

STATEMENT OF FUNDS

There are no pending external funds for this project. Needed funds in excess of the \$29,880 in this grant application will be sought internally through the Department of Surgery at our institution.

SUMMARY

Type 2 Diabetes Mellitus (T2DM) is a common co-morbid condition associated with morbid obesity, occurring in approximately 23% of morbidly obese patients.¹ Remission of T2DM following Roux-en-Y Gastric Bypass (RYGB) is now clearly established in the literature, although the mechanism for this occurrence is poorly understood. Proposed mechanisms for the improvement in insulin resistance and abnormal glycemic control include the bypass of a putative insulin resistance signal in the duodenum and proximal small intestine secondary to the anatomic reconfiguration of the gastrointestinal (GI) tract in RYGB. Secondly, the upregulation of GI hormones, including Glucagon-like Peptide 1 (GLP-1) produced in the distal small intestine is thought to play a significant role. GLP-1, the levels of which are known to be markedly higher after RYGB, stimulates insulin release and suppresses glucagon.²⁻⁴

More recent work in an animal model has demonstrated morphological adaptation of the Roux limb of the RYGB in association with reprogramming of intestinal glucose metabolism. Glucose transporter 1 (GLUT-1) was shown to be upregulated in the Roux limb of rats treated with RYGB. GLUT-1 is known to be abundantly present in fetal intestine, where it is thought to play a role in early intestinal tissue growth. GLUT-1 levels normally diminish from the high levels in the fetus to barely detectable in adult intestine. Therefore, its reappearance following RYGB is highly significant. Moreover, it was demonstrated that this morphological adaptation of the Roux limb led to an enhancement of intestinal glucose uptake and utilization, thereby contributing to the whole-body glucose disposal associated with RYGB.⁵ This phenomenon has yet to be studied in humans undergoing RYGB.

The aim of this study is to investigate small intestinal remodeling and reprogramming of glucose metabolism in patients with T2DM who undergo laparoscopic RYGB. Specifically, we aim to determine if the gene and protein expression levels of GLUT-1 are upregulated in the Roux limb and whether this is a major mechanism for the remission of T2DM following RYGB.

BACKGROUND

The problem and its significance

The prevalence of obesity rose significantly in United States in the last few decades of this past century, with 35.7% of US adults now obese. Along with the higher prevalence of obesity has come a rise in the incidence of Type 2 Diabetes Mellitus (T2DM). The Centers for Disease Control and Prevention (CDC) estimates that between 1980 and 2011 the number of adults diagnosed with Diabetes Mellitus increased from 5.5 million to 19.6 million. These trends clearly have an enormous public health⁶ and fiscal impact, with an estimated \$147 billion spent annually on obesity and related comorbidities. An estimate of global spending on diabetes in 2010 was at least \$376 billion and is projected to be \$490 billion in 2030.¹

The remission of T2DM following Roux-en-Y gastric bypass is well established. In fact, recent prospective randomized studies have demonstrated RYGB to be superior to the best available medical treatment for obesity-related T2DM.^{1,7} This undoubtedly highlights the crucial role of the gastrointestinal (GI) tract in glucose homeostasis.⁸ However, the precise mechanism for the remission is poorly understood, despite intense research in this area. Clear delineation of the role of the GI tract in glucose metabolism following RYGB is imperative.

Currently there are at least four procedures (Adjustable Gastric Banding, Sleeve Gastrectomy, RYGB, and Biliopancreatic Diversion with Duodenal Switch) routinely offered to morbidly obese patients with or without T2DM. Only the latter two operations involve altering the GI tract by transposing a distal intestinal segment to a more proximal location. Importantly, animal studies have shown that the Roux limb of the RYGB is important in glucose uptake and utilization.^{5,9} Results from our study could impact bariatric procedure selection for morbidly obese patients with T2DM. Moreover, elucidating the role of the Roux limb in glucose uptake and utilization will potentially allow manipulation of these mechanisms to develop less invasive surgical and non-surgical approaches to the treatment of Type 2 Diabetes Mellitus.

Prior Studies

Proposed mechanisms for the improvement in insulin resistance and abnormal glycemic control include the bypass of a putative insulin resistance signal in the duodenum and proximal small intestine secondary to the anatomic reconstruction of the gastrointestinal (GI) tract in RYGB. Additionally, the upregulation of GI hormones, including Glucagon-like Peptide 1 (GLP-1) produced in the distal small intestine is thought to play a significant role. GLP-1, the levels of which are known to be markedly higher after RYGB, stimulates insulin release and suppresses glucagon.^{2,3}

Morphological changes, including hyperplasia and hypertrophy, have been demonstrated in the Roux limb following RYGB. This evidence comes largely from animal studies.^{2,10,11} Most recently in a landmark study, Saeidi et al showed that the Roux limb of RYGB treated rats exhibited an increase in the RNA and protein levels of the basolateral glucose transporter-1 (GLUT-1). GLUT-1 is known to be abundantly present in fetal intestine, where it is thought to play a role in early intestinal tissue growth. GLUT-1 levels normally diminish from the high levels in the fetus to barely detectable in adult intestine. Therefore, its reappearance following RYGB is highly

significant. Moreover, this morphological adaptation of the Roux limb led to an enhancement of intestinal glucose uptake and utilization, thereby contributing to whole-body glucose disposal. PET/CT scanning using 2-deoxy-2-[18F]fluoro-D-glucose ([18]FDG) displayed intense uptake by the Roux limb of RYGB-treated rats versus sham operated rats. In PET/CT scanning, [18]FDG is administered intravenously, and entry into intestinal cells occurs through the basolateral, rather than the luminal side. Of crucial importance, Saeidi et al quantified the relative contribution of the intestine to whole-body glucose disposal. By biodistribution analysis using [18]FDG they demonstrated that the intestine displayed the highest rate of glucose uptake, thus becoming a major site for glucose disposal following RYGB. Glucose disposal per gram of tissue was shown to double in the intestine of RYGB-treated animals, with the glucose uptake by the Roux limb and common channel being higher in comparison with that in the jejunum of animals subjected to a sham operation.⁵

Preliminary work

Plasma glucose was measured fasting and at multiple points after standardized mixed-nutrient meals in a group of obese subjects with Type 2 Diabetes (n=9). The meal stimulation tests were performed before and 14 days after RYGB. As shown in the figure below, glucose absorption is significantly changed after RYGB.¹²

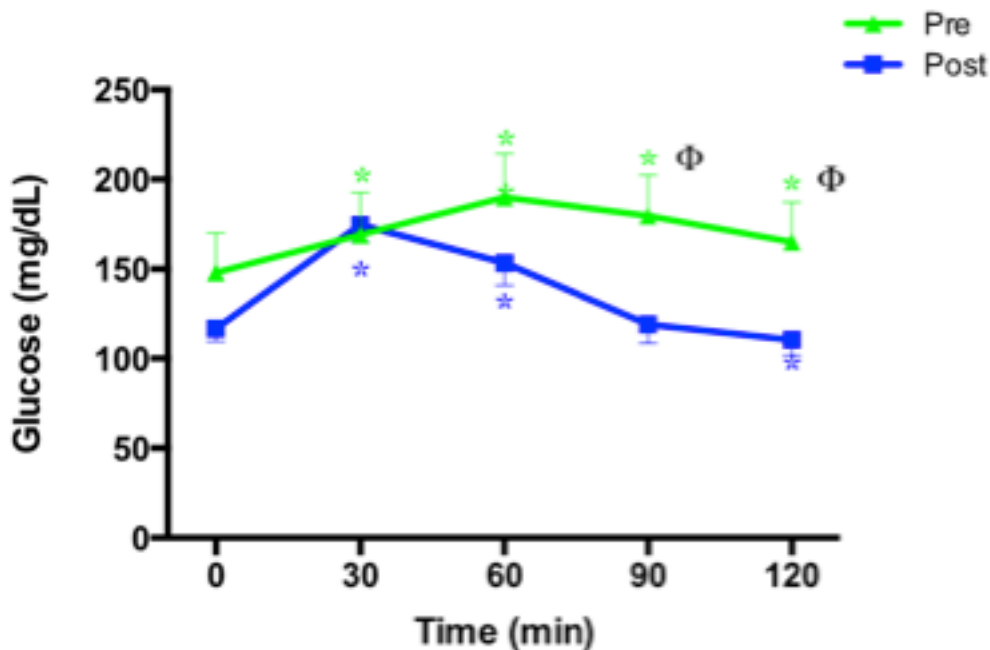


Figure: Plasma glucose levels during mixed meal stimulation. Triangles represent time point pre-RYGB and squares represent time point post-RYGB. Φ $P < 0.05$ for comparison within group between Pre- and Post-intervention. * $P < 0.05$ for comparison within group relative to baseline.

HYPOTHESIS

We hypothesize that small intestinal remodeling and reprogramming of glucose metabolism occurs in patients with T2DM who have undergone Roux-en-Y Gastric Bypass (RYGB). The surgically reconfigured intestinal segment (the Roux limb) undergoes an adaptive response characterized by increased glucose uptake and utilization, triggered by exposure to undigested nutrients. As a result of this change, the intestine becomes a major tissue for whole-body glucose disposal. We will test this hypothesis with the following specific aims:

Aim 1: Demonstrate that the basement membrane glucose transporter 1 (GLUT-1) is upregulated in the Roux limb following RYGB, and

Aim 2: Demonstrate that the upregulation of GLUT-1 is a major mechanism for the improvement in glycemic control observed in T2DM patients undergoing RYGB.

METHODS

Research Design

Aim 1: To demonstrate that the basement membrane glucose transporter 1 (GLUT-1) is upregulated in the Roux limb following RYGB.

To test this hypothesis, gene and protein expression levels of GLUT-1 will be analyzed from the specimens obtained intra-operatively (baseline) and at 2 months post-operatively to determine if levels are significantly elevated above baseline. Quantitative real-time PCR and Western blot techniques will be utilized as described in **C** below.

Anticipated results: Levels of GLUT-1 gene and protein expression as measured at 2 months will be significantly elevated above baseline.

Aim 2: To demonstrate that the upregulation of GLUT-1 is a major mechanism for the improvement in glycemic control observed in T2DM patients undergoing RYGB.

To test this hypothesis, change in GLUT-1 levels will be correlated with changes in fasting glucose, mixed meal stimulation test, and homeostasis model assessment (HOMA). Secondly, at 2 months post-operatively, whole-body positron emission tomography/computed tomography (PET/CT) scanning with Fluorodeoxyglucose (FDG) will be performed to evaluate glucose uptake and utilization in the Roux limb.

Anticipated results: There will be a significant correlation between the change in GLUT-1 expression and change in fasting glucose, mixed meal stimulation test, and HOMA. Moreover, there will be significant FDG uptake by the Roux limb.

A. Enrolment of Subjects

A total of 14 adult patients, who meet National Institutes of Health (NIH) criteria for bariatric surgery (Body Mass Index > 35) and have a diagnosis of Type 2 Diabetes Mellitus, undergoing laparoscopic Roux-en-Y Gastric Bypass (RYGB) at our institution will be enrolled in this prospective cohort study.

The study subjects will be recruited from the Duke University Center for Metabolic and Bariatric surgery. Patients will undergo routine preoperative evaluation to assess their candidacy for bariatric surgery. This multidisciplinary process includes evaluation by bariatric surgeons, registered dietitians, and licensed clinical psychologists. The center evaluates approximately 1200 patients annually, performing approximately 800-900 bariatric procedures yearly. Approximately 25% of these patients have a diagnosis of T2DM. Laparoscopic RYGB constitutes over 50% of the bariatric procedures performed at our institution. Therefore, patient accrual for the study is quite feasible.

Inclusion Criteria

1. Diagnosis of Type 2 Diabetes Mellitus
2. Age ≥ 18
3. BMI ≥ 35 kg/m²

Exclusion Criteria

1. Age < 18 or > 65
2. Patients undergoing revision from another bariatric procedure to RYGB
3. Presence of a seizure disorder (GLUT-1 deficiency syndrome)¹³
4. Use of Tricyclic antidepressants
5. Use of tobacco products

B. Anthropometric Data, Laboratory Data, and Specimen Collection

At initial evaluation, preoperative visit, and 2-month postoperative visit, patient height and weight will be measured and the BMI will be calculated.

The following laboratory studies will be obtained at the preoperative visit: Fasting Plasma glucose (FPG), insulin, and hemoglobin A1C (HbA1C). These will be obtained in addition to the routine preoperative laboratory studies.

A mixed meal stimulation test will be performed pre-operatively and at 2 months post-operatively as previously described.¹² Plasma insulin and glucose will be determined at each time point (0, 30, 60, 90, and 120 minutes).

Jejunal mucosa samples will be obtained from all subjects intra-operatively and post-operatively. The intra-operative tissue sample will be obtained by resection of a 2cm segment of the afferent portion of the Roux limb. Mucosal samples will be taken from this resected portion of Roux limb, snap frozen in liquid nitrogen, and stored at -80°C . Baseline levels of GLUT-1 gene (mRNA) and protein expression will be determined by quantitative real-time PCR and Western blot techniques respectively.

At 2 months post-operatively, study subjects will undergo upper endoscopy with biopsies of the corresponding segment of the Roux limb. Levels of GLUT-1 gene and protein expression will be determined by quantitative real-time PCR and Western Blot analysis.

C. Lysate preparation, Western Blot Analysis, Quantitative Real-time PCR

Frozen intestinal tissues will be crushed to powder and transferred to individual conical tubes. RIPA buffer containing protease inhibitors will be added to each sample. The protein concentration of each lysate sample will be determined using a commercially available protein assay (Bradford). Protein lysates will be separated sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE). Proteins will be transferred to PVDF membranes, blocked, and incubated with GLUT-1 antibody overnight at 4°C . Membranes will be developed using a standard Western blotting substrate.

Total RNA will be isolated using a commercially available kit. An aliquot from each sample will be converted to complimentary DNA (cDNA). Real-time PCR will be performed using GLUT-1 primer with NCBI accession # NM_138827.

D. Study Intervention

All enrolled patients will undergo laparoscopic RYGB after standard preoperative evaluation as described above. Standard multi-port laparoscopic RYGB will be performed in the following manner: A 30ml proximal gastric pouch is fashioned; the jejunum is divided 50cm distal to the ligament of Treitz; an antecolic Roux-en-Y gastrojejunostomy is created between the gastric pouch and the distal segment of divided jejunum using a linear stapler. Gastrointestinal continuity is restored by creating a stapled side-to-side jejunojejunostomy, resulting in a 100cm Roux (alimentary) limb and a 50cm Biliopancreatic limb.

The intra-operative tissue sample will be obtained by resection of a 2cm segment of the afferent portion of the Roux limb. Mucosal samples will be taken from this resected portion of Roux limb, snap frozen in liquid nitrogen, and stored at -80°C .

Post-operative management will be standard, with the initiation of oral intake of a full liquid diet on the first post-operative day. Patients will be discharged from the hospital when tolerating the diet without incident and meet all discharge criteria. Follow up will be at 2 weeks, 2 months, 6 months, and at 12 months per our institutional routine.

At 2 months post-operatively, study subjects will undergo upper endoscopy with biopsies of the corresponding segment of the Roux limb. Subjects will also undergo a repeat mixed meal stimulation test as previously described.¹²

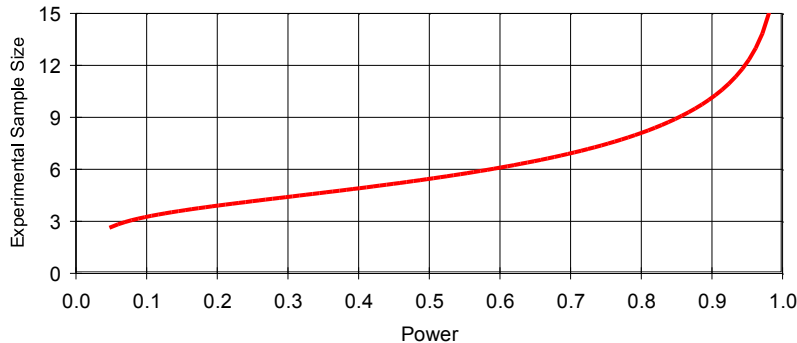
Lastly, at 2 months post-operatively, study subjects will undergo positron emission tomography/computed tomography (PET/CT) scanning with Fluorodeoxyglucose (FDG) to evaluate glucose uptake in the Roux limb. The rate of FDG uptake is proportional to the rate of glucose utilization within a tissue.

E. Statistical Analysis and Sample Size

Descriptive statistics, including means, standard deviations, and ranges for continuous parameters, as well as percent and frequencies for categorical parameters will be presented. Comparisons of continuous variables between pre- and post-operative time points will be completed by one sample t test. Categorical variables will be compared using the chi-square test or Fisher's exact test. The SPSS statistical software program (version 20.0, SPSS, Chicago, USA) will be used for all analyses. All tests will be 2-tail. P values of less than 0.05 will be considered to indicate statistical significance.

Power Analysis

We are planning a study of a continuous response variable (GLUT-1 RNA expression) from study subjects. Prior animal data from Saeidi et al.⁵ indicate that GLUT-1 RNA expression increased 0.8 ± 0.7 fold in the Roux limb of RYGB-treated rats compared with preoperative levels. Assuming that we will observe a similar magnitude of change in our human cohort, we will need to study 10 subjects to be able to reject the null hypothesis that this response difference is zero with probability (power) 0.9. The Type I error probability associated with test of this null hypothesis is 0.05. The enrollment target will be set at 14 patients assuming a 20% lost to follow up rate after the intraoperative biopsy.



F. Potential Pitfalls

A difference may not exist. In other words, contrary to what is observed in animal studies there may not be an upregulation of GLUT-1 in the Roux limb of patients undergoing RYGB. Therefore our study may not show that the intestine is a major tissue for glucose uptake and disposal via the GLUT-1 transporter mechanism. Still, it would be important to know that this specific glucose transporter is not involved in this process in humans, suggesting that other glucose transporters are involved, which can then be evaluated in future studies.

The optimal timing of these morphological changes in the Roux limb is unknown. However, given the rapid improvement glycemic control that is observed following RYGB we surmise that if the Roux limb is a major mechanism underlying this process, then we should be able to detect an upregulation in GLUT-1 within the first two months post-operatively.

SAGES RESEARCH GRANT APPLICATION BUDGET SHEET

SAGES grant 2014 BudgetSheet.xls

Detailed budget for 12 month period from July 1, 2014 through June 30, 2015 .

Dollar amount requested (Omit cents) \$29,880

Total for the grant request may not exceed \$30,000.

* 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.

NAME	POSITION TITLE	TIME/EFFORT		SALARY	FRINGE BENEFITS	SUB-TOTALS
		%	Hrs/ Week			
Philip Omotosho, MD	Principal Investigator*	20	12			
Alessandro Mor, MD	Post-doctoral Fellow	10	6	30,000	6000	3,600
3.						
4.						
5.						
CONSULTANT COSTS	Department of Surgery at our Institution provides statistician					0
EQUIPMENT (List all Items&Total Equipment Cost)	Dry ice, liquid nitrogen pipets, vials, gloves, labels, boxes					1000
SUPPLIES (List all Items&Total Supplies Cost)	Meal stimulation testing (140 insulin assays, 140 glucose assays) \$3,080; RT-PCR for GLUT1 \$3000					6,080
TRAVEL**	P.I. travel to present at SAGES					1,000
PATIENT CARE COSTS	Upper endoscopy with biopsies (\$1000 x 14 patients), Patient rembursement (\$300 x 14)					18,200
CONSORTIUM/CONTRACTUAL COSTS						
OTHER EXPENSES (List all Items & Total Cost)	PET/CT cost to be covered by divisional startup funding.					0
TOTAL DIRECT COSTS						29,880

REFERENCES

1. Mingrone G, Panunzi S, De Gaetano A, et al. Bariatric surgery versus conventional medical therapy for type 2 diabetes. *N Engl J Med* 2012; 366(17):1577-85.
2. Thomas S, Schauer P. Bariatric surgery and the gut hormone response. *Nutr Clin Pract* 2010; 25(2):175-82.
3. Park CW, Torquati A. Physiology of weight loss surgery. *Surg Clin North Am* 2011; 91(6):1149-61, vii.
4. Falken Y, Hellstrom PM, Holst JJ, et al. Changes in glucose homeostasis after Roux-en-Y gastric bypass surgery for obesity at day three, two months, and one year after surgery: role of gut peptides. *J Clin Endocrinol Metab* 2011; 96(7):2227-35.
5. Saeidi N, Meoli L, Nestoridi E, et al. Reprogramming of intestinal glucose metabolism and glycemic control in rats after gastric bypass. *Science* 2013; 341(6144):406-10.
6. Danaei G, Finucane MM, Lu Y, et al. National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants. *Lancet* 2011; 378(9785):31-40.
7. Schauer PR, Kashyap SR, Wolski K, et al. Bariatric surgery versus intensive medical therapy in obese patients with diabetes. *N Engl J Med* 2012; 366(17):1567-76.
8. Rubino F, Forgione A, Cummings DE, et al. The mechanism of diabetes control after gastrointestinal bypass surgery reveals a role of the proximal small intestine in the pathophysiology of type 2 diabetes. *Ann Surg* 2006; 244(5):741-9.
9. Taqi E, Wallace LE, de Heuvel E, et al. The influence of nutrients, biliary-pancreatic secretions, and systemic trophic hormones on intestinal adaptation in a Roux-en-Y bypass model. *J Pediatr Surg* 2010; 45(5):987-95.
10. Spak E, Bjorklund P, Helander HF, et al. Changes in the mucosa of the Roux-limb after gastric bypass surgery. *Histopathology* 2010; 57(5):680-8.
11. Stearns AT, Balakrishnan A, Tavakkolizadeh A. Impact of Roux-en-Y gastric bypass surgery on rat intestinal glucose transport. *Am J Physiol Gastrointest Liver Physiol* 2009; 297(5):G950-7.
12. Evans S, Pamuklar Z, Rosko J, et al. Gastric bypass surgery restores meal stimulation of the anorexigenic gut hormones glucagon-like peptide-1 and peptide YY independently of caloric restriction. *Surg Endosc* 2012; 26(4):1086-94.
13. Pong AW, Geary BR, Engelstad KM, et al. Glucose transporter type I deficiency syndrome: epilepsy phenotypes and outcomes. *Epilepsia* 2012; 53(9):1503-10.

INSTITUTIONAL REVIEW BOARD

Local Institutional Review Board (IRB) approval is pending.

AVAILABLE RESOURCES

Laboratory (Stedman Center):

The collaborator in this study occupies a laboratory space in the Stedman Metabolic Center in Durham, NC. This space provides access to equipment including quantitative real-time PCR; refrigeration; centrifuges; microcentrifuges; spectrophotometry; gel electrophoresis for protein, DNA, and RNA analysis; -80 C ultrafreezer; water baths; incubators; shakers; inverted contrast phase microscopy; and equipment for ELISA.

Clinic:

The Duke Metabolic and weight Loss Surgery Center has a fully functional and equipped clinic in which the principal investigator practices, with examination and procedure rooms available for clinical studies. This clinic also has a laboratory room.

Endoscopy Suite:

A modern, fully equipped, and functional endoscopy suite is available at our institution; the primary investigator and collaborator have full endoscopy privileges to perform the required upper endoscopy with biopsies.

Duke Nuclear Medicine:

The PET/CT scans will be performed at Duke University Nuclear Medicine. The Nuclear Medicine division provides diagnostic studies including laboratory studies such as quantitative glomerular filtration rates, planar imaging, SPECT imaging, SPECT/CT imaging, and PET/CT imaging.

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.**

NAME Omotosho, Philip Ayodeji	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, include postdoctoral training and residency training if applicable.)

INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
University of Maryland Baltimore County, Baltimore MD	BS	05/99	Biological Sciences
Penn State University College of Medicine, Hershey PA	MD	05/04	Medicine
Baystate Medical Center, Tufts University SOM, Springfield MA	Residency	06/09	General Surgery
Duke University Medical Center, Durham NC	Research Fellowship	06/10	Laparoscopic Surgery
Duke University Medical Center, Durham, NC	Clinical Fellowship	06/11	Laparoscopic Surgery

A. Personal Statement

The aim of the proposed research study is to investigate the role of the gastrointestinal tract in glucose uptake and disposal in morbidly obese patients who undergo Roux-en-Y gastric bypass (RYGB) surgery. Since the incidence of Type 2 Diabetes has risen along with the incidence of obesity, it is exceedingly important that the role of bariatric surgery (especially RYGB) be clearly delineated to guide therapy recommendations and future study. I am a minimally invasive surgeon with expertise in bariatric surgery, obesity, and metabolic disease. As a research fellow and junior faculty at Duke I have studied outcomes of bariatric surgery in different patient populations as well as the mechanisms for the improvement in insulin sensitivity after RYGB. I have a continued interest in the metabolic consequences of RYGB as it relates to the remission of Type 2 Diabetes. I have a career-long interest and dedication to this area of study and plan to pursue ongoing funding locally and at the national level to sustain the required research. For the aforementioned reasons, I am well suited to play a leadership role in the design, execution, and dissemination of the results of the proposed research study.

B. Positions and Honors

Positions and Employment

- 2004 – 2009 General Surgery Resident, Baystate Medical Center/Tufts University SOM, Springfield, MA
- 2004 – 2009 Clinical Associate, Tufts University School of Medicine, Springfield, MA
- 2009 – 2010 Research Fellow, Duke University Medical Center, Durham, NC
- 2010 – 2011 Clinical Fellow and Clinical Associate, Duke University Medical Center, Durham, NC
- 2011 - Assistant Professor, Department of Surgery, Duke University, Durham, NC

Other Experience and Professional Memberships

- 2007 - Member, Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)
- 2012 - Member, American Society for Metabolic and Bariatric Surgery (ASMBS)
- 2012 - Member, American Hernia Society
- 2013 - Member, Association for Academic Surgery
- 2013 - Fellow, American College of Surgeons

Program Director/Principal Investigator (Last, First, Middle): Omotosho, Philip A.

- 2013 - Member, Peer Review Committee, Duke Regional Hospital and Duke Raleigh Hospitals
- 2013 - Ad hoc Reviewer, Surgery for Obesity and Related Diseases

National Committees

- 2011 – 2012 Fundamentals of Laparoscopic Surgery Committee, SAGES
- 2013 - Fundamentals of Endoscopic Surgery Committee, SAGES
- 2013 - Hernia Task Force, SAGES
- 2013 - Chair, Retention Subcommittee, Membership Committee, SAGES

Honors

- 2004 Pathology Honor Society, Penn State University College of Medicine
- 2004 Gold Humanism Honor Society, Penn State University College of Medicine
- 2005 Intern of the Year Award, Department of Surgery, Baystate Medical Center
- 2006 – 2007 Excellence in Teaching Citation, Surgery Clerkship, Tufts University School of Medicine
- 2008 Excellence in Teaching Award, Class of 2008, Tufts University School of Medicine
- 2009 Arnold P. Gold Foundation Humanism and Excellence in Teaching Award

C. Selected Peer-Reviewed Publications

1. Baldisseri DM, Margolis JW, **Omotosho PA**, Volkman BF & Margolis FL. Sequence-specific NMR resonance assignments of the backbone atoms for the olfactory marker protein, OMP. *J Biomol NMR*. 2000 Jun; 17(4): 353-354.
2. **Omotosho PA**, Varnholt H, Tirabassi M, Prasad R, Moriarty K. Giant polypoid gastric heterotopia presenting with intermittent intussusception. *J Laparoendosc Adv Surg Tech*. 2007 Apr; 17(2): 249–251.
3. Romanelli JR, Mark L, **Omotosho PA**. Single port laparoscopic cholecystectomy with the Triport system: A case report. *Surg Innov*. 2008 Sep; 15(3): 223-8.
4. Diesen DL, Erhunmwunsee L, Bennett KM, Ben-David K, Yurcisin B, Ceppa EP, **Omotosho PA**, Perez A, Pryor A. Effectiveness of laparoscopic computer simulator versus usage of box- trainer for endoscopic surgery training of novices. *J Surg Educ*. 2011 Jul-Aug; 68(4):282-9.
5. **Omotosho PA**, Yurcisin B, Ceppa E, Miller J, Kirsch D, Portenier D. In vivo assessment of an absorbable and non-absorbable knotless barbed suture for laparoscopic single-layer enterotomy closure: A clinical and biochemical comparison against non-barbed suture. *J Laparoendosc Adv Surg Tech*. 2011 Dec; 21(10): 893-7.
6. Ceppa EP, Ceppa DP, **Omotosho PA**, Dickerson JA 2nd, Park CW, Portenier DD. Algorithm to diagnose etiology of hypoglycemia after Roux-en-Y gastric bypass for morbid obesity: case series and review of the literature. *Surg Obes Relat Dis*. 2011 Sep-Oct; 8(5): 641-7.
7. Earle DB, Romanelli JR, McLawhorn T, **Omotosho P**, Wu P, Rossini C, Swayze H, Desilets DJ. Prosthetic mesh contamination during NOTES transgastric hernia repair: a randomized controlled trial with swine explants. *Hernia*. 2012 Dec; 16(6): 689-95.
8. Ceppa EP, Rialon K, Burbride R, **Omotosho PA**, Jowell PS, Branch MS, Pappas TN. Endoscopic versus surgical ampullectomy: An algorithm to treat disease of the ampulla of vater. *Ann Surg*. 2013 Feb; 257(2): 315-22.
9. Shin JH, Worni M, Castleberry AW, Pietrobon R, **Omotosho PA**, Silberberg M, Ostbye T. The application of the comorbidity indices to predict early postoperative outcomes after laparoscopic Roux-en-Y gastric bypass: a nationwide comparative analysis of over 70,000 cases. *Obes Surg*. 2013 Jan; 23(5): 638-49.

D. Research Support

None at present

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.**

NAME Mor, Alessandro		POSITION TITLE	
eRA COMMONS USER NAME (credential, e.g., agency login)		Post-Doctoral Fellow	
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	MM/YY	FIELD OF STUDY
Catholic University, Rome, Italy	M.D.	03/2011	Medicine and Surgery

B. Positions and Honors

Positions and Employment

2012- Post-Doctoral Fellow, Division of Metabolic and Weight Loss Surgery, Duke University

Other Experience and Professional Memberships

2012- Member, SAGES

C. Selected Peer-reviewed Publications

- Mor A, Keenan E, Portenier D, Torquati A. Case-matched analysis comparing outcomes of revisional versus primary laparoscopic Roux-en-Y gastric bypass. Surg Endosc. 2012 Jul 18. [Epub ahead of print] PubMed PMID: 22806534.
- Mor A, Sharp L, Portenier D, Sudan R, Torquati A. Weight loss at first postoperative visit predicts long-term outcome of Roux-en-Y gastric bypass using Duke weight loss surgery chart. Surg Obes Relat Dis. 2012 Sep;8(5):556-60. Epub 2012 Jul 16. PubMed PMID: 22920966.
- Nanni G, Familiari P, Mor A, Iaconelli A, Perri V, Rubino F, Boldrini G, Salerno MP, Leccesi L, Iesari S, Sollazzi L, Perilli V, Castagneto M, Mingrone G, Costamagna G. Effectiveness of the Transoral Endoscopic Vertical Gastroplasty (TOGa®): a Good Balance Between Weight Loss and Complications, if Compared with Gastric Bypass and Biliopancreatic Diversion. Obes Surg. 2012 Sep 23. [Epub ahead of print] PubMed PMID: 23001571.
- Mor A, Lutfi R, Torquati A. Esophageal acid-clearance physiology is altered after Nissen-Collis gastroplasty. Surg Endosc. 2012 Oct 17. [Epub ahead of print] PubMed PMID: 23073687.
- Omotosho PA, Rodriguez JA, Spangler K, Mor A, Portenier DD, Torquati A. Predictors of long term success after Laparoscopic Roux-en-Y Gastric Bypass in African-American women. (Submitted to SOARD)

D. Research Support

SAGES PARTICIPATION

The Principal Investigator, Philip Omotosho, MD joined SAGES as a candidate member in 2008 and became a full member in 2010. He has submitted abstracts to SAGES meetings, participated in SAGES courses, and has served on SAGES committees. He currently serves on the Hernia Task Force, Fundamentals of Endoscopic Surgery, and Membership Committees.

Our post-doctoral fellow, Alessandro Mor, MD joined SAGES in 2014, and has submitted abstracts to SAGES meetings.



Duke Center for Metabolic and Weight Loss Surgery
DUKE UNIVERSITY HEALTH SYSTEM

Alfonso Torquati, MD, MSCI
Associate Professor of Surgery
Chief, Division of Metabolic and
Weight Loss Surgery
Director Obesity Research

October 24, 2013

Philip Omotosho, MD, FACS
Assistant Professor of Surgery
Duke University

Dear Phil,

I am delighted to serve as collaborator for your SAGES grant application titled **"Intestinal Remodeling and Reprogramming of Intestinal Glucose Metabolism Following Laparoscopic Roux-en-Y Gastric Bypass"**.

Our most recent collaborative work using the mixed meal stimulation test to characterize changes in intestinal glucose absorption has shown great promise. I look forward to continue our collaboration on the studies outlined in your research project. In particular, to support the measurement of GLUT-1 protein and RNA levels in the jejunal specimens.

We are more than happy to host the bench work for our collaborative. I would be happy to provide my expertise and assistance for the studies relative to the glucose metabolism after bariatric surgery.

Because of my expertise and long-standing interest in the remission of type 2 diabetes after bariatric surgery, I am very excited in continuing our collaboration. The mechanisms controlling glucose absorption after gastric bypass are obviously of critical importance for human health and in particular for obese patients suffering from type 2 diabetes.

Best regards,

A handwritten signature in blue ink, appearing to read 'Alfonso Torquati'.

Alfonso Torquati, MD, MSCI, FACS
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