c-Jun phosphorylation and KSHV reactivation. It is proposed that TPA induces KSHV reactivation through at least two arms. The first involves PKCdelta, ERK phosphorylation and c-Fos accumulation, whilst the second requires another PKC isoform that induces the phosphorylation of c-Jun. c-Fos and c-Jun jointly form an active AP-1 complex, which functions to activate the lytic cascade of KSHV.

Drake, C. L., C. Jefferson, T. Roehrs and T. Roth (2006). "Stress-related sleep disturbance and polysomnographic response to caffeine." *Sleep Med* **7**(7): 567-72. **Full-text Not Available / [Click for Article Request Form](#)**

BACKGROUND AND PURPOSE: To determine the sleep response to caffeine in individuals vulnerable to stress-related sleep disturbance as measured by polysomnography. **PATIENTS AND METHODS:** Eleven healthy individuals without insomnia scoring low (4 women, mean age=32.64+/-15.46 years) and 10 healthy individuals also without insomnia scoring high (6 women, mean age=34.20+/-13.73 years) on a measure of vulnerability to stress-related sleep disturbance were studied in a laboratory protocol. A moderate-low dose of caffeine (3mg/kg) was administered 1h prior to lights-out and compared to a counterbalanced control night with each condition separated by 1 week. Standard polysomnographic measures were assessed (i.e. total sleep time, sleep efficiency, latency to persistent sleep, and sleep stage percentages) for both control and caffeine nights. **RESULTS:** There were no between-group differences in sleep on the control night. Importantly, individuals reporting vulnerability to stress-related sleep disturbance had significantly prolonged latency to persistent sleep in response to the caffeine challenge (interaction; $P < 0.05$). **CONCLUSION:** Normal sleepers with an identified vulnerability to stress-induced sleep disturbance exhibited greater objectively verifiable sleep-reactivity in response to a caffeine challenge compared to non-vulnerable individuals. These results suggest that the construct of individual differences in vulnerability to sleep disturbance applies to a pharmacological 'stressor' (i.e. caffeine) as well as to previously assessed stressors such as a first-night effect. This finding provides further support for generalized trait vulnerability by demonstrating a sleep disturbance to a wake-promoting pharmacological challenge in specific a priori identified individuals.

Jee, W. S. (2006). "Harold M. Frost, M.D., D.Sc. (hon) -- one man's association." *J Musculoskelet Neuronal Interact* **6**(2): 113-21. **Full-text Not Available / [Click for Article Request Form](#)**

The author described how and when he first met Harold M. Frost, M.D., that began a journey from the Henry Ford Hospital to the University of Utah and Sun Valley Hard Tissue Workshops that sequentially developed the technology of dynamic cancellous bone histomorphometry, the ever-evolving mechanostat hypothesis and the Utah Paradigm for Bone Physiology.

Katramados, A., S. C. Patel and P. D. Mitsias (2006). "Non-invasive magnetic resonance myelography in spontaneous intracranial hypotension." *Cephalalgia* **26**(9): 1160-4. **[PDF Full-Text](#)**

Krzeminski, J. (2006). "Consumer Health Searcher: MerckSource." *Journal of Consumer Health on the Internet* **10**(2): 61-70. **Full-text Not Available / [Click for Article Request Form](#)**

Kumar, S. P., R. Mooney, L. J. Wieser and S. Havstad (2006). "The LATCH scoring system and prediction of breastfeeding duration." *J Hum Lact* **22**(4): 391-7. **Full-text Not Available / [Click for Article Request Form](#)**

This study aimed to determine whether LATCH scores assessed by professional staff during in-hospital stays are predictive of breastfeeding at 6 weeks. Participants were English-speaking breastfeeding women, 18 years or older, with healthy singletons. LATCH scores were obtained once every 8 hours on day 1 and daily subsequently until discharge. Data were obtained from hospital charts and telephone interviews on day 4 and week 6 postdelivery. At 6 weeks, 188 of 248 (76%) women were contacted and 66.5% were breastfeeding. LATCH scores were higher among women breastfeeding than those who had weaned. Using receiver operating characteristic (ROC) curves, a

score of 9 or above at 16 to 24 hours was the most discriminate of the 5 time periods examined (area under the ROC curve = 0.72). Furthermore, women who met this criterion were 1.7 times more likely to be breastfeeding at 6 weeks than women with lower scores. The LATCH assessment tool is a modest predictor of breastfeeding duration.

Malin, J. L., C. Ko, J. Z. Ayanian, D. Harrington, D. R. Nerenz, K. L. Kahn, J. Ganther-Urmie, P. J. Catalano, A. M. Zaslavsky, R. B. Wallace, E. Guadagnoli, N. K. Arora, M. D. Roudier and P. A. Ganz (2006). "Understanding cancer patients' experience and outcomes: development and pilot study of the Cancer Care Outcomes Research and Surveillance patient survey." Support Care Cancer **14**(8): 837-48. [PDF Full-Text](#)

GOALS OF WORK: The National Cancer Institute's Cancer Care Outcomes Research and Surveillance (CanCORS) Consortium is conducting a population-based study of newly diagnosed patients with lung and colorectal cancer to describe the experience of persons living with cancer and to understand which barriers present the most significant obstacles to their receipt of appropriate care. The keystone to this effort is the baseline patient survey administered approximately 4 months after diagnosis. **PATIENTS AND METHODS:** We developed a survey to obtain information from patients newly diagnosed with lung and colorectal cancer about their personal characteristics, decision making, experience of care, and outcomes. We conducted a pilot study to evaluate the feasibility of a lengthy and clinically detailed interview in a convenience sample of patients within 8 months of diagnosis (n=71). **MAIN RESULTS:** The median length of the interviews was 75 min for patients with lung cancer (range 43-130) and 82 min for patients with colorectal cancer (range 46-119). Most patients had received some form of treatment for their cancer: 66.1% had undergone surgery, 28.2% had received radiation therapy, and 54.9% were treated with chemotherapy. In addition, 26.7% reported their overall health was less than 70 on a 0-100 scale, demonstrating that patients with substantial health impairment were able to complete the survey. **CONCLUSIONS:** A clinically detailed survey of newly diagnosed lung and colorectal cancer patients is feasible. A modified version of this survey is being fielded by the CanCORS Consortium and should provide much needed population-based data regarding patients' experiences across the continuum of cancer care and their outcomes.

Maltsev, V. A., N. Silverman, H. N. Sabbah and A. I. Undrovinas (2006). "Chronic heart failure slows late sodium current in human and canine ventricular myocytes: Implications for repolarization variability." Eur J Heart Fail. Epub Ahead of Print. **Full-text Not Available / [Click for Article Request Form](#)**

BACKGROUND: Late Na(+) current (I(NaL)) in human and dog hearts has been implicated in abnormal repolarization associated with heart failure (HF). HF slows inactivation gating of late Na(+) channels, which could contribute to these abnormalities. **AIMS:** To test how altered gating affects I(NaL) time course, Na(+) influx, and action potential (AP) repolarization. **METHODS:** I(NaL) and AP were measured by patch clamp in left ventricular cardiomyocytes from normal and failing hearts of humans and dogs. Canine HF was induced by coronary microembolization. **RESULTS:** I(NaL) decay was slower and I(NaL) density was greater in failing hearts than in normal hearts at 24 degrees C (human hearts: tau=659+/-16 vs. 529+/-21 ms; n=16 and 4 hearts, respectively; mean+/-SEM; p<0.002; dog hearts: 561+/-13 vs. 420+/-17 ms; and 0.307+/-0.014 vs. 0.235+/-0.019 pA/pF; n=25 and 14 hearts, respectively; p<0.005) and at 37 degrees C this difference tended to increase. These I(NaL) changes resulted in much greater (53.6%) total Na(+) influx in failing cardiomyocytes. I(NaL) was sensitive to cadmium but not to cyanide and exhibited low sensitivity to saxitoxin (IC(50)=62 nM) or tetrodotoxin (IC(50)=1.2 muM), tested in dogs. A 50% I(NaL) inhibition by toxins or passing current opposite to I(NaL), decreased beat-to-beat AP variability and eliminated early afterdepolarizations in failing cardiomyocytes. **CONCLUSIONS:** Chronic HF leads to larger and slower I(NaL) generated mainly by the cardiac-type Na(+) channel isoform, contributing to larger Na(+) influx and AP duration variability. Interventions designed to reduce/normalize I(NaL) represent a potential cardioprotective mechanism in HF via reduction of related Na(+) and Ca(2+) overload and improvement of repolarization.

Mani, N. (2006). "Canadian Adverse Drug Reaction Monitoring Program (CADRMP) - Adverse Reaction (AR) Database." Journal of Consumer Health on the Internet **10**(3): 93-101. **Full-text Not Available / [Click for Article Request Form](#)**

Movsas, B., H. Diratzouian, A. Hanlon, H. Cooper, G. Freedman, A. Konski, E. Sigurdson, J. Hoffman, N. J. Meropol, L. M. Weiner, L. Coia, R. Lanciano, J. Stein, D. Kister and B. Eisenberg (2006). "Phase II trial of preoperative chemoradiation with a hyperfractionated radiation boost in locally advanced rectal cancer." [Am J Clin Oncol](#) **29**(5): 435-41. [PDF Full-Text](#)

PURPOSE: The purpose of this phase II study was to prospectively determine the efficacy of preoperative chemoradiation with a hyperfractionated (Hfx) RT boost to 61.8 Gy in locally advanced rectal cancer. **METHODS:** Eligibility stipulated that the primary lesion had to be either T4; or T3 and >4 cm or 40% of the bowel circumference. Radiation (RT) consisted of 45 Gy to the pelvis (1.8 Gy per fraction) followed by 1.2 Gy twice daily (to the gross tumor volume) to a total RT dose of 61.8 Gy. There was 5-FU infused at 1 g/m²/24 hours for 4 days during the 1st and 6th weeks of RT (concurrent with the Hfx boost). Surgical resection was planned 4 to 6 weeks later. Adjuvant chemotherapy (bolus 5-FU/leucovorin) was scheduled for 4 cycles at 28-day intervals. **RESULTS:** There were 22 patients, ages 22 to 81 years (median, 64) enrolled in the study. Of the 20 patients evaluable for response, 10 (50%) had evidence of clinical downstaging and 5 patients (25%) had > or =90% fibrosis in the resected specimen. With a median f/u of 40 months (7-158), the 4 years actuarial rate for all patients (n = 22) of OS was 64%, of DFS 62%, and of LC 84%. 3/21 patients (14%) had positive margins, all of whom developed a local failure (P < 0.001). **CONCLUSION:** This regimen of high dose preoperative chemoRT with a Hfx RT boost (to 61.8 Gy) in patients with bulky, locally advanced rectal cancer results in clinical downstaging in half of the patients with significant fibrosis in the operative specimen.

Murthy, S. and G. P. Reddy (2006). "Replisome: Complete machinery for DNA synthesis." [J Cell Physiol](#) **209**(3): 711-7. [PDF Full-Text](#)

Replication of nuclear DNA in eukaryotes presents a tremendous challenge, not only due to the size and complexity of the genome, but also because of the time constraint imposed by a limited duration of S phase during which the entire genome has to be duplicated accurately and only once per cell division cycle. A challenge of this magnitude can only be met by the close coupling of DNA precursor synthesis to replication. Prokaryotic systems provide evidence for multienzyme and multiprotein complexes involved in DNA precursor synthesis and DNA replication. In addition, fractionation of nuclear proteins from proliferating mammalian cells shows co-sedimentation of enzymes involved in DNA replication with those required for synthesis of deoxynucleoside triphosphates (dNTPs). Such complexes can be isolated only from cells that are in S phase, but not from cells in G(0)/G(1) phases of cell cycle. The kinetics of deoxynucleotide metabolism supporting DNA replication in intact and permeabilized cells reveals close coupling and allosteric interaction between the enzymes of dNTP synthesis and DNA replication. These interactions contribute to channeling and compartmentation of deoxynucleotides in the microvicinity of DNA replication. A multienzyme and multiprotein megacomplex with these unique properties is called "replisome." In this article, we summarize some of the relevant evidence to date that supports the concept of replisome in mammalian cells, which originated from the observations in Dr. Pardee's laboratory. In addition, we show that androgen receptor (AR), which plays a critical role in proliferation and viability of prostate cancer cells, is associated with replisome, and that identification of constituents of replisome in androgen-dependent versus androgen-independent prostate cancer cells may provide insights into androgen-regulated events that control proliferation of prostate cancer cells and potentially offer an effective strategy for the treatment of prostate cancer.

Nori, U. S., A. Manoharan, J. Yee and A. Besarab (2006). "Comparison of low-dose gentamicin with minocycline as catheter lock solutions in the prevention of catheter-related bacteremia." [Am J Kidney Dis](#) **48**(4): 596-605. [PDF Full-Text](#) / Authentication: ID: sladen - Password: library1

BACKGROUND: Catheter-restricted antibiotic lock solutions were found to be effective in the prevention of catheter-related bacteremia (CRB), but insufficient data are available about the ideal agent and dose. We hypothesized that a low concentration of gentamicin would be as effective as the high doses studied in the past. **METHODS:** In this prospective, open-labeled, randomized, clinical trial of patients on long-term hemodialysis therapy, patients were randomly assigned to administration of an antibiotic lock solution of gentamicin/citrate (4 mg/mL), minocycline/EDTA, or the control solution of heparin. Patients were followed up until the study end point of CRB was reached or a censoring event occurred. Interim data analysis was performed after 6 months to assess data safety; efficacy was noted and the study was terminated early. **RESULTS:** Sixty-two patients were enrolled into the study, evenly distributed in 3 arms, with data from 1 patient excluded from analysis. Seven of 20 patients in the

heparin group (4.0 events/1,000 catheter days), 1 of 21 patients in the minocycline group (0.4 events/1,000 catheter days), and none of 20 patients in the gentamicin group developed bacteremia. Results were statistically significant by using 2-tailed Fisher exact test; heparin versus gentamicin, $P = 0.008$, and heparin versus minocycline, $P = 0.020$. CONCLUSION: Antibiotic lock solutions are superior to the standard heparin lock alone in the prevention of CRBs, and low-dose gentamicin solution has efficacy similar to that of greater concentrations used in previous studies.

Okere, I. C., M. E. Young, T. A. McElfresh, D. J. Chess, V. G. Sharov, H. N. Sabbah, B. D. Hoit, P. Ernsberger, M. P. Chandler and W. C. Stanley (2006). "Low Carbohydrate/High-Fat Diet Attenuates Cardiac Hypertrophy, Remodeling, and Altered Gene Expression in Hypertension." Hypertension. Epub Ahead of Print. **Full-text Not Available / [Click for Article Request Form](#)**

The effects of dietary fat intake on the development of left ventricular hypertrophy and accompanying structural and molecular remodeling in response to hypertension are not understood. The present study compared the effects of a high-fat versus a low-fat diet on development of left ventricular hypertrophy, remodeling, contractile dysfunction, and induction of molecular markers of hypertrophy (ie, expression of mRNA for atrial natriuretic factor and myosin heavy chain beta). Dahl salt-sensitive rats were fed either a low-fat (10% of total energy from fat) or a high-fat (60% of total energy from fat) diet on either low-salt or high-salt (6% NaCl) chow for 12 weeks. Hearts were analyzed for mRNA markers of ventricular remodeling and activities of the mitochondrial enzymes citrate synthase and medium chain acyl-coenzyme A dehydrogenase. Similar levels of hypertension were achieved with high-salt feeding in both diet groups (systolic pressure of approximately 190 mm Hg). In hypertensive rats fed low-fat chow, left ventricular mass, myocyte cross-sectional area, and end-diastolic volume were increased, and ejection fraction was decreased; however, these effects were not observed with the high-fat diet. Hypertensive animals on low-fat chow had increased atrial natriuretic factor mRNA, myosin heavy chain isoform switching (alpha to beta), and decreased activity of citrate synthase and medium chain acyl-coenzyme A dehydrogenase, which were all attenuated by high-fat feeding. In conclusion, increased dietary lipid intake can reduce cardiac growth, left ventricular remodeling, contractile dysfunction, and alterations in gene expression in response to hypertension.

Ondra, S. L., S. Marzouk, A. Ganju, T. Morrison and T. Koski (2006). "Safety and efficacy of C2 pedicle screws placed with anatomic and lateral C-arm guidance." Spine **31**(9): E263-7. **PDF Full-Text**

STUDY DESIGN: This is a retrospective review of 150 C2 pedicle screw placements. Candidates had their C2 pedicle morphology assessed through three-dimensional imaging, including preoperative image guidance. After surgery, the patients were serially CT scanned. Follow-up, with fusion assessment, ranged from 1 to 12 years. **OBJECTIVE:** We will show that an open technique combined with lateral C-arm guidance provides rapid placement of C2 pedicle screws. **SUMMARY OF BACKGROUND DATA:** C2 pedicle screws can be successful anchors for a variety of cervical problems. Standard intraoperative image guidance, biplane fluoroscopy, or free hand techniques all have their drawbacks. **METHODS:** After adequate C2 exposure, the C2 pedicle is palpated. The dissector remains stationary to provide coronal orientation while a lateral C-arm radiograph is obtained for sagittal orientation. The drill trajectory is set, the C2 pedicle cannulated, and a cancellous screw placed. **RESULTS:** A total of 71 patients had bilateral screws placed and 8 patients had unilateral screws placed. The overall complication rate was 2.7%. **CONCLUSIONS:** In our series, we have found a consistent way to cannulate the C2 pedicle. C2 fixation serves as an integral part of cervical reconstruction. Preoperative planning, anatomic knowledge, and lateral C-arm orientation create a low morbidity method for C2 screw placement.

Ouellette, D. R. (2006). "The safety of bronchoscopy in a pulmonary fellowship program." Chest **130**(4): 1185-90. **PDF Full-Text**

STUDY OBJECTIVE: To determine the complication rate from supervised training bronchoscopy in a single pulmonary fellowship program, and to examine the effects of fellow and faculty experience on this complication rate. **DESIGN:** A retrospective review of preexisting quality improvement data from one center for the time period July 1, 1991, until June 30, 2005, was performed. The data were stratified based on the fellow year group and the staff experience level. The types of complications were recorded. **SETTING:** The study was performed at an accredited pulmonary and critical care fellowship program at a military medical center in the United States. **PARTICIPANTS:** Fifty-one pulmonary and critical care medicine fellows and 20 staff supervising

physicians performed the bronchoscopies that were included in this study. RESULTS: A total of 3,538 training bronchoscopies were performed during the study period with 73 complications for a complication rate of 2.06%. The most common complication was pneumothorax. The overall complication rates for first-year fellows (1stYFs), second-year fellows, and third-year fellows were not significantly different from the total complication rate. Training bronchoscopies supervised by junior staff had a complication rate not significantly different from that of senior staff. The cumulative complication rate for the first trimester for 1stYFs was 3.1%, whereas the cumulative complication rate for the second plus the third trimester for 1stYFs was 1.57% ($p < 0.05$). CONCLUSIONS: Training bronchoscopy performed during a pulmonary fellowship is a safe procedure in a supervised setting. Patients undergoing bronchoscopy performed by novice bronchoscopists have an increased complication rate during the first trimester of bronchoscopist training.

Rempel, S. A. and T. Mikkelsen (2006). Tumor invasiveness and anti-invasion strategies, Chapter 14. Handbook of Brain Tumor Chemotherapy. H. B. Newton, editor. New York, Elsevier: 193-218. **Full-text Not Available / [Click for Article Request Form](#)**

Rivera, P. P., M. K. Kole, D. M. Pelz, I. B. Gulka, F. N. McKenzie and S. P. Lownie (2006). "Congenital intercostal arteriovenous malformation." AJR Am J Roentgenol **187**(5): W503-6. [PDF Full-Text](#)

Rivers, E. P. (2006). "Patients are not airplanes and doctors are not pilots." Crit Care Med **34**(11): 2869-70. [PDF Full-Text](#)

Rogers, L. R., J. P. Rock, A. K. Sills, M. A. Vogelbaum, J. H. Suh, T. L. Ellis, V. W. Stieber, A. L. Asher, R. W. Fraser, J. S. Billingsley, P. Lewis, D. Schellingerhout and E. G. Shaw (2006). "Results of a phase II trial of the GliSite radiation therapy system for the treatment of newly diagnosed, resected single brain metastases." J Neurosurg **105**(3): 375-84. [PDF Full-Text](#) / Authentication: ID: sladen - Password: library1

OBJECT: The aim of this study was to evaluate the effectiveness of brachytherapy using the GliSite Radiation Therapy System in patients with a newly diagnosed resected single brain metastasis. The primary end point of the study was local tumor control. The secondary end points included patient survival, distant brain recurrence, quality of life, and treatment toxicity. METHODS: The authors conducted a prospective multiinstitutional phase II study of GliSite brachytherapy prescribed at a 60-Gy dose administered to a 1-cm depth after resection of a single brain metastasis. No whole-brain radiation therapy was given. Patients were assessed at 1 and 3 months after brachytherapy and every 3 months thereafter for up to 2 years. Seventy-one patients were enrolled at 13 centers. A GliSite balloon catheter was implanted in 62 patients. Fifty-four patients received brachytherapy. The median patient age was 60 years. The most common tumor (54%) was non-small cell lung cancer. Fifty-seven percent of patients had brain metastasis only, whereas 43% had extracranial metastasis. The median final administered dose was 60 Gy. The magnetic resonance imaging--determined local control rate, based on several different methods, was 82 to 87%. Both the median patient survival time and the median duration of functional independence were 40 weeks. Among the 35 patients who died, the cause of death was neurological in 11%. Thirteen patients underwent reoperation for suspected tumor recurrence or radiation necrosis, and histological diagnoses included radiation necrosis without tumor (nine patients), radiation necrosis mixed with tumor (two patients), and tumor only (two patients). Extracranial metastasis, tumor size, and radiation necrosis were significant factors affecting patient survival. CONCLUSIONS: In patients with a resected single brain metastasis, GliSite brachytherapy leads to a local control rate, median patient survival time, and duration of functional independence similar to those achieved with resection plus whole-brain radiation therapy.

Rosenzweig, T., A. Ziv-Av, C. Xiang, W. Lu, S. Cazacu, D. Taler, C. G. Miller, R. Reich, Y. Shoshan, Y. Anikster, G. Kazimirsky, R. Sarid and C. Brodie (2006). "Related to testes-specific, vespid, and pathogenesis protein-1 (RTVP-1) is overexpressed in gliomas and regulates the growth, survival, and invasion of glioma cells." Cancer Res **66**(8): 4139-48. [PDF Full-Text](#)

In this study, we examined the expression and functions of related to testes-specific, vespid, and pathogenesis protein 1 (RTVP-1) in glioma cells. RTVP-1 was expressed in high levels in glioblastomas, whereas its expression in low-grade astrocytomas and normal brains was very low. Transfection of glioma cells with small interfering RNAs targeting RTVP-1 decreased cell proliferation in all the cell lines examined and induced cell apoptosis in some of them. Overexpression of RTVP-1 increased astrocyte and glioma cell proliferation and the anchorage-independent growth of the cells. In addition, overexpression of RTVP-1 rendered glioma cells more resistant to the apoptotic effect of tumor necrosis factor-related apoptosis-inducing ligand and serum deprivation. To delineate the molecular mechanisms involved in the survival effects of RTVP-1, we examined the expression and phosphorylation of various apoptosis-related proteins. We found that overexpression of RTVP-1 decreased the phosphorylation of c-Jun-NH2-kinase and increased the expression of Bcl2 and that the protective effect of RTVP-1 was partially mediated by Bcl2. Finally, we found that RTVP-1 regulated the invasion of glioma cells as was evident by their enhanced migration through Matrigel and by their increased invasion in a spheroid confrontation assay. The increased invasive potential of the RTVP-1 overexpressors was also shown by the increased activity of matrix metalloproteinase 2 in these cells. Our results suggest that the expression of RTVP-1 is correlated with the degree of malignancy of astrocytic tumors and that RTVP-1 is involved in the regulation of the growth, survival, and invasion of glioma cells. Collectively, these findings suggest that RTVP-1 is a potential therapeutic target in gliomas.

Rufener, J. B., K. L. Yaremchuk and S. C. Payne (2006). "Evaluation of culture and antibiotic use in patients with pharyngitis." *Laryngoscope* **116**(10): 1727-9. [PDF Full-Text](#)

OBJECTIVES: The objectives of this study were to evaluate practice patterns for treatment of patients with pharyngitis with regard to testing for group A beta hemolytic streptococcal (GABHS) infection, frequency of antibiotic use, and appropriate choice of antibiotics. **STUDY DESIGN:** The authors conducted a retrospective review of billing data for 10,482 office visits for pharyngitis. **METHODS:** The 2004 billing database for a tertiary institution was queried for outpatient visits for pharyngitis or tonsillitis, group A Streptococcus tests (GAST), and antibiotic prescriptions filled after the visit. Patients were separated by age group and analyzed for the proportion of patients that received a GAST and proportion prescribed an antibiotic. Antibiotic prescriptions were also analyzed to determine whether they were appropriate for treatment of GABHS. **RESULTS:** A total of 68.7% of all patients and 82.2% of pediatric patients were tested for GAST. A total of 47.1% of adult patients and 44.9% of pediatric patients received an antibiotic. For adult patients for whom GAST was obtained, 48.6% were prescribed an antibiotic versus 53.6% of those not tested. Streptococcus testing was a significant predictor of antibiotic use ($P < .0001$), whereas age was not ($P = .22$). A total of 82.1% of all antibiotics prescribed were recommended for treatment of GABHS. **CONCLUSIONS:** Most patients seen for pharyngitis were tested for GABHS, but pediatric patients were tested more frequently than adults. Patients who received a GAST were less likely to receive antibiotics. The rates experienced in our tertiary academic institution are higher than previously quoted for community practice. When antibiotics were prescribed, they were usually appropriate for the treatment of GABHS based on current recommendations.

Rybicki, B. A., C. Neslund-Dudas, N. L. Nock, L. R. Schultz, L. Eklund, J. Rosbolt, C. H. Bock and K. G. Monaghan (2006). "Prostate cancer risk from occupational exposure to polycyclic aromatic hydrocarbons interacting with the GSTP1 Ile105Val polymorphism." *Cancer Detect Prev.* Epub Ahead of Print. **Full-text Not Available / [Click for Article Request Form](#)**

Background: Variation in the glutathione S-transferase (GSTP1) gene and occupational polycyclic aromatic hydrocarbons (PAH) exposure are putative prostate cancer risk factors. An Ile/Val polymorphism in codon 105 of GSTP1 affects its enzymatic activity toward PAH detoxification, a possible mechanism in prostate carcinogenesis. **Methods:** To determine whether the GSTP1 Ile105Val polymorphism modifies prostate cancer risk associated with occupational PAH exposure, we studied 637 prostate cancer cases and 244 controls of White and African-American race from the Henry Ford Health System in Detroit, Michigan. Occupational exposure to PAH from wood, petroleum, coal or other sources through respiratory and cutaneous routes was retrospectively assessed by expert review of job histories. The association of occupational PAH exposure and GSTP1 Ile105Val polymorphism with prostate cancer was tested in multiple logistic regression models adjusting for potential confounders. Cases were over sampled compared with controls to evaluate gene-environment interaction with the statistically efficient case-only analytic approach. **Results:** Neither carriage of the GSTP1 Val(105) variant allele nor occupational PAH exposure was significantly associated with prostate cancer. However, case-only analyses revealed that carriage of the GSTP1 Val(105) variant allele was associated with increasing levels of occupational respiratory PAH exposures

from any source and from petroleum (trend test $p=0.01$ for both). The GSTP1 Val(105) allele was observed most frequently in cases in the highest quartile of occupational respiratory PAH exposures from petroleum (OR=1.74; 95% CI=1.11-2.72) or from any source (OR=1.85; 95% CI=1.19-2.89). The gene-environment risk estimate in the highest PAH petroleum exposure quartile was greatest in men under age 60 (OR=4.52; 95% CI=1.96-10.41) or with a positive family history of prostate cancer (OR=3.02; 95% CI=1.15-7.92). Conclusions: Our results suggest men who carry the GSTP1 Val(105) variant and are exposed at high levels to occupational PAH have increased risk for prostate cancer. This increased risk is more pronounced in men under age 60 or with a family history of prostate cancer.

Ryu, S., A. Kolozsvary, K. A. Jenrow, S. L. Brown and J. H. Kim (2006). "Mitigation of radiation-induced optic neuropathy in rats by ACE inhibitor ramipril: importance of ramipril dose and treatment time." *J Neurooncol*. Epub Ahead of Print. [PDF Full-Text](#)

PURPOSE: Radiation-induced optic nerve damage was reduced by ramipril, a prodrug angiotensin-converting enzyme inhibitor (ACEI). This study was to determine the optimum dose and administration time of ramipril for mitigating radiation-induced optic neuropathy. **MATERIALS AND METHOD:** Adult Fischer 344 male rats were treated with a single dose radiation 30 Gy by using radiosurgical technique. After irradiation, the animals were randomly assigned into groups of different ramipril doses and administration time; control (no treatment), radiation alone, radiation + ramipril in different doses and starting times of drug. Ramipril was given 0.5-1.5 mg/kg/day and AT1R blocker Losartan 20 mg/kg/day in drinking water for 180 days. Functional endpoint with visual evoked potential (VEP) and anatomical endpoint with gross and histological analysis with immunohistochemical (IHC) stain were used. **RESULTS:** Normal VEP measurements in un-irradiated rats were 46.2 +/- 7.9 ms. There was no change of VEP value until 4 months, but was lengthened to 188.1 +/- 58.7 ms at 6 months after radiation. By ramipril treatment with the dose of 1.5 mg starting at 2 weeks after radiation, VEP was significantly shortened to 105.7 +/- 88.5 ms at 6 months. Gross and microscopic structure of the irradiated optic nerve was well preserved in the ramipril-treated group. **CONCLUSION:** Ramipril can mitigate the radiation-induced optic nerve damage and preserve the functional integrity of the nerve. The results support early treatment with a high dose of ramipril after radiation.

Sabbah, H. N., R. C. Gupta, S. Rastogi, S. Mishra, Y. Mika and D. Burkhoff (2006). "Treating heart failure with cardiac contractility modulation electrical signals." *Curr Heart Fail Rep* 3(1): 21-4. **Full-text Not Available / [Click for Article Request Form](#)**

Major advances have been made over the past two decades in the pharmacologic treatment of chronic heart failure (HF). Angiotensin-converting enzyme inhibitors, beta-blockers, and aldosterone antagonists have had a substantial impact on reducing mortality and morbidity in patients with HF and low left ventricular ejection fraction. These treatments delayed the progression toward advanced intractable HF but did not arrest progressive worsening of the disease. Patients on optimal medical therapy continued to deteriorate, albeit at a much slower pace, ultimately requiring further intervention. This gave rise to a host of device-based therapies that emerged in recent years to address this unmet need. Device therapies such as cardiac resynchronization, the CorCap cardiac support device (Acorn Cardiovascular, Inc., St. Paul, MN), and the OPTIMIZER System (Impulse Dynamics USA, Inc., Orangeburg, NY) are a few examples. This review addresses the progress made to date in the development and implementation of cardiac contractility modulation (CCM) as a device-based therapy for the treatment of patients with advanced HF. Treatment of patients with HF using CCM electrical signals is at present an investigational form of therapy.

Santra, M., M. Katakowski, R. L. Zhang, Z. G. Zhang, H. Meng, F. Jiang and M. Chopp (2006). "Protection of adult mouse progenitor cells and human glioma cells by de novo decorin expression in an oxygen- and glucose-deprived cell culture model system." *J Cereb Blood Flow Metab* 26(10): 1311-22. **Full-text Not Available / [Click for Article Request Form](#)**

We employed an in vitro hypoxia cell culture model system and gene transfer technology to examine the effect of the decorin gene on cell survival against oxygen and glucose deprivation (OGD). Ectopic expression of decorin in subventricular zone (SVZ) cells from adult male mouse brain and human glioblastoma U-87 cells kept the cells viable against 24 h of OGD. Fewer than 1% of decorin-synthesizing cells were apoptotic after 12 h of OGD. In contrast, 100% of the control cells were apoptotic even after 4 h of OGD. De novo decorin synthesis in SVZ and U-

87 cells induced expression of p21, p27 and Ras, AKT (acutely transforming retrovirus AKT8 in rodent T-cell lymphoma), and phosphorylated AKT. Blocking of phosphoinositide 3-kinase (PI-3K), Ras, and the epidermal growth factor receptor with specific inhibitors had no effect on induction of Ras, p21, and p27 at the messenger RNA level in decorin-synthesizing SVZ and U-87 cells. PI-3K inhibitors significantly increased apoptosis in decorin-expressing cells. Our data indicate that induction of p21, p27, Ras, AKT, and phosphorylated AKT by decorin inhibits apoptosis and protects U-87 and SVZ cells against OGD. Therefore, our data suggest that decorin is a potent trophic factor that protects neuronal progenitor cells and glioma cells from OGD.

Sun, L., A. M. Hui, Q. Su, A. Vortmeyer, Y. Kotliarov, S. Pastorino, A. Passaniti, J. Menon, J. Walling, R. Bailey, M. Rosenblum, T. Mikkelsen and H. A. Fine (2006). "Neuronal and glioma-derived stem cell factor induces angiogenesis within the brain." Cancer Cell **9**(4): 287-300. **Full-text Not Available / [Click for Article Request Form](#)**

Stem cell factor (SCF) is overexpressed by neurons following brain injury as well as by glioma cells; however, its role in gliomagenesis remains unclear. Here, we demonstrate that SCF directly activates brain microvascular endothelial cells (ECs) in vitro and induces a potent angiogenic response in vivo. Primary human gliomas express SCF in a grade-dependent manner and induce normal neurons to express SCF in brain regions infiltrated by glioma cells, areas that colocalize with prominent angiogenesis. Downregulation of SCF inhibits tumor-mediated angiogenesis and glioma growth in vivo, whereas overexpression of SCF is associated with shorter survival in patients with malignant gliomas. Thus, the SCF/c-Kit pathway plays an important role in tumor- and normal host cell-induced angiogenesis within the brain.

Tunceli, K., K. Li and L. K. Williams (2006). "Long-term effects of obesity on employment and work limitations among U.S. Adults, 1986 to 1999." Obesity (Silver Spring) **14**(9): 1637-46. **Full-text Not Available / [Click for Article Request Form](#)**

OBJECTIVE: To determine the relationships between BMI and workforce participation and the presence of work limitations in a U.S. working-age population. **RESEARCH METHODS AND PROCEDURES:** We used data from the Panel Study of Income Dynamics, a nationwide prospective cohort, to estimate the effect of obesity in 1986 on employment and work limitations in 1999. Individuals were classified into the following weight categories: underweight (BMI < 18.5), normal weight (18.5 < or = BMI < 25), overweight (25 < or = BMI < 30), and obese (BMI > or = 30). Using multivariable probit models, we estimated the relationships between obesity and both employment and work disability. All analyses were stratified by sex. **RESULTS:** After adjusting for baseline sociodemographic characteristics, smoking status, exercise, and self-reported health, obesity was associated with reduced employment at follow-up [men: marginal effect (ME) -4.8 percentage points (pp); p < 0.05; women: ME -5.8 pp; p < 0.10]. Among employed women, being either overweight or obese was associated with an increase in self-reported work limitations when compared with normal-weight individuals (overweight: ME +3.9 pp; p < 0.01; obese: ME +12.6 pp; p < 0.01). Among men, the relationship between obesity and work limitations was not statistically significant. **DISCUSSION:** Obesity appears to result in future productivity losses through reduced workforce participation and increased work limitations. These findings have important implications in the U.S., which is currently experiencing a rise in the prevalence of obesity.

Vazquez, J. A. (2006). "The safety of anidulafungin." Expert Opin Drug Saf **5**(6): 751-8. **Full-text Not Available / [Click for Article Request Form](#)**

The echinocandins are a new class of antifungal that have shown promising results in treating a variety of fungal infections. Anidulafungin is the newest approved echinocandin and may have some advantages over existing antifungals. It has activity against a broad range of fungi. It is unique because it undergoes a process of slow chemical degradation rather than being metabolised. Studies evaluating the use of anidulafungin in combination with other commonly used drugs have not demonstrated any significant drug-drug interactions or adverse events. Thus far, anidulafungin appears to have an excellent safety profile with few adverse events. Based on early clinical experience, it appears that anidulafungin will be a valuable and safe asset in the management of serious and difficult-to-treat fungal infections.

Velanovich, V. (2006). "The lasso technique for laparoscopic distal pancreatectomy." Surg Endosc **20**(11): 1766-1771. **[PDF Full-Text](#)**

BACKGROUND: Laparoscopic distal pancreatectomy with or without splenectomy is becoming an acceptable alternative to open resection for selected pancreatic lesions. One of the difficulties with this approach is manipulating the pancreas with laparoscopic instruments to avoid unnecessary injury to the pancreas, and yet obtain adequate margins. The described technique accomplishes these goals. **METHODS:** Data from all patients who underwent laparoscopic distal pancreatectomy (always with splenectomy) were reviewed for age, gender, laparoscopic completion of the resection, postoperative complications, length of hospital stay, and pathology. The essential component of the technique is use of a Penrose drain around the neck or proximal body of the pancreas as a "lasso" for atraumatic manipulation. This technique is described in detail. **RESULTS:** A total of 11 patients have undergone laparoscopic distal pancreatectomy with splenectomy using the lasso technique. Two patients (18%) underwent conversion to an open laparotomy: the because of bleeding from the pancreatic parenchyma and the other due to local invasion of a pancreatic adenocarcinoma. The average operating time was 162 +/- 39 min, and the median length of hospital stay was 3 days. There were two (18%) pancreatic leaks, both of which were treated conservatively with resolution. Pathologic examination, found six cystic neoplasms, two neuroendocrine tumors, two masses of chronic pancreatitis, and one adenocarcinoma. **CONCLUSIONS:** The lasso technique simplifies intraoperative manipulation of the pancreas during laparoscopic distal pancreatectomy. It allows for safe manipulation of the pancreas and may expand the indications for the laparoscopic approach to pancreatic resection.

Williams, L. K., R. A. McPhee, D. R. Ownby, E. L. Peterson, M. James, E. M. Zoratti and C. C. Johnson (2006). "Gene-environment interactions with CD14 C-260T and their relationship to total serum IgE levels in adults." *J Allergy Clin Immunol* **118**(4): 851-7. [PDF Full-Text](#)

BACKGROUND: Both endotoxin exposure and a single nucleotide polymorphism in one of its receptors, CD14 C-260T, have been separately associated with total serum IgE levels. Furred pets might also influence IgE levels through their effects on endotoxin levels. However, how these factors interact to influence total IgE levels is not well known, especially in adults. **OBJECTIVE:** We sought to investigate the interactive relationship between endotoxin levels, pet exposure, and CD14 C-260T genotype on total serum IgE levels in adults. **METHODS:** Mothers enrolled in an ongoing cohort study were genotyped for the CD14 C-260T polymorphism. Exposure to pets was assessed by using questionnaires and dust allergen levels collected in the home. Endotoxin exposure was estimated by using dust collected from mothers' bedroom floors. The primary outcome measure was total serum IgE level. **RESULTS:** CD14 C-260T genotype was assessed in 517 (85.2%) of the 607 women enrolled in the study. The CD14 C-260T genotype was significantly associated with total IgE levels; however, this relationship appeared to be modified by the level of endotoxin exposure. Similar interactions between CD14 C-260T and pet exposure were not seen, regardless of the measure of pet exposure used. **CONCLUSIONS:** The CD14 C-260T genotype and endotoxin exposure together appear to influence total serum IgE levels in adults. The absence of a similar gene-environment interaction for pet exposure suggests separate mechanisms of action. **CLINICAL IMPLICATIONS:** A common polymorphism in the endotoxin receptor, CD14 C-260T, and dust endotoxin levels in the home might interact to influence total serum IgE levels into adulthood.

Zacharek, M. A., K. J. Fong and P. H. Hwang (2006). "Image-guided frontal trephination: a minimally invasive approach for hard-to-reach frontal sinus disease." *Otolaryngol Head Neck Surg* **135**(4): 518-22. [PDF Full-Text](#)

OBJECTIVES: Peripherally located frontal sinus pathology may be unreachable with standard endoscopic techniques. Patients with superiorly or laterally based lesions often undergo osteoplastic flap with or without obliteration. Image-guided frontal trephination (IGFT) can localize pathology and provide excellent exposure. We present 13 patients in whom this technique was applied. **STUDY DESIGN:** Medical records of 13 patients undergoing IGFT were retrospectively reviewed. **RESULTS:** The patients' mean age was 49.2 years, (range 14-79); follow-up time was 29.9 months (range 12-39). Indications for IGFT were superiorly or laterally based mucoceles (3), fibrous dysplasia or osteoma (3), type 4 frontal cells (3), and frontal recess stenosis or ossification (4). In five patients, IGFT was combined with endoscopic transethmoid frontal sinusotomy; eight patients were treated through a trephination approach, and three patients underwent trephination with unilateral frontal sinus obliteration. One patient required revision; all others remain symptom free. **CONCLUSIONS/SIGNIFICANCE:** IGFT offers an attractive alternative to osteoplastic flap.

Zhang, X., F. Jiang, S. N. Kalkanis, H. Yang, Z. Zhang, M. Katakowski, X. Hong, X. Zheng and M. Chopp (2006). "Combination of Surgical Resection and Photodynamic Therapy of 9L

Gliosarcoma in the Nude Rat." Photochem Photobiol. Epub Ahead of Print. **Full-text Not Available / [Click for Article Request Form](#)**

The objective of the present study was to investigate the combination treatment of 9L gliosarcoma brain tumor in the rat with surgical resection and photodynamic therapy (PDT). Nude rats with intracranial 7-day-old 9L gliomas were randomly subjected to no treatment, PDT alone (Photofrin(R): 2 mg/kg, optical: 80 J/cm²), surgical resection alone, or resection combined with 2 mg/kg Photofrin(R)-mediated PDT at an optical dose of 80J/cm². All animals were sacrificed 14 days after tumor implantation. Hematoxylin-and-eosin and immunohistochemical stainings were performed to assess the tumor volume, the expression of vascular endothelial growth factor (VEGF) in the brain adjacent to tumor (BAT), as well as the tumor cell apoptosis and proliferation. Our data show that both surgical resection alone and PDT alone significantly decreased tumor volume, but furthermore, surgical resection combined with PDT significantly reduced the tumor volume and reduced local tumor infiltration compared to either surgical resection or PDT alone treatment. PDT treatment with or without resection increased tumor apoptosis, but resection alone did not alter the tumor cell apoptosis, compared with non treatment control group. Both surgical resection alone and PDT alone induced a significant increase in VEGF expression in the BAT; however, intraoperative PDT did not further increase VEGF expression, compared with surgery alone or PDT alone. No significant differences were found in tumor cell proliferation, as indicated by Ki67 immunoreactivity, among the four groups. Our results suggest that PDT enhances the efficacy of surgical resection in the management of malignant gliomas without increasing VEGF expression in the BAT.

Zhuo, J. L., O. A. Carretero, H. Peng, X. C. Li, D. Regoli, W. Neugebauer and N. E. Rhaleb (2006). "Characterization of N-Acetyl-Seryl-Aspartyl-Lysyl-Proline (Ac-SDKP) Receptor Binding Sites Using [¹²⁵I]-Hpp-Aca-SDKP in Rat Cardiac Fibroblasts." Am J Physiol Heart Circ Physiol. Epub Ahead of Print. **[PDF Full-Text](#)**

We have shown that the tetrapeptide Ac-SDKP inhibited endothelin 1 (ET-1)-induced cell proliferation and collagen synthesis in cultured rat cardiac fibroblasts (CFs) and reduced left ventricle collagen deposition in rats with aldosterone-salt- and angiotensin II (Ang II)-induced hypertension. However, it is not known whether these effects are mediated by receptor binding sites specific for Ac-SDKP. We hypothesized that Ac-SDKP exerts anti-fibrotic effects by binding to specific receptor sites in cultured rat CFs, which mediate the inhibitory effects of Ac-SDKP on ET-1-stimulated collagen synthesis. Ac-SDKP binding sites in rat CFs and hearts were characterized using a specific radioligand, [¹²⁵I]-Hpp-Aca-SDKP, a biologically active analogue of Ac-SDKP. [¹²⁵I]-Hpp-Aca-SDKP bound to rat CFs and fractionated membranes with similar affinities and specificity and in a concentration- and time-dependent fashion. Scatchard plot analysis revealed a single class of high-affinity Hpp-Aca-SDKP binding sites (B_{max}: 1704 +/- 198 fmol/mg protein; K_d: 3.3 +/- 0.6 nM). [¹²⁵I]-Hpp-Aca-SDKP binding in CFs was displaced by unlabeled native peptide Ac-SDKP (K_i: 0.69 +/- 0.15 nM) and the analogue Hpp-Aca-SDKP (K_i: 10.4 +/- 0.2 nM), but not the unrelated peptide Ang II or ET-1 (10 microM). In vitro, both Ac-SDKP and Hpp-Aca-SDKP inhibited ET-1-stimulated collagen synthesis in CFs in a dose-dependent fashion, reaching a maximal effect at 1 nM (control: 7.5 +/- 0.4; ET-1: 19.9 +/- 1.2; ET-1+/-SDKP: 7.7 +/- 0.4; ET-1+Hpp-Aca-SDKP: 9.7 +/- 0.1 mg/mg protein; p <0.001). Ac-SDKP also significantly attenuated ET-1-induced increases in intracellular calcium and mitogen-activated protein kinase ERK 1/2 phosphorylation in CFs. In the rat heart, in vitro autoradiography revealed specific [¹²⁵I]-Hpp-Aca-SDKP binding throughout the myocardium, primarily interstitial in location. We believe these results demonstrate for the first time that Hpp-Aca-SDKP is a functional ligand specific for Ac-SDKP receptor binding sites, and that both Ac-SDKP and Hpp-Aca-SDKP exert anti-fibrotic effects by binding to Ac-SDKP receptors in rat CFs. Key words: Collagen synthesis, Endothelin 1, Heart, Intracellular calcium, ERK 1/2 phosphorylation.

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