DEPARTMENT OF SURGERY

Research Meeting
February 6, 2012

GI, TUMOR & ENDOCRINE DIVISION

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Martin McCarter, MD
Paul Montero, MD
Nathan Pearlman, MD
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Christopher Raeburn, MD
Thomas Robinson, MD
Kevin B. Rothchild, MD
Jonathan Schoen, MD
Gordon K. Lindberg, MD, PhD
Michael J. Schurr, MD

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Research – Breast

Finlayson, Tina

Sentinel Node biopsy for T1-2 breast cancer, with bone marrow aspiration. Early study that confirmed SNBx as an appropriate staging procedure for early breast cancer. Bone marrow aspiration results not conclusive. Currently in long-term patient follow up.

Randomized study of axillary node dissection vs. observation for patients with a positive SNBx. Did not accrue well nationally, so closed early. Results of those who did participate published 18 months ago, suggest that axillary node dissection is not required in all patients with a positive sentinel node biopsy. Still in long-term follow up.

Sentinel node biopsy after neoadjuvant chemotherapy for patients with positive axillary LN at presentation. All patients after neoadjuvant chemotherapy had sentinel biopsy followed by axillary dissection. Question asked is if a SNBx done after chemotherapy provides sufficient axillary staging information to avoid an axillary dissection if the SN is negative. Enrollment completed about 15 months ago and currently in long-term follow up.
Erythropoiesis in Burn Patients – Prospective Randomized clinical trial using IV iron and exogenous erythropoietin to decrease blood transfusions in burn patients. Completing IND for IV iron through FDA. Preliminary data shows Hepcidin over expression, iron sequestration and aberrant red blood cell synthesis in burn patients. Moving toward Hepcidin protocol.
Research – Burn

Schurr, Michael

Stratatech, Inc. SBIR Phase II from NIGMS (R44 GM065025) Expression of Angiogenic Growth Factors in Keratinocytes - Long-lived keratinocyte that recapitulates normal human skin with full barrier function. The initial focus has been to develop a universal donor skin for use in burn and traumatic wounds. We have completed an IND, our first phase I trial and are proceeding with our second phase IIb trial funded by the DOD. The trial is multi-site and the first UCH patient will be enrolled this week. We also have been able to modify the keratinocyte to express interesting proteins. We have completed an IND for our first construct (expression of antimicrobial defensins) and have been awarded funding by the NIH to proceed with Phase I clinical trial in diabetic foot ulcers. I have no conflict of interest with this entire body of work.

Cutaneous Wounds - Our team includes veterinary sciences, microbiology, chemical engineering, and surgery. We have developed antimicrobial polyelectrolyte multi-layers that can be stamped onto biologic dressings. The hallmark example is Biobrane, which has widespread application in pediatric burns. We have been able to transfer low dose silver to the biobrane and dramatically reduce the incidence of infection in 2 different animal models. This body of research reached the limits of development under the university setting and has spun off Imbed Corporation of which I am a founding member. We are currently looking at several antimicrobials, have focused on Biobrane and Integra for the use in burn patients, and are attempting to duplicate our success with implantable biologics for abdominal wall reconstruction.
Research – Endocrine

McIntyre, Robert C.

A Phase III, Randomized, Multicenter, Double-Blind, Double Dummy, Parallel-Group, Comparative Study to Determine the Efficacy, Safety, and Tolerability of Ceftazidime Avibactam plus Metronidazole versus Meropenem in the Treatment of Complicated Intra-Abdominal Infections in Hospitalized Adults.

A Novel Pulse Oximetry Parameter in a Hospital Setting: This study consists of measuring parameters related to respiration in subjects in a hospital setting on the general care floor, by means of non-invasive pulse oximetry monitoring devices pulse oximetry sensors, and other closely related non-invasive devices without altering clinical care of the subject. The primary objective of this study is to assess equivalency, performance and accuracy of Respiration Rate V1.0 algorithm that extracts respiratory information from a pulse oximetry system.
SAGES electrosurgery project: With Dr. Matthew Fox (PGY-3) interrogation of electrosurgical ("bovie") generators to document and analyze the settings and power modes used (cut versus coag, 30 versus 20 watts, etc). This project was accepted for poster presentation at SAGES 2012 and we intend to complete a manuscript. Not surprisingly, surgeons most commonly use Coag mode (>90%) rather than Cut mode, and 30 watts is the most common power setting. We feel this emphasizes that electrosurgical technology is underused.

SERF surgical curriculum deficiencies project: Part of Surgical Education Research Fellowship with the Association of Surgical Education, needs assessment involving electronic surveys sent to 4 residency programs which has identified surgical topics that residents feel are not taught well in the curriculum, textbook, journals, or on-the-job training. An associated abstract was not accepted for the APDS. The next step is to create educational modules on these topics (mesh, hemostatic agents, and surgical staplers).

APDS preliminary resident project: Along with Claire Travis, Dr. Nehler, and Dr. Powell, data collected regarding the career planning and outcomes of our preliminary residents over the last 7 years. This abstract was accepted for oral presentation at the APDS this March and an accompanying paper will be written. We found that ~80% of preliminary residents go on to match in a categorical position.

AEF ergonomics project: An AEF grant was obtained to carry out a project involving FLS simulators, laparoscopic suturing, and ergonomics. The COMIRB application is nearly complete and we will begin obtaining necessary equipment. Collaboration with Dr. Appleton of the GYN department and on simulator training and an associated curriculum. The study is anticipated to be underway this spring, with aims for preliminary results by the fall. Subsequent grant money based on this project will be sought either this fall or next fall from SAGES.
Research – Endocrine

Raeburn, Christopher

Notch signaling in thyroid cancer. Examining the role of Notch1 in human thyroid cancer cell lines. Abstract accepted to American Association of Endocrine Surgeons meeting May 2012. Manuscript in progress. Will use this data to submit for extramural funding in Spring 2012.

Proteomic analysis of differential protein expression in adrenal tumorigenesis. Continue to maintain and add to my adrenal tumor bank. Limitation has been in gaining enough malignant tumors to do meaningful comparison.

Collaboration with Endocrine Division in patient recruitment for and maintenance of UCH Thyroid cancer tissue bank and clinical database. One manuscript is in submission.


A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Intravenous Ulimorelin Administered Post-Operatively to Accelerate Recovery of Gastrointestinal Motility in Subjects Who Have Undergone Partial Bowel Resection (TZP-101-CL-P008), 2011-12, PI for Denver VAMC


A placebo controlled trial of L-Tryptophan supplementation on post-operative delirium in older adults undergoing major elective operations.
Specific aim: To determine if post-operative supplementation with L-tryptophan reduce the incidence and/or duration of post-operative delirium.

Evaluation of a geriatric specialty pre-operative risk assessment strategy for prediction of post-operative complications, institutionalization and cost.
Specific aim: To determine the diagnostic accuracy of geriatric specialty pre-operative evaluation in predicting post-operative adverse events.

Defining clinical complication profiles of novel monopolar radiofrequency energy coupling pathways in the operating room.
Specific aim: To determine if antenna coupling of radiofrequency energy occurs and whether this phenomena can create thermal injuries in common operating room scenarios.
Research – Endocrine/Bariatric

**Schoen, Jonathan**

Mechanisms of Improvement of Type 2 Diabetes Mellitus Following Bariatric Surgery. COMIRB and CTRC approval pending. Funding: Dept of Surgery AEF $40,000 seed grant.

Sleeve Gastrectomy as a Primary Weight Loss Procedure. COMIRB # 06-0371 (study in progress)

Bustamante A, Dinarello C. The Effects of Obesity and Bariatric Surgery - Mediated Weight Loss on Expressible and Inducible Cytokine Production Including the Use of Proteomics. C011IRB #06- 1138 (study in progress).

Consultant, Cornier M- P.I. Neuronal Responses to Effective Weight Loss Maintenance Strategies. NIH R01: #R01DK089095, $521,372 (study in progress).

Coinvestigator. Nonalcoholic Fatty Liver among Obese Patients Undergoing Bariatric Surgery: The Effect of Weight Loss on Liver Histopathologic Features and Examination of Potential Biochemical and Genetic Factors in Disease Pathogenesis and Progression/Regression. COMIRB # 10-0585 (in progress).
Focus on metastatic disease. Investigating transfusion related immunomodulation and funded by the American Cancer Society to examine the effect of blood transfusion on pancreas cancer progression.

Examine the role of blood transfusion on pancreas cancer progression and examine the role of transfusion in terms of its effect on the metastatic tumor microenvironment. In the course of this research, we have discovered previously undescribed sex dimorphism between male and female mice with pancreas cancer and have further demonstrated that these genotypic differences result in tumor microenvironment differences as demonstrated by changes in tumor associated neutrophil: macrophage ratios and in the activation states of tumor associated macrophages. We are now exploring these findings in an immunocompetent colon cancer and melanoma model.

The affect of metastatic cancer on coagulation profiles in immunocompetent mice. This work has demonstrated clinically useful perturbations in the coagulation system, which is dose dependent and reproducible.

Examining the hepatic microenvironment and the effect of hepatic resection and ablation on tumor growth and progression.
Study the significance of RET proto-oncogene in desmoplastic melanoma primary tumors.

Investigate the effects of neoadjuvant systemic treatment on surgical outcomes in stage III melanoma patients. The objective of this trials is to examine if the combination of bio-chemotherapy and regional lymphadenectomy can be delivered in a safe and effective manner. The study has reviewed >150 charts.
Research – Surgical Oncology

**McCarter, Martin**

**Co-operative group**
Institutional PI for ACOSOG GI cancer clinical trials for GIST and Pancreas
Institutional PI for NSABP GI surgery trials (Colon and Rectal Cancer)

**Industry**
PI for ongoing studies investigating post-operative ileus (Helsinn)
PI for Coloprint early stage colon cancer recurrence risk assessment (Agendia)
PI for Phase II 5 year Imatinib therapy for high risk GIST (Novartis)

**Outcomes research**
NCDB and NISQP databases focused on surgical cancer patients (particularly esophageal cancer, colon cancer, and general DVT risk) Database review projects with surgical residents and faculty regarding melanoma patients with regard to large melanoma sentinel lymph node experience (in preparation for size of sentinel node metastasis, outcomes for negative SLNBx patients, Outcomes for ear melanoma).
Maintain IRB approved surgery specific databases tracking our experience and outcomes with Hyperthermic Intraperitoneal Chemotherapy (HIPEC) and extra-hepatic Radiofrequency Ablation of abdominal and pelvic tumors (published and in preparation).

**Basic Science**
Basic and translational research investigating the immunosuppressive effects of melanoma on normal immune cells.

**Other ongoing collaborations:**
Tumor banking for gastrointestinal tumors and melanoma (William Robinson).
Recruitment for the GI tumor xenograft program (Ekhardt et al.).
Collaborate with Sarah Cheng on post-op DVT prevention program for high risk surgery patients.
Collaborative efforts investigating the immunology of HIV with researchers in the department of Infectious Diseases (Cara Wilson, Liz Connick, Amie Meditz).