

The Innovator

Baystate  Health

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ENHANCING LIVES.



Research Pilot Award Program (RPAP) sees success over several years since its inception



Paul Visintainer, PhD, oversees the RPAP program.

The Research Pilot Award Program (RPAP) is an internal grants program designed to help UMMS-Baystate faculty test study designs and collect preliminary data to support a larger external grant application. The program is underwritten completely with indirect funds obtained through existing federal grant awards.

Beginning in the summer of 2016, the program has solicited applications and funded proposals each year. The application

process is competitive, and funding depends on the number and quality of the applications, as well as the availability of funds. A committee of experienced clinical researchers reviews and scores each application on three criteria: the experience of the investigator with conducting research, the feasibility and fundability of the proposed study, and whether the study is consistent with the mission of Baystate.

To date, the program has

funded 16 clinical investigators across several departments and disciplines. The studies that have been completed have supported four grant applications, two published papers, and three further manuscripts in preparation. Moreover, these pilot studies have provided the investigators critical information about their protocols – patient eligibility, recruitment, subject compliance, measurement of variables, required staffing, collaborations with external agencies, as

examples. As these studies illustrate, it is difficult to overstate the importance of pilot studies: they tell us what works – and what doesn't – enabling us to correct and modify our approaches, thereby producing more competitive, feasible, and clinically-relevant applications.

In this issue, we consider six RPAP studies that have been completed thus far. Future issues of *The Innovator* will highlight ongoing and new RPAP studies and their principal investigators.

A Pilot Randomized Controlled Study of Non-Invasive Ventilatory Support for Acute Hypoxemic Respiratory Failure: High Flow Nasal Oxygen vs. Helmet-Non-Invasive vs. Mask-Non-Invasive Ventilation

Mark Tidswell, MD, Associate Professor of Medicine at UMass Medical School-Baystate; Associate Professor of Medicine, Tufts University School of Medicine

Non-invasive ventilatory modes such as noninvasive positive pressure ventilation (NIPPV) and high-flow nasal cannula oxygen (HFNO) improve gas exchange, reverse hypoxemia, and may prevent intubation and the risks associated with invasive mechanical ventilation including need for sedation, delirium, lung injury, and nosocomial pneumonia.

Traditionally, NIPPV is delivered through a

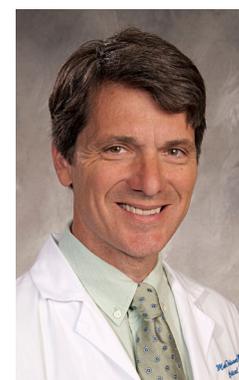
face-mask, but patient intolerance and air leaks are frequent with mask-NIPPV. More recently, delivery of NIPPV through a helmet interface resulted in better tolerance than the face-mask and allowed the use of higher levels of positive pressure ventilation (PEEP).

No studies have yet compared all three modalities (HFNO, mask-NIPPV and helmet-NIPPV) in a population of patients with hypoxemic respiratory

failure. We proposed a pilot randomized controlled trial to assess the effect of HFNO and helmet-NIPPV on intubation rate among patients with AHRF. These rates were compared with historical data obtained from the literature for mask-NIPPV intubation rates in similar population. Our main objective was to collect feasibility data on helmet NIPPV and other clinical elements in preparation for a full-scale randomized

trial based on findings of this pilot study.

The project was terminated early because of difficulty achieving recruitment targets. What we learned is that the selection criteria were likely too rigid, which restricted the size of the potential patient pool and increased the time and effort required for patient screening. Finally, patient participation was lower than expected.



Mark Tidswell, MD

Novel Scoring to Increase Sensitivity of Polysomnography (PSG) for Clinical Significant Obstructive Sleep Disordered Breathing

Karin Johnson, MD, Vice Chair for Academic Affairs and Associate Professor, Department of Neurology, UMass Medical School-Baystate

My RPAP project led to two publications so far: "Cardiovascular and Somatic comorbidities and sleep measures using three hypopnea criteria in mild sleep disordered breathing: sex, age and body mass index differences in a retrospective sleep cohort" in *Journal of Clinical Sleep Medicine*² and "Flow Limitation/Obstruction With Recovery Breath (FLOW) Event For Improved Scoring of Mild Obstructive Sleep Apnea without Electroencephalography" in



Karin Johnson, MD

*Sleep Medicine*¹.

Overall, the RPAP provided me with the connections within the outstanding research,

IRB, and epidemiology teams at Baystate and provided a foundation that has facilitated other research projects. I was able to be a research mentor for several summer students, college students, and PURCH medical students. This included becoming site PI for an investigational drug for Idiopathic Hypersomnia patients and research on readmission rates in inpatients undergoing sleep studies as well as the impact of COVID-19 on sleep laboratories.

1: Johnson KG, Johnson DC, Thomas RJ, Feldmann E, Lindenauer PK, Visintainer P, Kryger MH. Flow limitation/obstruction with recovery breath (FLOW) event for improved scoring of mild obstructive sleep apnea without electroencephalography. *Sleep Med.* 2020 Mar;67:249-255.

2: Johnson KG, Johnson DC, Thomas RJ, Rastegar V, Visintainer P. Cardiovascular and somatic comorbidities and sleep measures using three hypopnea criteria in mild obstructive sleep-disordered breathing: sex, age, and body mass index differences in a retrospective sleep clinic cohort. *J Clin Sleep Med.* 2020 Oct 15;16(10):1683-1691.

Improving Patient-Centered Outcomes for Adolescents with Depressive Illness through the Massachusetts Child Psychiatry Access Project (MCPAP)

Bruce Waslick, MD, Associate Professor of Psychiatry, UMass Medical School-Baystate

There is increasing evidence that various models of primary care supports and enhancements are effective in increasing detection of depressive illness in adolescents and facilitating families' access to effective care services.

The Massachusetts Child Psychiatry Access Project (MCPAP) model of primary care practice support was established as a state-wide system of care enhancement in Massachusetts in 2004 and has been replicated and widely disseminated in over 25 other states and regions. While the use of MCPAP by primary care providers improves access



Bruce Waslick, MD

to mental health care for their patients, the program has not been evaluated in terms of improving mental health outcomes compared with interventions such as screening/referral alone. Thus, the overall aim of this proposal was to evaluate the

effectiveness of the MCPAP model in the evaluation and treatment of adolescent depression in primary care. The MCPAP-supported model employs screening, assessment, intervention and referral support in primary care pediatric practices.

The project was terminated in its first year due to several unanticipated obstacles, including inability to recruit and enroll primary care practices in a timely fashion and disparate medical record systems, which made collecting comparable data across practices challenging and demanding on time and effort.

Engaging School Nurses in Diabetes Care Team to Improve Diabetes Self-Management Skills, Adherence, and Glycemic Control in Children with T1DM

Ksenia N. Tonyushkina, MD, Pediatric Endocrinologist and Assistant Professor of Pediatrics, UMass Medical School-Baystate

The overall objective of this pilot proposal was to evaluate the feasibility of monthly insulin dose adjustments for students with T1DM through collaboration between pediatric diabetes clinic and school nurses and impact of this intervention on diabetes control. Specifically, the goals were to evaluate the changes in A1C, diabetes self-management (DSM) behaviors in children with T1DM and their families, and to determine patient acceptance and satisfaction with this intervention.

We showed that school nurses could be engaged in a diabetes care team and model diabetes care at school with on-going support and education by the



Ksenia N. Tonyushkina, MD

diabetes clinic team. We also found a trend toward better diabetes control during the school year vs. summer. The study suggested that involvement of school nurses could improve care of high-risk students in need of intensive diabetes care coordination and supervision.

Exercise Prescription in Cardiac Rehabilitation: A Pilot Randomized Controlled Trial

Quinn R. Pack, MD, MSc, Associate Professor of Medicine, UMass Medical School-Baystate; Adjunct Associate Professor of Medicine, Tufts University School of Medicine

As of October 2020, our RPAP was in the final stages of completion. We had 48 total patients enroll and complete baseline stress tests, of which 4 dropped out, 20 discontinued the protocol prematurely due to COVID, and 24 completed the full protocol. We were successful in implementing our protocols. Patients randomized to a target heart rate range increased their exercise intensity by about 5 beats per minute and increased their exercise capacity by an additional 1 MET. Patient satisfaction was high.

In June 2020, Dr. Pack utilized these pilot findings to apply for a Physician-Scientist Early Stage Investigator R01 grant from the NHBLI. In August 2020, Meredith Shea defended her dissertation



Quinn R. Pack, MD, MSc

and was awarded a PhD from Springfield College. In October 2020, she presented this data at the national meeting of the American Association of Cardiovascular and Pulmonary Rehabilitation and won the Beginning Investigator Award. Three manuscripts are planned and are in various stages of submission.

Evaluation of AntiGD2-PolyMPC-Dox Prodrugs in a Neuroblastoma Tumor Model

Michael Tirabassi, MD, Assistant Professor of Surgery, UMass Medical School-Baystate

The use of polymer-prodrug strategies has demonstrated many advantages for enhanced chemotherapeutic drug delivery with improved tumor targeting, reduced adverse effects, and superior efficacy. These agents achieve these benefits by covalently binding the small chemotherapeutic molecule to a bulky polymer, preventing the extravasation of the drug from systemic vascular endothelium until it reaches the “leaky” tumor bed capillaries. This mechanism (known as the enhanced permeation and retention (EPR) effect⁷⁻⁹), passively selects for the desired site of action and promotes drug exposure over a longer time-frame, resulting in less frequent dosing requirements. Polymer prodrugs thus permit administration of a higher maximum tolerated



Michael Tirabassi, MD

dose (MTD), enabling delivery of more drug to the cancer target while reducing off-target side-effects.

The Schneider lab at PVLSI has shown that polymethacryloyloxyethyl phosphorylcholine (polyMPC) *in vivo* are safe and efficacious in toxicity and immunogenicity experiments in mice. We proposed to combine the benefits of anti-GD2 immunotherapy with the polyMPC prodrug platform. Success in this project would represent

a potential breakthrough in neuroblastoma by decreasing the toxic effects, as well as the frequency and duration of chemotherapy, improving their quality of life during therapy, in addition to their survival. This is a cutting-edge approach not only for the treatment of neuroblastoma, but for that of all cancer types.

While success in this project would represent a potential breakthrough in neuroblastoma therapy, the project was hampered by technical hurdle of attaching the chemotherapeutic molecule to the polymer. Consequently, the project was halted. As therapeutic polymer formulations advance, this project may be reconsidered.

Dr. Tirabassi was also a past participant in the Research Faculty Development Program (RFDP).

Closing RPAP statement from Paul Visintainer, PhD

A senior military commander once rued, “No battle plan survives contact with the enemy.” The same may be said of research. Ideas and protocols may appear elegant and feasible on paper, only to fall short once they are attempted in practice. Consequently, the efforts above are not without their obstacles.

For some of the studies, the challenges proved too substantial to overcome, given the available time and funding. Technical barriers at the basic science level or inability to identify

and recruit a sufficient number eligible patients led to early termination of studies. It is important to recognize, however, that this pilot phase is where protocols are evaluated and refined.

As William Whewell, a historian and philosopher noted, “Every failure is a step to success”. This is the goal of the RPAP – to give clinicians who are committed to a career in research an opportunity to present their ideas and refined their approaches in an effort to develop a robust research project.

Kudos: Laura Sorci appointed to national committee with NRG Oncology

Laura Sorci, Sr. Clinical Research Coordinator, was recently appointed as a member of the CRA Subcommittee of NRG Oncology as of January 2021. Her appointment will last for 3 years. She is assigned to the Quality Control working group within the organization.

This role will be a great experience for her and Baystate Health as an institution.

Her appointment reflects her expertise and dedication to participating in NRG Oncology cancer clinical trials.

Congratulations, Laura!

News from UMass CCTS

THE NATIONAL COVID COHORT COLLABORATIVE (N3C)

The National COVID Cohort Collaborative (N3C) Data Enclave is now open to scientists looking for evidence-based answers to COVID-19 research questions. This centralized and secure national data analytics platform is for COVID-19 research, including studying potential risk factors, protective factors and long-term health consequences, as the pandemic continues to evolve. Its data and analytics capabilities will grow over time.

CCTS SPARK PROGRAM

Rolling application deadline. This program's priorities



are to support studies that impact clinical care and research methodologies, support students/trainees, and provide access to funds to generate pilot and preliminary data for external grant submissions. For more information, visit umassmed.edu/ccts/funding/spark-program.

CCTS SMALL CONFERENCE GRANTS

Rolling application deadline. This funding facilitates the development of faculty-to-faculty networks within the University

system. Visit the following link for more information: umassmed.edu/ccts/funding/small-conference-grants.

K-CLUB: Dr. Mihaela Stefan has just been added as a co-leader. Baystate faculty are encouraged to join! umassmed.edu/ccts/education/k-club

QUESTIONS?

Contact Nate Hafer, PhD at 508-856-2511, by emailing Nathaniel.Hafer@umassmed.edu, or visit umassmed.edu/CCTS.



Select Recent Awards

OB/GYN

NEENA QASBA, MD, Access, Contraceptive Coverage, Expected Supply in our State, ACCESS Study Part 3, Baystate Health, Inc., RPAP.

CHILD PSYCH

BARRY SARVET, MD, MCPAP Medical Director Jul-Dec 2020, Beacon Health Options.

EMERGENCY

HOWARD SMITHLINE, MD, PReventing Emerging infections through Vaccine Effectiveness Testing—COVID (Project PREVENT), University of CA/LA Olive View, CDC.

CRITICAL CARE

JAY STEINGRUB, MD, Surveillance of Respiratory Viruses in the Critically Ill: 2020-2021 IVY Network Surveillance Study, Vanderbilt University Med. Ctr., CDC.

JAY STEINGRUB, MD, Phase 2, Randomized, Double-Blind, Placebo-Controlled Study of the Effect of Anti-CD14 Treatment in Hospitalized Patients with COVID-19 (DAIT-COVID-19-003), Benaroya Research Inst. (BRI), Nat. Inst. Allergy Infect. Disease.

MARK TIDSWELL, MD, A Multicenter, Adaptive, randomized Controlled Platform Trial of Safety and Efficacy of Antithrombotic Strategies in Hospitalized Adults with COVID-19, NYU School of Medicine, Nat. Heart Lung Blood Inst.

PEDIATRICS

MANDI SUMMERS, FY21 CPS Administration, MA Exec. Office Public Safety, US Dept. of Highway Safety.

Remembering Alan Schneyer, PhD, friend and colleague

Alan Schneyer was a vital part of the community at Baystate Medical Center, and therefore, his death on November 18th, 2020 has impacted many of us. He was a researcher, a teacher, an entrepreneur and, most valued, he was a friend and colleague to many of us. Alan was a frequent guest for Grand Rounds in the Division of Endocrinology at Baystate Medical Center, invited lecturer at UMass Amherst and a guest lecturer in courses. He was a collaborator in science locally as well as nationally and internationally. Alan's obituary can be found at bit.ly/3grYZxx. His life is a reminder of what we have all lost, and especially his wife, Elissa Brown, and children, Jon and Becca.

A Life in Science

After more than 20 years as a researcher at Massachusetts General Hospital in Reproductive Endocrinology, Alan was recruited to join the Pioneer Valley Life

Sciences Institute in 2007. Alan was a fixture in the research community of Western Massachusetts with faculty appointments at both Baystate Medical Center and the University of Massachusetts-Amherst. The move to western Massachusetts was stimulated by his creation of a mouse model for polycystic ovarian disease. But his work demonstrated unexpected effects of follistatin-like proteins on the function of pancreatic beta cells and their role in diabetes. This result caused him to shift the focus of his research to diabetes. He could see the potential for a completely new strategy to manage diabetes. This was to devise therapeutics to restore the function of the pancreatic beta cells rather than simply provide insulin by daily injections to patients. A grand idea, but he was unwilling to be satisfied with simply an idea and he committed himself to the task of building this new therapy.

To support new innovations in diabetes care,



Dr. Alan Schneyer, pictured above, passed away on November 18, 2020.

Alan obtained grants from the Juvenile Diabetes Research Foundation and the National Institutes of Health supporting his work. But to drive this work forward to a viable therapeutic would require a more focused approach. Therefore, in 2014 he started Fairbanks Pharmaceuticals, Inc. The company was awarded a patent for their therapeutic in fall 2020. Fairbanks continues with this work and will provide a legacy that most of us aspire to. Some of Alan's posts can

be found at the company's website (fairbankspharma.com/author/aschneyer).

A Friend and Colleague

We remember Alan as the indomitable optimist, an individual who could see opportunities as well as the hurdles. He provided support for those around him. He was recognized for his patience as a teacher. The success of his students and staff reflect his ability to both communicate and stimulate a passion for research. For us, Alan represented the best of science and the effort to use science to improve the lives of people. That included the joy of discovery, the challenge of wrestling with technical problems as well as developing new therapies and the relentless desire to never give up on a dream. Throughout all of this, his compassion was ever-present. He also brought joy when we talked about cycling, watching an ultimate tournament or discussing

a weekend with his family. Alan was much more than a colleague. Though he is sorely missed, Alan leaves us with many more joys for having known and worked with him.

Since Dr. Schneyer's death, the work of Fairbanks Pharmaceuticals has been continued through the leadership of his wife, Elissa Schneyer, and scientific guidance of his collaborator Dr. Melissa Brown together with the staff at Fairbanks Pharmaceuticals. A manuscript by the group has been accepted for publication in *Endocrinology* and will be available online shortly. The title is "FSTL3 Neutralizing Antibodies Enhance Glucose-Responsive Insulin Secretion In Dysfunctional Male Mouse And Human Islets". This work demonstrates the efficacy of a new therapy for treatment of diabetes that serves to preserve the function of pancreatic beta cells, and thus, delaying the need for replacement of insulin.

News from Tufts CTSI



Scholarships Available for Health Economics & Outcomes Research (HEOR) Certificate Program

Baystate Health employees may be eligible for a 40% scholarship to the new Certificate Program in Health Economics and Outcomes Research (HEOR)!

The HEOR Program is offered by the Tufts University Graduate School of Biomedical

Sciences (GSBS) Clinical and Translational Science (CTS) Graduate Program, and is co-directed by David Kent, MD, CM, MSc, Director of the CTS Graduate Program, and Peter Neumann, ScD, Director of the Center for Evaluation of Value and Risk (CEVR).

Individuals seeking an introduction to HEOR, including clinicians and other health care professionals, professionals in the pharmaceutical and biotechnology industry, graduate degree holders, and graduate degree students, are encouraged to apply.

The Program is

designed to accommodate the schedules of learners who are already immersed in professional careers or other training programs. To apply for a scholarship, please email Elizabeth Leary, PhD, Graduate Program Manager, at ewiltrout@tuftsmedical-center.org.

Introducing Tufts CTSI I LEARN!

Tufts Clinical and Translational Science Institute (CTSI) recently launched Tufts CTSI I LEARN (ilearn.tuftsctsi.org), a modern, interactive online learning portal offering non-degree professional education

and training opportunities in clinical and translational research.

Tufts CTSI I LEARN includes live-streamed, blended synchronous and asynchronous courses, self-paced courses, and recorded seminars, workshops, and trainings to support the professional development of research stakeholders including investigators, coordinators, community members, and research participants. The user-friendly platform was built in the D2L Brightspace learning management system.

Anyone interested in exploring Tufts CTSI



I LEARN should create a free user account to access more than 100 learning opportunities. Users of the original I LEARN platform will need to register for new accounts. With a Tufts CTSI I LEARN account, users can keep track of their courses and earn certificates of course completion. Questions? Please email training@tuftsctsi.org.