Do Adipose Derived Stem Cells Improve Tensile Strength and Wound Remodeling in Hiatal Hernia Repair?

Principal Investigator: Dana A. Telem, MD

Amount Requested: $30,000.00

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Co-investigators:
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Gabriel Pagnotti  MS, PhD candidate
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Aurora D. Pryor, MD
Mark A. Talamini, MD
Summary

Hiatal hernia is a common disorder characterized by a widening of the diaphragm which allows for protrusion of the stomach and/or other abdominal viscera into the thorax. Although hiatal hernia is present in up to 60% of the population older than 50 years of age, only approximately 10% of patients are symptomatic. Repair of hiatal hernia is recommended when symptoms become clinically relevant, are refractory to medical therapy or interfere with activity of daily living. Such symptoms include gastroesophageal reflux, dysphagia, weight loss, gastrointestinal bleeding secondary to ulceration, chest pain, shortness of breath and other respiratory complications. Repair of these hernias can be quite challenging. In larger defects re-approximation of the crura may be under tension or the general tissue of poor quality. As such, the recurrence rate following repair is reported anywhere from 10 to 59 percent. To improve recurrence rates, consideration is made to reinforcement of the crural repair with synthetic or biologic mesh. If mesh is placed, current preference favors biologic mesh secondary to concerns for intraluminal esophageal erosion with permanent mesh. Prospective randomized trials demonstrate that while biologic mesh improves short term recurrence rates, from 19 to 9 percent, the long term efficacy remains uncertain leading some to question the utility of mesh placement all together. Additionally, mesh also has the propensity to elicit a host response which may diminish its efficacy to augment crural repair. Improvement in recurrence rates following hiatal hernia repair is a high priority, as evidenced in a recent survey of SAGES members presented in 2013. Recurrent operations can be technically challenging and patients at increased risk for complication and poor long-term functional outcomes. To date, a novel effective solution for this nearly 10% recurrence rate has yet to be described. Recent research involving autologous stem cells in tissue remodeling; however, has the potential to become a solution. Use of autologous stem cells for wound healing and remodeling is an emerging field with promising results to date. Adipose tissue provides an excellent source of stem cells and is an abundant tissue which is easily accessed. The purpose of this study is to determine whether the addition of autologous adipose derived mesenchymal stem cells (AD-MSC) to a biologic matrix will augment hiatal remodeling resulting in increased tensile strength of the repair as demonstrated in a porcine model. The premise of this study is that the mesh will serve as a biologic scaffold to mechanically and biologically support AD-MSC as healing occurs. Using platelet rich plasma (PRP) to stimulate differentiation, we anticipate that the AD-MSC will differentiate into either myocytes with potential to improve diaphragm regeneration or fibroblasts which will increase collagen synthesis and deposition. The ultimate result being increased tensile strength and improved tissue remodeling.
Background, Supporting Concepts and Data

Wound healing is a continuous process which involves three overlapping stages: inflammation, proliferation and remodeling. The main objective of this cycle is to close the wound and produce collagen. The inflammatory phase serves as a recruitment period for cells that secrete several important cytokines and growth factors that will result in collagen production by fibroblasts. Initially fibroblast cells produce type III collagen which appears at day 4 and is random and immature in its fiber organization. Collagen remodeling, namely transition from collagen type III to type I, then occurs which increases the tensile strength of the wound. This process starts at approximately week 3 and can continue from months to years. Over time, cross-linking and shortening of the collagen fibers promotes formation of a tight, strong scar. While peak tensile strength of the wound is achieved at 60-90 days, regeneration does not fully restore tissue to prior strength levels which likely accounts for hernia formation or recurrence. As such, development of factors that improve healing and prevent hernia formation is a burgeoning and evolving field which has traditionally centered on utilization of mesh, both synthetic and biologic. While mesh augments tensile wound strength and promotes wound remodeling, it is not without its pitfalls. In the most exaggerated form, the host response to mesh is to treat it as a foreign body creating persistent inflammation, fibrotic encapsulation, and degradation of biomaterials. This in part may explain hiatal hernia recurrence following placement of an onlay biologic or synthetic mesh. Although the mesh provides initial tensile strength, changes in properties and host reaction to the foreign material may diminish its effect over time. As such, rethinking the way we use mesh in the purview of emerging biologic technologies could result in a novel way to decrease hernia recurrence. In addition to providing tensile strength on its own, biologic mesh can be used as a mechanical and biologic scaffold to support these novel technologies during wound healing.

Autologous adult stem cells represent precursor cells with the ability to differentiate into diverse specialized cell types. Stem cell therapy has the potential to dramatically change the treatment of multiple human disease processes. Current application of stem cell therapies include malignancy, degenerative neural diseases, spinal cord injury, cardiac muscle regeneration and repair of muscle and bone damage. Assessing the properties and potential of these cells implicate their potential role in wound healing. Investigation into this topic is currently underway. Biologic technologies including platelet rich plasma (PRP), and adipose and bone marrow derived mesenchymal stem cells already demonstrate advantages in wound healing and tissue remodeling. Recently, two novel papers evaluated the impact of adult mesenchymal stem cells on tensile strength and healing of abdominal wall hernias. The first of these papers assessed the effect of bone marrow derived stromal cells (BM-MSC) and PRP on fascial healing. This study demonstrated that in a rodent model, the addition of BM-MSC with PRP resulted in a fourfold increase in tensile wound strength at 4 weeks postoperatively. Vascularization and collagen abundance were also significantly increased at the study end points of 4 and 8 weeks. The
second study builds off of kinetics data demonstrating the ability of stem cells to adhere to an acellular porcine matrix and investigated the addition of adipose derived stem cells to biologic mesh for ventral hernia repair in a rodent model. This study demonstrated that biologic mesh that had been pre-seeded with stem cells exhibited increased cellular proliferation and enhanced vascularity at the musculofascial /graft interface. This finding suggests addition of stem cells to a biologic matrix may in fact enhance incorporation of the biologic matrix into the anterior abdominal wall. While ventral hernia and diaphragmatic hernia differ, the same principles of wound healing apply. To the authors knowledge, only one study to date has investigated BM-MSC use in hiatal hernia repair and was performed in a rodent model with non-autologous cells. In this study, BM-MSC was added to a collagen impregnated vicryl knitted mesh. Results demonstrated thicker autologous tissue with increased capillary incorporation in rodents with BM-MSC seeded mesh as compared to mesh alone. No gross advantages were demonstrated however, on histologic examination. Major limitations of this study included functional analysis was not performed and BM-MSC were not stimulated with factors promoting differentiation.

As aforementioned, PRP therapy alone also augments tissue regeneration as demonstrated in burn and orthopedic literature where it is used to promote healing. This independent effect is likely secondary to promotion of fibroblast proliferation. PRP refers to the portion of the plasma fraction of autologous blood having platelet concentrations above baseline and is comprised of a multitude of growth factors essential during the proliferative phase of wound healing. Growth factors include: vascular endothelial growth factor, platelet derived growth factor, epidermal growth factor, basic fibroblast growth factor, and transforming growth factor. While PRP alone is effective, studies demonstrate increased tensile strength and wound remodeling when used in conjunction with autologous stem cells. PRP stimulates stem cell differentiation into fibroblasts making it an ideal agent to achieve an end goal of increased collagen synthesis and deposition.

Study Purpose
The purpose of this study is to determine whether the addition of autologous adipose derived mesenchymal stem cells (AD-MSC) and PRP to an acellular biologic matrix improves the tensile strength of the hiatal closure as well as augments crural healing, graft incorporation and tissue remodeling.

Time-line and Future Directions
This study represents the first phase in assessing application of autologous biologic technologies to the wound healing processes. The anticipated length of time it will take to complete this project is 12 months. Assuming results are favorable, further investigation into optimal scaffold and stem cell lineage will ensue. The ultimate purpose of this translational research is reduction in both short and long-term hiatal hernia recurrence. Other hernia types will also be studied. As both PRP and AD-MSC are FDA approved technologies, human clinical trials, particularly with PRP alone, are likely achievable within a 5 year time frame.
Hypotheses and Specific aims

**Hypothesis #1:** The addition of AD-MSC in conjunction with PRP to a porcine acellular matrix will augment crural healing during hiatal hernia repair. This will result in significantly improved mean tensile strength, increased collagen deposition, increased vascularity and increased incorporation at the mesh/hiatal interface of the crural repair as compared to standard repair with or without biologic mesh.

**Specific aims:**

1) Determine if the addition of AD-MSC + PRP to a porcine acellular matrix augments tissue regeneration and wound healing as histologically assessed by vascularization, collagen deposition, cell incorporation, differentiation and quantification as compared to controls in a swine model at 8 weeks

2) Determine if the addition of AD-MSC + PRP to a porcine acellular matrix increases the mean tensile strength of the crural repair as assessed by biomechanical analysis compared to controls in a swine model at 8 weeks

**Hypothesis #2:** The addition of PRP alone to a porcine acellular matrix will augment crural healing during hiatal hernia repair. This will result in significantly improved mean tensile strength, increased collagen deposition, increased vascularity and increased incorporation at the mesh/hiatal interface of the crural repair as compared to standard repair with or without biologic mesh but inferior to repair with PRP + AD-MSC.

**Specific aims:**

1) Determine if the addition of PRP alone to a porcine acellular matrix augments tissue regeneration and wound healing as histologically assessed by vascularization, collagen deposition, cell incorporation, differentiation and quantification as compared to controls at 8 weeks

2) Determine if the addition of PRP alone to a porcine acellular matrix increases the tensile strength of the hiatal repair as assessed by biomechanical analysis compared to controls at 8 weeks
Methods

Study population: The swine model for hiatal hernia repair is well defined and has been utilized in multiple research models. For this study, healthy Yorkshire male pigs weighing 30 to 40 kg will be utilized and obtained from an institutionally approved vendor.

Study Groups and statistical justification:
1) Hiatus repair alone (n=6)
2) Hiatus repair + acellular porcine matrix (n=6)
3) Hiatus repair + acellular porcine matrix + PRP (n=6)
4) Hiatus repair + acellular porcine matrix + PRP + AD-MSC (n=6)

Study Power: An a priori power analysis was performed to calculate sample size and was based on number samples needed to assess tensile strength. Based on available literature which demonstrates 4 times increased mean tensile wound strength in rodents following ventral hernia repair with stem cell seeded mesh, a large effect size was anticipated. Using an anticipated effect size, Cohen’s d of 0.6, probability level of 0.05 and desired statistical power level of 0.8, the minimal samples necessary per group was 26. As a minimum of 6 samples are generated per porcine hiatus, each group will contain 6 animals. An additional animal has been placed in each group in the event an animal dies prematurely or an issue with specimen retrieval is encountered.

Pre-operative protocol: Animal procedures and both pre-operative/post-operative care will take place at the Stony Brook Animal Research Facility in Stony Brook, NY. All animals will be cared for by both members of the investigational team and veterinary staff. The animals will be transitioned to a clear liquid diet 24 hours prior to the procedure and fasted for 12 hours prior to the operation. Pre-anesthesia will consist of Telazol 4.4mg/kg intravenous (IV); atropine sulfate 0.4mg/kg IV, and xyazine 2.2mg/kg IV. General anesthesia will be achieved using 1% to 3% isoflurane on a semi closed inhalation circuit after general endotracheal intubation. Cefazolin 1gm IV will be administered immediately prior to the procedure.

Procedure: The Stony Brook animal facility is equipped with 4 fully functional large animal operating rooms. Following the induction of general anesthesia, the abdomen will be prepped and draped in sterile fashion using a betadine prep. Five trocars will be placed within the abdomen under direct vision. The hiatus will be identified, circumferentially dissected and a retroesophageal window created to adequately expose the diaphragmatic crura. The crura will then be closed with interrupted 0-Ethibond sutures in a caudal to cranial fashion leaving an approximately 1.5cm hiatal opening and ensuring the esophagus is not kinked against the closure. Once this has been completed, Cook Biodesign® mesh (Cook, Bloomington, In) with or without PRP/AD-MSC will be placed and secured with 2-0 silk sutures– specific details pertaining to this protocol will follow. Upon completion of this the trocars will be removed and skin sutured closed. Sterile dressings will be applied. Cook Biodesign® was selected as it is an acellular matrix which is available at our institution.
Post-operative care: Post-operatively animals will be immediately fed a clear liquid diet for 36 hours and then transitioned to soft solids. Cephalexin 250mg BID will be administered for 24 hours following the procedure. Animal monitoring will be jointly performed by the investigational team and the veterinary staff. All animals will receive a fentanyl patch (25mcg) for analgesia. Animals will be followed for lethargy, poor feeding, decreased activity, vomiting, fever and inability to tolerate po. If an animal is determined to be ill, early sacrifice may be recommended by the veterinary staff. At 8 weeks animals will be sedated and euthanized. At the completion of the animal study, necropsy will be performed. At necropsy the hiatus will be examined. In addition, the peritoneum and mediastinum will also be examined for evidence of abscess, fluid collection, hemorrhage or other abnormality. Eight weeks was selected as 60-days represents the time frame corresponding to peak tensile strength.

PRP and Stem Cell Isolation
Preparation and storage of PRP as well as stem cell isolation, maintenance and storage will be performed in collaboration with the Stony Brook Biobank. Established in 2004, the purpose of this facility is to cryogenically store tissue and cell lines as well as facilitate translational research. This facility is fully equipped with the supplies and expertise necessary for PRP preparation as well as stem cell isolation and growth.

- **Platelet rich plasma (PRP) Preparation and Mesh Application**
  For swine receiving PRP (n=12) a blood draw will be performed 2-3 days prior to operation and processed according to a protocol described by Maekawa et al. Animals will be anesthetized by subcutaneous injection of Telazol (4.4mg/kg) and xylazine (2.2 mg/kg). Blood (5mL) will then be drawn from the ear or jugular vein with a 14-gauge needle into a 10mL syringe containing 3.2% sodium citrate. Whole blood will then be centrifuged at 200 × g for 10 minutes at room temperature. The upper fraction (plasma layer) will be aspirated and centrifuged at 700 x g for 10 minutes at room temperature. The platelet poor upper fraction will then be aspirated, placed in a sterile tube and stored at -20 degrees Celsius. One mL of this platelet poor layer will be kept with the platelet pellet which will be resuspended using 5% (5ul) DMSO. This preparation will be placed in a cryovial and slowly frozen to –80ºC where it will be stored until use. Prior to application, the platelet poor plasma that had been stored at -20 degrees will be thawed to 37 degrees and 1mL placed into a centrifuge tube. The platelet pellet that had been stored at -80 degrees Celsius will then be thawed until the ice pellet dislodges and can be placed into the reserved 1mL of warmed plasma. This mixture will then be centrifuged at 700 x g for 10 minutes at 4 degrees Celsius. The plasma portion will be aspirated and discarded and the platelet pellet resuspended in 5mL. In animals receiving PRP alone, the mesh will be steriley saturated in this medium immediately prior to hiatal application.
  The mesh will then be placed as previously described.

- **Adipose derived Stem Cell Isolation and Labelling**
  Adipose tissue was selected as it is abundant, easy to harvest and an excellent source of stem cells with the capacity to differentiate into distinct tissue lineages including those of interest, myocyte and fibroblast. Following induction of anesthesia as described above, a 2-3cm incision will be made under sterile conditions and a 2x2 cm piece of
caudal adipose tissue harvested as described within the literature. This procedure will occur 2 weeks prior to hialtal operation. The incision will be sutured closed with interrupted 2-0 nylon suture and postoperative analgesia administered as previously described. Tissue processing will occur by one of two methods: mechanical versus manual.

**Mechanical Isolation:** Mechanical isolation of cells will be the preferred method of stem cell extraction. Adipose derived stem cells will be isolated using the iCellator ® (Tissue Genesis, Inc., Honolulu) Adipase ® protocols. The iCellator® is a commercially available FDA approved device which takes adipose tissue and in a completely automated and reproducible process, isolates cells in approximately one hour. An agreement for purchase of this device has been made by our institution with anticipated arrival for use 12/2013.

**Manual Isolation:** In the event there are difficulties with mechanical extraction, manual isolation will be performed. Obtained adipose tissue will be carefully dissected, minced and placed for 90 min at 37°C on a shaker with Liberase Blendzyme 3 (Roche) at a concentration of 4 units per gram of fat tissue in PBS. The resulting digested tissue will then be centrifuged for 10 mins at 450g and the supernatant will be placed for 2 h at 37°C in 15 ml Hank’s balanced salt solution (HBSS) containing 0.2 % (w/v) collagenase type 1 and 20 ll penicillin/streptomycin for enzymatic digestion. Enzyme neutralization will be performed by adding growth medium (GM) containing Modified Eagle’s Medium (a-MEM; Invitrogen, Paisley, UK), 20 % (v/v) fetal bovine serum (FBS), 2 mM glutamine (Cellgro), and 1 % (v/v) penicillin/streptomycin (Gibco, Grand Island, NY, USA). The samples will be centrifuged at 1,200g for 5 min and the resultant stromal cell pellet will be resuspended in GM. Subsequently, the solution will be passed through a 70-lm filter to remove remaining undissociated tissue, centrifuged at 1,000g for 5 min and the pellet resuspended in GM.

**Cell Culture and Growth:** Extracted AD-MSCs will be propagated and plated in a tissue culture flask at 37°C with 5 % CO2 and maintained at sub-confluent levels with passage by trypsin/EDTA (Invitrogen, UK). After confluence of ASCs (passage 0), cells will be seeded at a density of 3,000 cells/cm² (passage 1). At 60% confluence AD-MSCs will be transfected with a lentiviral vector carrying enhanced green fluorescent protein (GFP) as previously described in the literature.

- **AD-MSC + PRP Mesh Seeding**
  Previous kinetics studies assessing fixation of stem cells to an acellular matrix demonstrate 92% cell adherence at 30-minutes following mesh seeding and 96% at 120 minutes. An acellular porcine matrix will be obtained. At the start of the operation the mesh will be steriley saturated with 1x10⁶ cells in 5mL of growth medium mixed with 5mL of PRP for a period of at minimum 30 minutes (total of 10mL). Following completion of this time period the mesh will be introduced into the abdomen and secured into place at the hiatus as previously described.
Outcomes analysis: At 8-weeks, the distal esophagus with hiatus will be harvested en bloc for analysis. The integrity of the hernia repair will be assessed by gross examination. At minimum, 6 cross sectional biopsy specimens oriented across the repair (including matrix and hiatus) will be excised for biomechanical, histologic and immunohistochemical analysis. Tissue specimens for histologic analysis will be placed in 10% formalin for fixation and then embedded in paraffin. Specimens will be cut into serial sections 4mm thick and examined for tissue architecture and cellular infiltration. Additional sections will be prepared for immunofluorescent studies using primary antibodies against GFP and vascular marker PECAM-1. The interface zone (zone where acellular matrix abuts hiatus) will also be analyzed separately to assess incorporation as defined by degree of vascularity and cellular proliferation. All specimens will be prepared, sectioned and stained by an experienced research histology technician and evaluated by a board certified pathologist.

a) Biomechanical analysis - Standard tensiometric analysis will be performed to determine average tensile strength using the Instron 3343. This axial/torsion testing system has a load capacity of 1 kN and maximum pressure of 90 PSI. The hiatal tissue from each animal will be sectioned longitudinally across the healed defect. The tensiometer will then be utilized to record force and tissue deformation. Biomechanical properties to be analyzed and recorded include: maximum stress tolerated by tissue (tensile strength), viscoelasticity, energy needed to completely rupture the tissue and stress required to strain/deform the tissue. Univariate analysis will be utilized to compare groups.

b) Histologic assessment of specimens will be compared by univariate analysis where appropriate:

1) Vascularization - Degree of vascularization will be assessed histologically by averaging the total number of blood vessels present on five non-overlapping fields of tissue from the hiatal closure. Additionally, staining with PECAM1 will be performed and angiogenesis quantitatively compared.

2) Collagen deposition – A comparative analysis of collagen organization, abundance and myocyte degeneration based on hemotoxylin and eosin staining will be performed. Based on existing literature, specimens will be scored using a semi-quantitative scale and compared.17

3) AD-MSC incorporation, differentiation and migration - Immunofluorescent detection of GFP labeled AD-MSC to assess viability and cellular differentiation using specific markers will be performed. Based on studies by Fuchs et al. GFP labeled stem cells are detectable in vivo up to 12 months following transfection.32 Additionally, binary assessment for migration of AD-MSC into esophagus or other local tissue by immunofluorescent quantification will also be evaluated.

4) Histologic examination of mesh hiatal interface zone – The degree of inflammation will be quantitatively compared based on presence and number of inflammatory cells. A comparative analysis of degree of incorporation will also be performed.
Statement of Funds

We are currently engaged in discussions for possible funding of extended phases of this project, however no funds are currently available or guaranteed. If this grant is funded by SAGES and additional funds are obtained, they will be used for unique aspects of the project not delineated in this application. Mesh for this project will be donated by Cook biomedical. In addition, the Stony Brook Biobank has also agreed to process the PRP (n=12) and 6 stem cell lines at no cost for this initial project.

Local/Institution Review Boards

Animal care committee approval has been submitted for this project and is pending final approval.

Available Resources and Committed Personnel

1) Stony Brook Biobank
   a. PRP preparation and storage
   b. Stem cell isolation, growth, GFP transfection and storage – mechanical/ manual
      i. iCellator® – purchase contracted with estimated date of arrival 12/2013
   c. Personnel: Angelique Corthals, PhD

2) Biomechanical resources
   a. Instron 3343 – available at present, tensile testing and analysis
   b. Personnel: Gabriel Pagnotti MS biomedical engineering, PhD candidate

3) Pathology support and specimen analysis
   a. Stony Brook Department of pathology – Research histology core laboratory
   b. Specimen processing, paraffin embedding sectioning for H&E, trichromes, immunohistochemical staining and analysis
   c. Personnel: Kenneth Shroyer, MD,PhD, Mallory Korman BS

4) Stony Brook animal facilities
   a. Pre- and post-operative animal maintenance
   b. Fully equipped large animal ORs
   c. Personnel (in addition to study investigators): Thomas Zimmerman, DVM, MPVM, DACLAM

5) Additional grant collaborators (data acquisition, analysis and research support)
   a. Maria Altieri, MS, MD
   b. Aurora D. Pryor, MD
   c. Mark A. Talamini, MD
SAGES Participation (PI): Dana A. Telem

Awards: SAGES Researcher in Training (2012)

Committees: Research and Career development (2012-present), Flexible endoscopy (2012-present)

Submitted abstracts/invited presentations/education:

Invited faulty, Sages Mini-Medical school boot camp (2012-2013)

Invited faculty, SAGES advanced laparoscopic course for residents – October 2012

Invited faculty, SAGES basic laparoscopic course for residents – August 2013


Podium Presentation, NOTES transanal rectosigmoid resection with total mesorectal excision in a large human cadaver series. Scientific Session of the 15th World Congress of Endoscopic Surgery, March 7th-10th, 2012, San Diego, CA. Podium presentation

Podium Presentation, Laparoscopic subtotal colectomy for medically refractory ulcerative colitis: The time has come.” Scientific Session of the 12th World Congress of Endoscopic Surgery, April 22nd-25th, 2009, Phoenix, AZ.


References

1 Goyal Raj K, "Chapter 286. Diseases of the Esophagus". Harrison's Principles of Internal Medicine, 17e.


## SAGES RESEARCH GRANT APPLICATION
### BUDGET SHEET

Detailed budget for 12 month period for 4/1/2013 to 4/1/2014

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<td>Principal Investigator</td>
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**Salary funds should be used for staff required to execute the study, but should not be used for salary support for the primary investigator. If salary support exceeds 50% of the project budget, then specific justification is required.**

**Funds requests for travel for the presentation of a SAGES funded study should be limited to $1,000.**

### CONSULTANT COSTS
- Pathology Consultation:
- Gross prep, processing, immunohistochemistry $15.00/sample x 156 samples: $2,340.00

### EQUIPMENT

#### List all Items & Total Equipment Cost

### SUPPLIES

#### List all Items & Total Supplies Cost

### TRAVEL**

#### ANIMAL COSTS
- Sheep $250.00/animal x 24 animals: $6,000.00
- Per diem cost $12.50/day x 24 animals x 65 days: $19,500.00
- Surgical suite, anesthesia and basic support charge $90.00 x 24 animals: $2,160.00

### CONSORTIUM/CONTRACTUAL COSTS

### OTHER EXPENSES

#### List all Items & Total Cost

### TOTAL DIRECT COSTS
- $30,000.00
BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2. Follow this format for each person. DO NOT EXCEED FOUR PAGES.

NAME
Dana A Telem, MD

POSITION TITLE
Assistant Professor of Surgery

eRA COMMONS USER NAME (credential, e.g., agency login)

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)

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<tr>
<td>University of Pennsylvania, Philadelphia PA</td>
<td>BA</td>
<td>9/95-6/99</td>
<td>Biology with minor in Chemistry and English</td>
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<tr>
<td>Jefferson Medical College, Philadelphia PA</td>
<td>MD</td>
<td>7/01-6/05</td>
<td>General Surgery</td>
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<tr>
<td>The Mount Sinai Hospital, New York NY</td>
<td>Resident</td>
<td>7/05-6/11</td>
<td>Advanced laparoscopic and bariatric surgery</td>
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<tr>
<td>Massachusetts General Hospital, Boston MA</td>
<td>Fellow</td>
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A. Personal Statement

My research interests lie in clinical outcomes and translation research. I am interested in developing and implementing innovative approaches to answer ongoing clinical questions; in particular as they relate to the operative management of hiatal hernia. Biogenic technologies are at the forefront of current practice in many surgical fields and represent the likely future for hernia repair. I feel very strongly that this technology will improve the high recurrence rate witnessed in the operative management of this disease. I have experience in both basic and clinical research and have assembled a research team with the expertise in pathology, biomedical engineering and stem cell technology necessary to perform and complete high-quality research in this area. Through this collaboration novel approaches to hiatal hernia will be developed, incorporating the best of translational medicine into our clinical practice.

B. Positions and Honors

POSITIONS

7/2008-6/2009 Assistant medical student clerkship director and teaching resident
7/2010-6/2011 Administrative chief resident, The Mount Sinai Medical Center, New York, NY
7/2011-7/2012 Instructor in Surgery, Harvard Medical School, Boston, MA
8/2012-present Assistant Professor of Surgery, Stony Brook University, Stony Brook, NY
Associate Director Metabolic and Weight Loss Center
Associate Fellowship Director – Minimally invasive Surgery
Clerkship Director for Third Year Medical Students - SBU

PROFESSIONAL AWARDS AND HONORS

2003-2004 Society of Academic Emergency Medicine Medical Student Research Grant
2005 Francis Torrens Stewart MD Clinical Surgery Prize
2010 The Medical Student Teaching Award
2011 David A. Dreiling Award for Excellence in Scholarly Activities
2011 Center of Expertise Medical Education Research Grant
2012 SAGES Researcher in Training Award
2012-present Editorial board, Gastroenterology and Hepatology Research
2012-present SAGES flexible endoscopy committee
2012-present SAGES research and development committee
2012-present SSAT program subcommittee (video)
2013-present ACS committee on video based education
2013-present Stony Brook University Department of Surgery Research Grant
2013-present SSAT Diversity Task force
Selected National Invited Presentations
Video session II: Breakfast at the movies. Digestive Disease Week, May 17th–May 21st, 2013, Orlando, FL. Session moderator.


NOTES transanal rectosigmoid resection with total mesorectal excision in a large human cadaver series. Scientific Session of the 15th World Congress of Endoscopic Surgery, March 7th-10th, 2012, San Diego, CA. Podium presentation

Prospective study for selective management of patients with acute biliary pancreatitis: Interim Results. Digestive Disease Week, May 7th – May 10th, 2011, Chicago, IL. Plenary podium presentation.

Can virtual reality simulators predict future surgeons? American College of Surgeons Clinical Congress, October 11th-14th, 2009, Chicago, IL. Podium presentation

Risk factors for anastomotic leak following gastrointestinal surgery: A case-control study. American College of Surgeons Clinical Congress, October 11th-14th, 2009, Chicago, IL. Podium presentation

Laparoscopic subtotal colectomy for medically refractory ulcerative colitis: The time has come.” Scientific Session of the 12th World Congress of Endoscopic Surgery, April 22nd-25th, 2009, Phoenix, AZ. Podium presentation

C. Selected Peer-Reviewed Publications


Palaniappa N, Telem DA, Ranasinghe, Divino CM. Incidence of Iatrogenic Ureteral Injury Following Laparoscopic Colectomy. Arch Surg


D. Research Support

Active
N/A (PI: Telem) 01/01/13- Present. Stony Brook Medicine Department of Surgery Seed Grant
“Sleeve Gastrectomy for Morbid Obesity and Gastroesophageal Reflux Disease (GERD): Determining a Correlation” Role: Principle Investigator, Funding: $15,000.00

Inactive
N/A (PI: Gee) 10/20/11-10/01/12 Center of Expertise Medical Education Research Grant
“Can virtual reality simulators achieve endoscopic proficiency in novice surgical residents” Role: Co-investigator, Funding: $3,000.00
A. Personal Statement

As director of the new BioBank at Stony Brook Medicine, I am happy to collaborate with Dr. Dana Telem on biological hernia repair using adipose tissue stem cells. If validated, this new technique could revolutionize hernia repair and lower significantly the rate of patient re-admission. It would become a paradigm shift with very high clinical impact.

In this proposal, the BioBank will put all of its service at the disposition of Dr. Telem, including stem-cell cultures both mechanically (using the iCellator®) and manually. We will also extract and prepare PRPs and voucher tissues extracted at all major steps of the protocols, both for the sake of reproducibility of results and further investigation.

Maintaining a high quality collection of specimens, which serve as a basis for study and are retained as a reference has become one of the most pressing issues of the medical community and bio-repositories at large. This is in this light that the new BioBank at Stony Brook Medicine has been created, in collaboration between the department of Pathology and the Cancer Center. Dr. Marchenko’s study will be of great value to the facilities and the research community at large.

The BioBank Collection now house over 15,000 aliquots in an array of liquid nitrogen freezers (-150 degree Celsius), which represents over 3000 individual cases. Each sample is archived in a barcoded and human readable vial generated by the facilities relational database, Freezerworks Unlimited™.

B. Positions and Honors

Employment
2012 to present  Assistant Professor, Dept. of Pathology, SUNY, Stony Brook University Medical School, NY
2009 to 2012  Assistant Professor, Dept. of Sciences, CUNY, John Jay College of Criminal Justice, NY
2009  Consultant on HIV viral load. Médecins Sans Frontières (Doctors without Borders); Campaign for Access to Essential Medicines; Geneva, Switzerland – Johannesburg, South Africa
2008 to 2009  Adjunct Professor, Anthropology Dept., Stony Brook University, NY.
2006 to 2008  Lecturer in Biomedical and Forensic studies, Faculty of Life Sciences, University of Manchester (UK)
April 2003-2006  Curatorial Associate (Director), American Museum of Natural History (AMNH), Ambrose Monell Cryo-Collection, New York, NY
2000-April 2003  Collection Manager, American Museum of Natural History (AMNH), Ambrose Monell Cryo-Collection, New York, NY
1999  Research Assistant, University of Oxford, England, Dept of Zoology, Goldstein Laboratory
Scientific and professional experience
2006 to 2008: Scientific expert and consultant for the DNA team led by Dr. Yehia Gad at the National Research Centre, Cairo and the Supreme Council of Antiquities.
2007 to present: Scientific expert and consultant for the building of a dedicated ancient DNA laboratory on the new campus facilities of the American University in Cairo.
2007: Scientific expert and consultant for the Hatshepsut Project, in collaboration with the National Research Centre in Cairo, the Supreme Council of Antiquities, the American University in Cairo and Discovery Channel.
2006-7: Scientific consultant and cast member of the IMAX documentary 'Mummies: Secrets of the Pharaohs' (Opens in the US May 25)
2005: Consultant for the 3D replica and analysis of the remains of CopperMan, a 550 AD Chilean mummy on view at the American Museum of Natural History and at the Museo de Arte Precolombino, Santiago de Chile
2004 to present: referee for Naturwissenschaften, Journal of Egyptian Archaeology
2003 to present: Scientific consultant in methods of DNA preservation for: Canadian Museum of Nature, Ottawa; Molecular Laboratory of the Institute von Humboldt, Cali, Colombia; Museum of High Mountain Archaeology, Argentina; Natural History Museum, London; Smithsonian National Museum of Natural History, Genetic Resources Board; South African National Biodiversity Institute DNA Banking, Cape Town; Walter Reed Military Hospital, Washington DC; Wildlife Biological Resource Center, Pretoria
2004: Sat on the first board meeting of the Barcode of Life Project, Washington, May
2004: Organisation of the Society for Preservation of Natural History Collection (SPNHC) and International Society for Biological and Environmental Repositories (ISBER) annual meeting at AMNH, May 2004
2003: Collaborator on the NSF FIBR grant Wolbachia project, AMNH-TIGR-UC Riverside-UC Santa Cruz-STRI-MBL
2001-05: Mentor to students from NSF funded programs Ascend, Inside View, UMEB, REU

Honors and Awards
2007 European Research Council grant (grant accepted for funding Friday July 13\textsuperscript{th}, 2007) Wrath of the gods: Diseases, Landscapes and Climate in Ancient Egypt (€ 2,000,000; £1,500,000)
2005 NSF BRC grant (Status: Meritorious) Development of best practice for archiving microbial communities. ($300,000)
2004 The Explorers Club Elected Resident Fellow
2004 NSF Biological Research Collections Grant (Fund if Possible) Protecting unique genetic resources at the American Museum of Natural History 1. ($290,000)
2004 Black Rock Forest Consortium Grant Black Rock Forest Consortium, Cornwall, New York ($3,900)
2001 Employee Recognition Award American Museum of Natural History, New York, NY

C. Selected Peer-reviewed Publications

Peer-Reviewed Journals relevant to this proposal


**Edited Books relevant to this proposal**


**Chapters in Edited Books relevant to this proposal**


**Other Peer-Reviewed Journals**


**Other Chapters in Edited Books**


**D. Research Support**

**Ongoing Support**

2013  Equipment Grant ($21,000, granted on April 15, 2013)  LILaC, Long Island League against Cancer, Plainview, NY

2011  Equipment Grant ($17,000, granted on May 13th, 2011)  Program for Research Initiatives for Science Majors (PRISM), John Jay College of Criminal Justice
**BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2. Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

<table>
<thead>
<tr>
<th>NAME</th>
<th>Gabriel M Pagnotti</th>
</tr>
</thead>
<tbody>
<tr>
<td>POSITION TITLE</td>
<td>Graduate Research Assistant</td>
</tr>
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| eRA COMMONS USER NAME (credential, e.g., agency login) |  |

**EDUCATION/TRAINING** (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)

<table>
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<th>INSTITUTION AND LOCATION</th>
<th>DEGREE (if applicable)</th>
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<th>FIELD OF STUDY</th>
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<tr>
<td>University of Central Florida</td>
<td>BS</td>
<td>12/02</td>
<td>Electrical Engineering</td>
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<tr>
<td>University of Central Florida</td>
<td>Post-Baccalaureate</td>
<td>08/03-05/05</td>
<td>Molecular &amp; Microbiology</td>
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<tr>
<td>University of South Florida</td>
<td>MS</td>
<td>05/08</td>
<td>Biomedical Engineering</td>
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<tr>
<td>University of South Florida</td>
<td>Certificate</td>
<td>05/08</td>
<td>Health Sciences</td>
</tr>
<tr>
<td>Stony Brook University</td>
<td>Ph.D.</td>
<td>09/14 (expected)</td>
<td>Biomedical Engineering</td>
</tr>
</tbody>
</table>

**NOTE:** The Biographical Sketch may not exceed four pages. Follow the formats and instructions below.

**A. Personal Statement**

The goal of the investigation undertaken by this team is aimed at utilizing a primitive autologous stem cell population in combination with a biological scaffold and a series of growth factors in order to recapitulate the tissue integrity of the lower esophageal sphincter. This regenerative therapy is expected to improve outcomes resulting from dysfunctional esophageal reflux by recapitulating lost functionality and tissue strength. My role in this study stems from my multidisciplinary education, prior industry experience, and vested interests in regenerative medicine. I began my undergraduate education (1998) studying Electrical Engineering and, subsequently, began post-baccalaureate classes (2003-2005) in Molecular and Microbiology at the University of Central Florida in order to expand my knowledge of the medical sciences. At that time, I began my professional career in systems engineering within the intelligent traffic systems industry, which allowed me to gain a practical edge on high-speed fiber optic, wireless, and copper-based communication system design, installation, and maintenance, while fostering responsibilities in team management, problem-solving, and project estimation for multi-million dollar contracts for various Departments of Transportation and other state entities. While gaining industry experience and in pursuit of an opportunity to gain practical experience in the medical sciences, I volunteered my evening and weekend time in a molecular parasitology lab where the driving focus was understanding the primary trafficking mechanisms in the malarial parasite, Plasmodium falciparum, providing me with practical lab bench-work experience. Since having completed my Master’s degree at the University of South Florida in Biomedical Engineering (2008), I have shifted my focus to a full-time graduate career in Biomedical Engineering and am currently a fifth-year doctoral student at Stony Brook University in the Rubin Musculoskeletal Lab. Currently, my personal research interests are focused on the utility of exercise as a means to curb musculoskeletal loses in the face of cancer. Additionally, I have been appointed to oversee training and maintenance of the interdepartmental micro-CT imaging systems. Considering my involvement in an array of ongoing translational research in collaboration with multiple departments at Stony Brook University and other medical research institutions and with my varied skillset, I am poised to contribute to the development and advancement of this project.
B. Positions and Honors

**Intelligent Traffic Systems Field Engineer**
*MasTec North America: ITS Division - Orlando, FL* 2004 - 2008
*Gord and Associates, Inc. – Tampa, FL* 2008 - 2009

**Molecular Parasitology Lab Assistant**
*University of Central Florida Biomolecular Research Annex* 2005 - 2006
*Chakrabarti Lab for Infectious Diseases*

**Graduate Research Assistant**
*SUNY Stony Brook: (SBU) Biomedical Engineering Department* 2009 - Ongoing
*Rubin Lab for Musculoskeletal Research*

**Mentorship**
**Instructor: Women in Science and Engineering (WSE)** 2011 - 2012
Developed and instructed an 8-week course for freshman students receiving academic honors who are awarded involvement in the WSE Honor Program wherein they were exposed to practical and fundamental science and engineering laboratory techniques specifically in the Biomedical Engineering Department.

**Senior Design Group: Biomedical Engineering Department** 2011 - 2012
Mentored a Biomedical Engineering Senior Design group with regards to programming, designing, and testing a prototypical device conceived and developed to administer low magnitude mechanical signals focused on a localized cutaneous region with use on future chronic wound healing applications.

**Undergraduate Research Assistant Training** 2012 - 2013
Mentored undergraduate biomedical engineering students in the areas of microscopy, histological analyses, cell culture, and tissue preparation. These skills will be used to conduct both collaborative and individual studies on co-localization of cancer and bone-resorbing cells within the bone marrow niche.

**Community Outreach**
**Judge: New York State Science and Engineering Fair (NYSSEF)** Winter 2013
Judged the annual competition among New York State high school students for qualification at the *Intel International Science and Engineering Fair* 2013; Flushing Meadows, Queens, NY.

**Teacher: Early Engineering Education - The Jewish Academy** Spring 2013
Participated in and assisted in the development of a pilot outreach program for NIH grant submission intended to create a curriculum for elementary school students (grades 1-6) in order to foster early exposure to engineering-based principles as well as provide practical, hands-on applications; Northport, Long Island, NY.

**Academic Honors**
**Presidential Poster Award Recipient** 2011
*The Annual American Society for Bone and Mineral Research Conference*

**Endocrinology Fellowship Forum** 2011
*The Fifth Annual EFF/ADA Fellows Forum on Metabolic Bone Diseases*

**College of Engineering Dean’s List** 2001-2002
University of Central Florida
National Memberships and Affiliations

Biomedical Engineering Society (BMES) 2009-2011
American Society of Bone and Mineral Research (ASBMR) 2013-2014
International Bone and Mineral Society (IBMS) 2013-2014

C. Selected Peer-reviewed Publications

Peer-Reviewed Journals

D. Research Support

Low Magnitude Mechanical Signals Mitigate Osteopenia without Compromising Longevity in an Aged Murine Model of Spontaneous Granulosa Cell Ovarian Cancer (Completed)
Rubin (PI)
Determine the safety and efficacy in mechanical signaling in affecting the longevity and offsetting bone loss in a spontaneous model of ovarian cancer.

Immunomodulatory Role of Mechanical Signals in Regulating the Expansion of Hematopoietic Precursors in a Murine Model of Multiple Myeloma.
Rubin (PI)
Project aimed at investigating the immunomodulatory role of mechanical signals on the BM niche during the onset of a primary bone cancer.

Improved Bone Quality in Diet-Induced Obesity by Low Intensity Vibrations is Paralleled by Suppressed Bone Marrow Adiposity and Reduced Pro-Inflammatory State of Mesenchymal Stem Cells.
Rubin (PI)
Biomedical engineering project designed to explore how low intensity vibrations influence the bone marrow environment and, more particularly, the skeletal-immune system interplay during obesity.

Running Decreases Marrow Adipose Tissue in Chow and High Fat Fed Mice
Styner (PI)
Stony Brook BME collaboration with UNC Chapel Hill Department of Medicine seeks to quantify the effects of exercise on the integrity of the skeletal system following a high-fat diet regimen.

Mechanical Signaling to Promote the Osseo-integration of an Implant into Sheep
Hart (PI)
Collaboration with the Ohio State University Biomedical Engineering Department to study the osseo-integrative abilities of mechanical loading to facilitate the integration of a novel implant into the limbs of sheep.

Low Intensity Vibrations for Pain Management and as a Means to Improve Postural Stability
Rubin/Durkin/Beneveniste (Co-PI's)
Multi-departmental clinical collaboration facilitated by the Pain Management Center (SBU) and the Biomedical Engineering Department whereby patients are subjected to a mechanical loading regimen to mitigate indices of pain and improve muscle quality in order to increase postural stability.
Image Processing Software Development to Quantify Tumor Infiltrating and Tumor Associated Lymphocytes in Human Serous Carcinoma
Shroyer (PI)
Collaboration with the Department of Pathology in the College of Medicine (SBU) to develop an automated ImageJ – based program used to distinguish and quantify particular immunohistochemical lymphocyte staining patterns in patient samples of serous carcinoma.
BIOGRAPHICAL SKETCH

NAME
Shroyer, Kenneth Reed

POSITION TITLE
Marvin Kuschner Professor and Chairman

Department of Pathology
Stony Brook University Medical Center

eRA COMMONS USER NAME
SHROYER.KEN

EDUCATION/TRAINING

<table>
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<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
<th>YEAR(s)</th>
<th>FIELD OF STUDY</th>
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<td>Colorado College, Colorado Springs, CO</td>
<td>B.A.</td>
<td>1978</td>
<td>Biology</td>
</tr>
<tr>
<td>Univ. of CO Graduate School, Denver, CO</td>
<td>Ph.D.</td>
<td>1983</td>
<td>Experimental Pathology</td>
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<tr>
<td>Univ. of CO School of Medicine, Denver, CO</td>
<td>M.D.</td>
<td>1987</td>
<td>Medicine</td>
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A. Personal Statement

Dr. Shroyer completed his graduate training in Experimental Pathology under the supervision of Dr. Paul K. Nakane, the inventor of the immunoperoxidase method. Dr. Shroyer is Board Certified in Anatomic and Clinical Pathology (1991), with subspecialty certification in Cytopathology (1995). He is an experienced surgical pathologist and cytopathologist and has also maintained continuous federally-funded grant support since 1993. He invented the method of DNP labeling of nucleic acid probes, was a pioneer in the development of methods for in situ hybridization of mRNAs in the early 1980s, and was the first to report the molecular analysis of x-chromosome inactivation in archival tissues as a marker of clonality. He participated in the early validation of tyramide-based signal amplification technology for in situ hybridization and high sensitivity immunohistochemistry. He has also been engaged in the development of novel approaches for antibody labeling using nanoparticles for both in vivo imaging and for immunohistochemical applications in collaboration with scientists in biomedical engineering for over six years. In addition to his roles as Chair of the Department of Pathology, staff surgical pathologist and cytopathologist, Dr. Shroyer is the Director of the Pathology Core Histology Laboratory at Stony Brook Medicine.

B. Positions and Honors

Positions and Employment:

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<th>Year(s)</th>
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<tr>
<td>1987-1988</td>
<td>Intern in Anatomic and Clinical Pathology, University of Colorado Health Sciences Center</td>
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<tr>
<td>1988-1991</td>
<td>Resident in Anatomic and Clinical Pathology, Univ. of Colorado Health Sciences Center</td>
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<tr>
<td>1991</td>
<td>Chief Resident in Pathology, University of Colorado Health Sciences Center</td>
</tr>
<tr>
<td>1991-1997</td>
<td>Assistant Professor of Pathology, University of Colorado Health Sciences Center</td>
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<td>1997-2001</td>
<td>Associate Professor with tenure, University of Colorado Health Sciences Center</td>
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<tr>
<td>2002-2007</td>
<td>Professor with tenure, University of Colorado Health Sciences Center</td>
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<tr>
<td>1991-2007</td>
<td>Graduate Faculty, University of Colorado Health Sciences Center, Graduate School</td>
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<tr>
<td>1993-2007</td>
<td>Director of Cytopathology, University of Colorado Health Sciences Center</td>
</tr>
<tr>
<td>2000-2007</td>
<td>Director of Surgical Pathology, University of Colorado Health Sciences Center</td>
</tr>
<tr>
<td>2007-</td>
<td>Marvin Kuschner Professor and Chair, Department of Pathology, Stony Brook University Medical Center, State University of New York</td>
</tr>
<tr>
<td>2007-</td>
<td>Graduate Faculty, Molecular and Cellular Biology Program, Molecular Pharmacology, and Genetics Programs, Stony Brook University Medical Center</td>
</tr>
<tr>
<td>2013-</td>
<td>Vice Chair, Board of Directors, Clinical Practice Management Plan, Stony Brook Medicine</td>
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</table>
Other Experience and Professional Memberships:
2004- Editorial Board, Human Pathology
2006- Associate Editor, Journal of Clinical Virology
2001- National Cancer Institute Study Section member, including IMAT, Applied Emerging Technologies for Cancer Research, Alliance of Glycobiologists for Detection of Cancer and Cancer Risk, SPOREs in Breast, Cervical, Endometrial, Ovarian, Skin Cancers, Lymphoma, Genitourinary, and Gastrointestinal Cancers and In Vivo Cellular and Molecular Imaging Centers (ICMICs), Indo-US Collaborative Program on Low-Cost Medical Devices, Cancer Target Discovery and Development (CTDD) Network, The Chernobyl Tissue Bank-Coordinating Center (Chair), AIDS and Cancer Specimen Resource (ACSR) (Chair), Cancer Diagnostics and Treatments (CDT)
1991- United States and Canadian Academy of Pathology (Member of the Scientific Advisory Board)
1991- American Association for Cancer Research
1993- American Society of Cytopathology
2002- American Society for Investigative Pathology
2011-2015 Member External Advisory Board, National Institutes of Health, National Center for Research Resources, University of Hawaii

Honors (selected):
2009-2013 Best Doctors in America
2009 Recognition for authorship of one of Human Pathology’s top 10 cited articles
1991 Robert H. Fennell, Jr., M.D. Award, Department of Pathology, University of Colorado HSC
1985-1987 Edgar and Marion Adler Scholar Award (only medical student to receive this award in two consecutive years), University of Colorado HSC
1987 Joseph and Regina Glaser Research Award, University of Colorado HSC

Invention (selected):
DNP-labeling of Nucleic Acid Probes (This invention was the first use of non-radioactive tags to detect nucleic acid probes that did not involve the use of radiochemicals).
Inventor
June, 1982

Regulation of B7-H4 Expression by miR-34 and its Clinical Utility
Stony Brook University Research Foundation Reference Number: R-8128
Co-Inventor with Jingfang Ju
Disclosure Date: 9/11/2008

C. Selected Peer-reviewed Publications (from 141 peer-reviewed publications)


D. Research Support

**Active**

Department of Veterans Affairs Merit Review Grant (Zucker) 10/01/09-09/30/13

Department of Veterans Affairs

Reversibility of Epithelial Mesenchymal Transition in Prostate Cancer.
The goal of this project is to identify mechanisms that enable reversal of EMT pathways in prostate cancer.
Kenneth R. Shroyer, Co-I

Overlap: None

1R33CA140084. (Robinson, Shroyer: Subcontract PI) 09/08/10-08/31/13

NIH

Specific Detection of Cervical Cancers Using Cytometry-Based Molecular Diagnostics.
The goal of this project is to develop a cytometry based method to screen for cervical cancer in cytology specimens.
Pre-clinical Evaluation of Carbon Nanostructure-Based High-Performance Contrast Agent for Magnetic Resonance Imaging
The goal of this project is to develop graphene nanoparticles for enhanced MRI imaging.
Kenneth R. Shroyer, Clinical PI

Completed

Tumor-targeting single-wall carbon nanotubes for microwave-based imaging and hyperthermia treatment of breast cancer: A small animal study.
Kenneth R. Shroyer, Consultant

Multifunctional Carbon Nanostructure-Based Platforms for Breast Cancer Theragnostics.
Kenneth R. Shroyer, Co-I

Identifying Biomarkers for Pre-malignant and Invasive Cervical Cancer.
Kenneth R. Shroyer, PI

Evaluation of a Newly Designed Device for Breast Cancer Screening.
Kenneth R. Shroyer, Co-I

R33 phased innovation and application award p16 and HPV in low-grade cervical cytologic specimens.
Kenneth R. Shroyer, PI

Multifunctional Carbon Nanostructure-Based Platforms for Breast Cancer Theragnostics.
Kenneth R. Shroyer, Co-I
NAME
Aurora Dawn Pryor

POSITION TITLE
Professor of Surgery
Vice Chair for Clinical Affairs

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)

<table>
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<th>FIELD OF STUDY</th>
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<td>Duke University, Durham NC</td>
<td>BS</td>
<td>05/1991</td>
<td>Biomedical and Electrical Engineering</td>
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<tr>
<td>Duke University, Durham NC</td>
<td>MD</td>
<td>05/1995</td>
<td>Molecular Biology</td>
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<tr>
<td>Duke University, Durham NC</td>
<td></td>
<td>1995 - 2002</td>
<td>General Surgery Resident</td>
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<tr>
<td>Duke University, Durham NC</td>
<td></td>
<td>1997-1999</td>
<td>Postdoctoral Fellow in Biochemistry and Experimental Surgery</td>
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<tr>
<td>Duke University, Durham NC</td>
<td></td>
<td>07/2003</td>
<td>Clinical Endosurgery Fellow</td>
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A. Personal Statement
I lead many multidisciplinary research efforts to study the optimal management and outcomes of surgical disease. I am particularly interested in upper gastrointestinal and bariatric surgical issues. As PI of many previous studies, I have experience in both basic and clinical projects. I am comfortable with the IACUC and IRB process and patient follow-up expectations. I have trained 15 previous fellows, and have mentored many residents and junior faculty. I am very interested in optimizing the management of hiatal hernia, and feel strongly that we can improve on the high recurrence rate witnessed in the surgical management of this disease. By collaborating with Dr. Telem, we can develop novel approaches to hiatal hernia repair, incorporating the best of translational medicine into our practice.

B. Positions and Honors

Work Experience

**Director, Bariatric and Metabolic Weight Loss Center.** Stony Brook University Medical Center 2011 - present

**Vice Chairman (Clinical Affairs).** Department of Surgery. Stony Brook University Medical Center 2011 - present

**Division Chief, General Surgery, Trauma, Critical Care and Burns.** Stony Brook University Medical Center 2011 - present

**Professor, General Surgery.** Laparoscopic and Bariatric Surgery, Stony Brook University Medical Center 2011 - present

**Associate Professor, General Surgery.** Laparoscopic and Bariatric Surgery, Duke University Medical Center 2009 - 2011

**Division Chief, General Surgery, Durham Regional Hospital** 2009 - 2011

**Director, Duke Minimally Invasive Surgery at Durham Regional Hospital** 2009 - 2011

**Director, Duke Bariatric and Minimally Invasive Surgery Fellowship at Durham Regional Hospital** 2006 - 2011
Program Director/Principal Investigator (Last, First, Middle): Pryor, Aurora Dawn

Assistant Professor, General Surgery. Laparoscopic and Bariatric Surgery, Duke University Medical Center 2003 - 2009

Professional Awards and Honors

American Board of Surgery Associate Examiner 2008, 2011
American Federation for Clinical Research Trainee Investigator Award for Excellence in Scientific Research 1994
ASMBS Program Subcommittee Chair 2009 - present
ASMBS Program Committee 2006 - present
ASMBS Emerging Tech Committee 2006 - present
ASMBS Emerging Tech Committee, Co-Chair 2011 - present
Association for Academic Surgery Medical Student Research Award 1995
Blue Cross Blue Shield Bariatric Centers of Distinction Advisory Board 2011 - present
Editorial Board: Bariatric Times 2010 - present
Editorial Board: Surgical Endoscopy 2010 - present
SAGES Board of Governors 2009 - present
SAGES Membership Committee Chair 2013 – present
SAGES Resident Education Committee Member 2007 - present
SAGES Research and Career Development Chair 2008 - 2013
Weck Closure Systems Award for Excellence in Basic Science, First Place 1999

C. Selected Peer-reviewed Publications

Most relevant:
Yoo, JS, Pryor AD. Abdominal access techniques used in laparoscopic surgery. UpToDate. 2011-2012.


Additional Recent Publications:


D. Research Support

**Ongoing Research Support:**


ASMBS, 2010 $50,000, Early Intervention in Patients with Predicted Poor Long-Term Outcome Following Laparoscopic Roux-en-Y Gastric Bypass: A Prospective Randomized Study. *Principal Investigator*

**Completed Research Support:**

Covidien Pryor PI 9/2009-6/2010
Gastric Pouch Creation with Duet Staple Line Reinforcement. This was a prospective study of gastric pouch creation using a novel preloaded stapler with reinforcement. Role: *Principal Investigator*

Trocar Site Hernias Following Laparoscopic Roux-en-Y Gastric Bypass. A retrospective multicenter study to assess the incidence and predictors of hernia following gastric bypass. Role: *Multicenter PI*

Use of Standardized Patients in Resident Education. Funding supported a standardized patient interaction for residents to teach difficult skills and assess physician-patient interaction. Role: *Co-PI*

Simulator versus Box-Training for Surgical Skills Acquisition. A prospective randomized study of surgical skills acquisition in surgical residents. Role: *Responsible Co-Principal Investigator*

Valleylab Pryor PI 9-12/2003
Mesenteric Division with Ligasure. An animal model investigation of ideal mesenteric division techniques for gastric bypass. Role: *Principal Investigator*

NIH NRSA Pryor PI 1/1998-7/1999
A yeast two-hybrid study of interactions with BRCA-2. Role: *Trainee Investigator.*

Four Schools Physician Scientist Training Program 1993
Full tuition support for 2 years of medical school
**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2. Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

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<th>POSITION TITLE</th>
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<tbody>
<tr>
<td>Mark A. Talamini, M.D.</td>
<td>Professor of Surgery</td>
</tr>
<tr>
<td>eRA COMMONS USER NAME</td>
<td>Chairman, UCSD Department of Surgery</td>
</tr>
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</table>

**EDUCATION/TRAINING** *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

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<td>Johns Hopkins University</td>
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<td>1978</td>
<td>Natural Sciences</td>
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<td>Johns Hopkins University</td>
<td>MD</td>
<td>1981</td>
<td>Medicine</td>
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**A. Positions and Honors.**

**Positions and Employment**

1981 – 1987 Fellow, The Johns Hopkins University School of Medicine
1987 – 1988 Instructor, The Johns Hopkins University School of Medicine
1988 – 1995 Assistant Professor, Department of Surgery, The Johns Hopkins University School of Medicine
1988 – 2005 Assistant Director, Nutrition Support Team, The Johns Hopkins Hospital
1992 – 2005 Director, Minimally Invasive Surgery, Johns Hopkins Hospital, School of Medicine
1995 – 2002 Associate Professor, Department of Surgery, The Johns Hopkins University School of Medicine
2002 – 2005 Professor, Department of Surgery, The Johns Hopkins University School of Medicine
2005 – present Professor and Chairman, Department of Surgery, University of California, San Diego

**Other Experience and Professional Memberships**

1999 – present FDA Advisory Panel Consultant
2001 – 2004 Chairman, Technology Committee, Society of American Gastrointestinal Endoscopic Surgeons
2003 – present Chairman, Finance Committee, Society of American Gastrointestinal Endoscopic Surgeons
2003 – present Treasurer, Society of American Gastrointestinal Endoscopic Surgeons
2003 – present Publication Committee, Society of American Gastrointestinal Endoscopic Surgeons
2004 – present American College of Surgeons Ad Hoc Committee on Surgical Skills Centers
2006 – present Chairman, Southern California District #4 Committee on Applicants of the ACS for 2007
2008 – 2009 President, Society of American Gastrointestinal Endoscopic Surgeons

**Awards**

1980 MAP-RDIF Fellowship-Internship in Bangladesh
1995 RW Hart Prize for Excellence in Developing Concepts for Telemedicine Systems
2002 Alpha Omega Alpha Honor Medical Society

**B. Selected peer-reviewed publications (in chronological order).**

**Publications Selected from 105 Peer-Reviewed Publications**


Chang DC, Talamini MA. A review for clinical outcomes research: hypothesis generation, data strategy, and hypothesis-driven statistical analysis. Surg Endosc. 2011 Feb 27.

C. Research Support

Mapping Vascular Proteome for Organ Targeting in Vivo
(7RO1HL074063-06) August 2009-December 2009
Sponsor: NIH/NHLBI
$582,249

Targeting Vessels in Tumors (Principal Investigator)
(7R01CA104898-05) September 2009-August 2010
Sponsor: NIH/NCI
$3,346,734

Nanotechnology Platform for Targeting Solid Tumors (Principal Investigator)
(7R01CA119378-05) September 2009-June 2010
Sponsor: NIH/NCI
$985,717
Principal Investigator/Program Director (Last, First, Middle): Talamini, Mark A.
Technology to Map Endothelial Targets in Human Renal Tumors (Principal Investigator)
(7R33CA118602-04)
September 2009-May 2010
Sponsor: NIH/NCI
$364,123