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Title*  A Monte Carlo simulation of the dosimetry of extraorally applied photobiomodulation therapy

Authors*  Anna N. Yaroslavsky, Wendy B. London, Christine Duncan, Amy F. Juliano, Stephen T. Sonis, Ather Adnan, Nathaniel S. Treister

PI*  Nathaniel S. Treister
Background: Oral mucositis (OM) often occurs after myeloablative hematopoietic cell transplantation. We explore extraoral photobiomodulation therapy (PBMT) for the prevention of OM in children. Objective: To use modeling of PBMT to determine optimal treatment sites and parameters for a safe and efficacious treatment. Methods: MRI images from eighteen pediatric patients were analyzed to obtain morphological information on tissues along each of six trajectories passing through the cheek; lips; submandibular and submental regions; neck, transversely and anteroposteriorly. Eighteen simulations were performed for each trajectory using the Monte Carlo method to calculate light distribution and finite difference method to solve the heat transfer equation. Our model accounts for the geometry of emitter, optical, thermal, and morphological tissue properties, as well as possible changes of the optical properties during the therapy. We have used a layered tissue model. The optical and thermal properties of tissues were assigned to each pixel individually using published data on the properties of relevant tissues. We evaluated spatially resolved fluence rate and absorbed power. Results and Conclusions: At 850nm and 399mW/cm2, the median dose transmitted ranged from 0.18–2.4J/cm2. Our results reveal that extraoral PBMT shows promise for the prevention of OM in children.

Lay Summary (MUST be limited to 200 words, anything beyond 200 words will be truncated for print). Please keep in mind - Discover Brigham is open to the public, this lay summary needs to be appropriate for lay audiences with NO scientific background. *

Oral mucositis is a painful side-effect of stem cell transplantation. Children currently have no FDA-approved treatment for oral mucositis. A new kind of light therapy called photobiomodulation therapy is a promising treatment for oral mucositis in children who undergo stem cell transplantation. However, we do not know the best way to apply photobiomodulation therapy in order to treat oral mucositis. In this study, we used a computer-generated model of photobiomodulation therapy applied to the head and neck. We simulated the transmission of light through the head and neck under various conditions and found the best settings to apply photobiomodulation therapy for the prevention of oral mucositis.

Clinical Implications (MUST be limited to 40 words and accessible to a lay audience) - please describe the clinical implications of your research.*

Our model has allowed us to determine a potential protocol using photobiomodulation therapy to treat oral mucositis. If validated, our model could potentially revolutionize the treatment of oral mucositis in children from a palliative approach to a preventative one.

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Title*
Generation of Contractile Muscle Fibers and MuSCs from Human Pluripotent Stem Cells

Authors*
Ziad Al Tanoury, Olivier Pourquie

PI*
Olivier Pourquie

Abstract Body (MUST be limited to 200 words, anything beyond 200 words will be truncated for print)*
During embryonic development, skeletal muscles arise from somites, which derive from the presomitic mesoderm (PSM). Based on our understanding of PSM development in vivo and mouse embryonic stem cell differentiation in vitro, we
established conditions allowing efficient differentiation of cultures of human pluripotent cells (hES/hPS) into PSM-like cells without introduction of exogenous genetic material. Our strategy allowed for the production of contractile fibers and Muscle Stem Cells (MuSC) from human pluripotent cells, thus recapitulating stepwise early differentiation of the paraxial mesoderm in vivo. In this context, we used the CRISPR/Cas9 technology and generated several hiPS reporter cell lines recapitulating the posterior PSM development, as well as the earliest and the latest stages of skeletal muscle differentiation. We used our recently published serum-free protocols (Chal et al 2015, Nat Biotechnol and Chal, Al Tanoury et al 2016, Nat Protoc) to generate striated contractile muscle fibers intermingled with PAX7yfp+ progenitors that show MuSC-like characteristics including the ability to regenerate muscle fibers when engrafted into wild-type or dystrophic mice models (mdx). Beyond the study of myogenesis, our strategy offers an attractive platform for the development of relevant in vitro models of muscle dystrophies and drug screening strategies, as well as provides a unique source of cells for tissue engineering and cell therapy approaches.

Lay Summary (MUST be limited to 200 words, anything beyond 200 words will be truncated for print). Please keep in mind - Discover Brigham is open to the public, this lay summary needs to be appropriate for lay audiences with NO scientific background.

During embryonic development, skeletal muscles arise from somites, which derive from the presomitic mesoderm (PSM). Based on our understanding of PSM development in mouse and chicken embryos, we established conditions allowing the efficient production of contractile skeletal muscle fibers and muscle stem cells from human pluripotent stem cells (PSC). Here we used the CRISPR/Cas9 gene editing technology to generate several PSC lines harboring fluorescent reporters recapitulating defined stages of the PSM development and skeletal muscle formation. We provide efficient protocols for the generation of striated, contractile fibers and muscle stem cells able to regenerate muscle fibers when engrafted into wild-type or dystrophic mice models. Beyond the study of myogenesis, our strategy offers an attractive platform for the development of relevant in vitro models of muscle dystrophies and drug screening strategies, as well as provides a unique source of cells for tissue engineering and cell therapy approaches.

Clinical Implications (MUST be limited to 40 words and accessible to a lay audience) - please describe the clinical implications of your research.

Satellite cells (also called MuSCs) represent the ideal candidate for cell therapy approaches that aim at reconstructing muscles and thus, an access to an unlimited source of MuSCs differentiated from PSC could open the possibility of developing cell therapy strategies for muscular dystrophies and drug screening.

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If you selected 'other' please specify your research area:

Title*
Optimizing Seizure Control during Pregnancy with Therapeutic Drug Monitoring

Authors*  PI*
Emile Ansari, Stephanie C. Allien, P. Emma Voinescu, Li Chen, Suna Park, Page B. Pennell  Dr. Page Pennell

Abstract Body (MUST be limited to 200 words, anything beyond 200 words will be truncated for print)*
Prescribing anti-epileptic drugs (AEDs) in pregnant women with epilepsy (PWWE) is complicated by increasing clearances. Prior studies by our group have shown decreasing AED concentrations result in seizure worsening. The magnitude of dose changes needed for the most common AEDs used, lamotrigine and levetiracetam, is not well-known. Our hypothesis was that the two AEDs would be similar.

Methods: PWWE treated in the epilepsy-obstetrics clinic at BWH were tracked prospectively in a longitudinal database. Monthly AED concentrations were obtained and dosages adjusted to maintain the individualized target concentration, as per standard care. The primary aim was to determine and compare the ratios of maximal pregnancy to preconceptional daily dose for lamotrigine and levetiracetam. Only the most recent pregnancy was used. Results Sixty-two lamotrigine and 43 levetiracetam subjects were identified. The mean ratios were 2.30 (+0.99) for maximal pregnancy to baseline preconceptional daily dosage for lamotrigine and 2.13 (+1.00) for levetiracetam, and did not differ (p=0.39, two-tailed t-test). Conclusions These findings provide clinically relevant information to treat PWWE. On average, two-fold or greater dose adjustments are needed for both lamotrigine and levetiracetam. Also, this can reassure PWWE that dose increases are expected and a common strategy to prevent seizure worsening.

Lay Summary (MUST be limited to 200 words, anything beyond 200 words will be truncated for print). Please keep in mind - Discover Brigham is open to the public, this lay summary needs to be appropriate for lay audiences with NO scientific background.*

Optimal clinical care of a woman with epilepsy during pregnancy requires special attention by her health care team and includes obtaining monthly serum anti-epileptic drug (AED) blood levels. During pregnancy, most AEDs are eliminated from the body more efficiently and the blood levels can drop dramatically, leading to seizure worsening. This study examined the dosing changes for the two most commonly used AEDs in women with epilepsy during pregnancy, lamotrigine and levetiracetam. Average ratios of final pregnancy to pre-pregnancy daily doses were 2.3 times for lamotrigine and 2.1 for levetiracetam, although the ratios varied substantially between women. These findings give clinicians a better idea of how much they should expect to increase doses of these AEDs during pregnancy and should provide reassurance to women with epilepsy that dose increases are expected during pregnancy and a common strategy to prevent seizure worsening.

Clinical Implications (MUST be limited to 40 words and accessible to a lay audience) - please describe the clinical implications of your research.*

Dose increases are expected and a common, successful strategy for management of AEDs during pregnancy. Further use of this knowledge allowed our team to conclude that the LTG and LEV ratios would be similar, which was proven through this study.

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If you selected 'other' please specify your research area:

Title*
Iatrogenic inner ear dehiscence after skull base surgery: treatment quandary.

Authors*
Ryan Bartholomew, C. Eduardo Corrales MD

PI*
C. Eduardo Corrales

Abstract Body (MUST be limited to 200 words, anything beyond 200 words will be truncated for print)*
A complication of lateral skull base surgery not well characterized in the literature is iatrogenic inner ear dehiscence. Dehiscence of the otic capsule, the classic example being superior semicircular canal dehiscence, can disrupt the transmittance of vibroacoustic energy within the inner ear. This results in hearing loss (pseudo-) and third-window phenomena including autophony, pulsatile tinnitus, oscillopsia, bone conductive hyperacusis, and sound and pressure induced vertigo. We describe three patients with inner ear dehiscence following lateral skull base surgery and present a management algorithm including intra-operative identification and repair, as well as transcanal round window reinforcement for patients with delayed dehiscence recognition. Two patients had iatrogenic inner ear dehiscence identified only after presenting for third-window symptoms. They subsequently underwent transcanal round window reinforcement resulting in improvement of their symptoms and self-reported quality of life. For one patient, inner ear dehiscence was successfully identified and repaired intra-operatively. This patient experienced expected post-operative hearing deficit but was spared third-window symptoms. Should intra-operative repair not be possible, due either to technical considerations or failure to identify the dehiscence, transcanal round window reinforcement is a minimally invasive intervention which can improve quality of life for patients suffering from third-window symptoms.

Lay Summary (MUST be limited to 200 words, anything beyond 200 words will be truncated for print). Please keep in mind - Discover Brigham is open to the public, this lay summary needs to be appropriate for lay audiences with NO scientific background. *

A complication of lateral skull base surgery is unintended drilling through the bony capsule of the inner ear. This is known as iatrogenic inner ear dehiscence and it can result in hearing loss, vertigo, and a disruptive ability to hear one’s own body sounds including creaking joints, eye movement, and heartbeat. We describe three patients with this complication from lateral skull base surgery. For two patients, the complication was only discovered after being evaluated for the previously mentioned auditory and vertigo symptoms. They subsequently underwent a minimally invasive surgery, transcanal round window reinforcement, which improved their symptoms and quality of life. For another patient, the surgeons identified the complication during the original surgery and were able to repair the damage. This patient was spared many of the symptoms experienced by the prior two patients. In summary, should iatrogenic inner ear dehiscence occur during lateral skull base surgery, attempts to intra-operatively identify and repair the dehiscence should be made. Otherwise, transcanal round window reinforcement is a minimally invasive surgery which can be done at a later time to improve symptoms resulting from the complication.

Clinical Implications (MUST be limited to 40 words and accessible to a lay audience) - please describe the clinical implications of your research.*

Transcanal round window reinforcement is a minimally invasive intervention which can improve quality of life for patients with symptoms caused by unintended drilling through the inner ear during lateral skull base surgery.
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- Regenerative Medicine
- Women's Health & Gender Biology

If you selected 'other' please specify your research area:

Title*
The BabySeq Project: Early Observations from a Randomized Trial of Exome Sequencing in Newborns

Authors*

PI*
Robert C. Green
The BabySeq Project is the first randomized trial examining the implications of returning a newborn’s genomic sequencing (GS) information to their parents and clinicians. Infants are enrolled from the well baby nursery and the ICU. All families receive state-mandated newborn screening and a family history assessment, while half are randomized to additionally receive exome sequencing. We report monogenic disease risk, carrier status for recessive conditions, and limited pharmacogenomic (PGx) risk. To date, GS information has been returned for 96 healthy and 15 ICU infants. Variants associated with monogenic disease risk were found in 8 healthy infants indicating risk for dilated cardiomyopathy, supravalvular aortic stenosis, hearing loss, biotinidase deficiency and atypical hemolytic-uremic syndrome. Monogenic variants associated with hypoplastic left heart, hereditary cancer, and KBG syndrome were identified in 3 ICU infants. Carrier status variants were identified in 96 infants. 207 carrier variants were reported in 148 genes with infants averaging 2 variants each (range 0-6). PGx variants associated with atypical responses to medications that may be relevant in childhood were identified in 6 infants. By surveying parents and clinicians, we aim to better understand the impact of GS on newborn healthcare and how best to integrate GS into clinical pediatric care.

Variants associated with monogenic disease risk were found in 8 healthy infants indicating risk for dilated cardiomyopathy, supravalvular aortic stenosis, hearing loss, biotinidase deficiency and atypical hemolytic-uremic syndrome. Monogenic variants associated with hypoplastic left heart, hereditary cancer, and KBG syndrome were identified in 3 ICU infants. Carrier status variants were identified in 96 infants. 207 carrier variants were reported in 148 genes with infants averaging 2 variants each (range 0-6). PGx variants associated with atypical responses to medications that may be relevant in childhood were identified in 6 infants. By surveying parents and clinicians, we aim to better understand the impact of GS on newborn healthcare and how best to integrate GS into clinical pediatric care.

How would knowing one’s entire genetic blueprint from birth affect a person’s life? Could this information improve healthcare? Such questions inspired the BabySeq Project, the first randomized clinical trial exploring the impact of genomic sequencing in newborns. Infants are enrolled from the well baby nursery and the ICU. All receive the standard of care and a family history assessment, while half also receive genomic sequencing. Genetic results have been returned for 96 healthy and 15 sick infants. 8 healthy infants and 3 sick infants were found to be at risk for diseases including heart conditions, hereditary cancer, hearing loss, vitamin deficiency, kidney disease and a neurodevelopmental syndrome. 96 infants were carriers for recessive genetic disorders, relevant for family planning, but not expected to have a direct impact on the infant’s health. On average, each infant was found to be a carrier for 2 disorders (range 0-6). 6 infants were found to have genetic changes that may affect their response to certain medications. Surveys are administered to the infant’s parents and clinicians. By analyzing responses to these surveys, we hope to better understand the impact of GS on newborn healthcare, and how best to integrate it into clinical pediatric care.

Genomic newborn sequencing has the potential to provide comprehensive and clinically useful information on many conditions. The BabySeq Project is the first randomized clinical trial exploring the impact of genomic sequencing on healthy and ICU infants, their parents and clinicians.
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Title*  
Functionally Clustered microRNAs for GBM Reprogramming and Therapy

Authors*  
Vivek Bhaskaran, Mahmoud Idriss, Josie L Hayes, Sean E Lawler, E Antonio Chiocca, Jakub Godlewski, Pier Paolo Peruzzi

PI*  
Pier Paolo Peruzzi

Abstract Body (MUST be limited to 200 words, anything beyond 200 words will be truncated for print) *
Deregulation of microRNAs, a class of small non-coding RNAs which work by repressing protein translation, is a hallmark of GBM. The study of their role in the tumor pathobiology, however, has been almost exclusively limited to investigating the biological effect of single microRNAs, failing to recognize the possible importance of their combinatorial action. MicroRNA expression analysis from more than 500 GBM specimens revealed that there are a small number of microRNAs, down regulated in all tumors, whose expression is strongly correlated. The vast majority of these microRNAs are physiologically expressed together in neurons, suggesting that these "clustered" microRNAs could work as a functional network determining proper control of cellular biology and lineage determination. Consequently, we found that stepwise re-expression of a progressively increasing number of these "clustered" neuronal microRNAs in patient-derived GBM stem cells expands the number of targeted oncogenic proteins, including several proteins involved in epigenetic control of gene expression and maintenance of stemness. In comparison to single microRNAs, combinatorial re-expression of multiple neuron specific microRNAs resulted in a greater ability to induce differentiation toward a more benign neuronal phenotype, and decreased proliferation and tumorigenicity in vivo. Importantly, we also show that it is possible to engineer an artificial polycistronic microRNA cluster to simultaneously encode multiple neuronal microRNAs, thus creating a novel GSC-reprogramming construct. This artificial gene can be successfully delivered to GSCs by lentiviral vectors, resulting in proper expression of the multiple microRNAs and consequent profound biological effects.

Lay Summary (MUST be limited to 200 words, anything beyond 200 words will be truncated for print). Please keep in mind - Discover Brigham is open to the public, this lay summary needs to be appropriate for lay audiences with NO scientific background. *

The most common and aggressive brain tumor is called glioblastoma. It occurs at any age but it is vastly more frequent between 50-70 years. Glioblastoma is a killer. Patients with this form of cancer rarely survive longer than 12-14 months from the time the tumor is diagnosed. Cancer cells that constitute glioblastoma can interact with the cells of the normal brain and exploit them to better survive, grow and invade the surroundings. The currently accepted mainstay of treatment for GBM is surgery followed by radiation and chemotherapy with TMZ. Yet, despite this intensive regimen, median survival is less than 15 months. It is crucial to develop new strategies to improve tumor control and patient survival. The more diverse such strategies are, the higher the likelihood that they could be used in combination, thus increasing the chances of an effective clinical benefit. Conventional gene therapy has not had much impact on GBM treatment to date, mainly because single gene targeting. Our proposal changes this paradigm suggesting that multiple gene delivery would achieve a broad and significant effect. Hence, microRNAs are ideal candidates, by virtue of their unique features like extremely small size which allows multiple genes to be fitted into a delivery vector, thus allowing re-expression of specific microRNA clusters concomitantly. Since therapeutic microRNAs are highly expressed in non-tumor cells, their delivery to the tumor should have few, if not any “off-target” effects on surrounding normal tissues.

Clinical Implications (MUST be limited to 40 words and accessible to a lay audience) - please describe the clinical implications of your research.*

We provide a rationale for using multiple microRNAs as a new weapon for GBM therapy, synergistic with the current standard of care, specifically we believe that microRNAs can be used to reduce GBM escape from current standard therapies, thus augmenting their efficacy and prolonging survival.

* 

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Title*
Effects of prenatal vitamin D exposure on somatic growth and development in infancy: Results of the VDAART trial

Authors*
Adrianna Boulin, Nancy Laranjo, Vincent J. Carey, BJ Stubbs, Jessica Wolfe, Augusto A. Litonjua, Scott T. Weiss

PI*
Scott T. Weiss

Abstract Body (MUST be limited to 200 words, anything beyond 200 words will be truncated for print)*
The Vitamin D Antenatal Asthma Reduction Trial (VDAART) was a randomized, double-blind, placebo-controlled trial conducted in three sites across the United
States. The objective of the study was to determine whether prenatal vitamin D supplementation could prevent asthma or recurrent wheeze in early childhood. Four hundred and forty women were randomized to receive 4000 IU vitamin D plus a prenatal vitamin containing 400 IU vitamin D daily, and 436 women were randomized to receive a placebo plus a prenatal vitamin containing 400 IU vitamin D daily. In addition to asthma outcomes, anthropometric data was evaluated to determine if vitamin D supplementation or levels affected growth measures. We found no significant effects of Vitamin D supplementation or maternal vitamin D levels at baseline or third trimester on weight or head circumference at birth, year 1, or year 3 in models adjusting for common covariates (all $p \geq 0.089$). However, there was an effect of cord blood Vitamin D level on Birth weight in the adjusted model. Children born prematurely were excluded in this analysis. Irrespective of treatment, VDAART growth curves estimated with lmsqreg (https://rdrr.io/rforge/lmsqreg/) show accelerated growth in weight after two years compared to CDC references.

**Lay Summary (MUST be limited to 200 words, anything beyond 200 words will be truncated for print). Please keep in mind - Discover Brigham is open to the public, this lay summary needs to be appropriate for lay audiences with NO scientific background.**

The Vitamin D Antenatal Asthma Reduction Trial (VDAART) was a study with participants across three sites in the United States sorted into two groups: a study group and a control group. The objective of the study was to determine whether prenatal vitamin D supplementation could prevent asthma or recurrent wheeze in early childhood. Both the participant and study staff were unaware of who was sorted into what group. The study group received a daily dose of 4000 IU of vitamin D and a prenatal vitamin containing 400 IU vitamin D, while the control group just received a daily dose of the prenatal vitamin containing 400 IU vitamin D. Supplementation of vitamin D showed no major effects on weight or head circumference at birth, year 1 or year 3 in adjusted models. However, cord blood vitamin D levels were associated with slightly heavier babies.

**Clinical Implications (MUST be limited to 40 words and accessible to a lay audience) - please describe the clinical implications of your research.**

Our study showed no significant effects of vitamin D supplementation on growth measures. However, vitamin D supplementation may provide other clinical benefits.

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Title*
Focused Ultrasound Platform for Delivering Mechanical Stimulation to Epileptic Tissue in Humans

Authors*
Spencer Brinker, Ellen Bubrick, Timothy Mariano, Nathan McDannold

PI*
Ellen Bubrick

Abstract Body (MUST be limited to 200 words, anything beyond 200 words will be truncated for print)*
The platform presented in this project is intended for investigating the safety and efficacy of delivering long term, repeated exposure of Pulsed Low Intensity
Focused Ultrasound (PLIFU) to epileptic tissue in humans with refractory epilepsy. Sixty-five million people are affected worldwide by epilepsy while 30% of patients continue having seizures despite medication or cannot handle surgery based on health reasons. Noninvasive neuromodulation such as transcranial magnetic stimulation has failed to produce any positive outcomes in reducing seizures. This warrants investigations using alternative forms of brain stimulation like PLIFU. A focused ultrasound piezoelectric transducer is mounted and submerged underwater within a probe. The ultrasound beam is noninvasively transmitted to the brain through a water bag coupled between the probe and head. A manual positioner is combined with a neuronavigation system and pretreatment MRI for positioning the ultrasound focal area in epileptic tissue regions. The probe design allows PLIFU delivery to multiple locations while only using one coupling position of the water bag. Novel acoustic emission detection and electroencephalography scalp sensors are used in the platform for monitoring focused ultrasound transmission and electrophysiological assessment, respectfully of the brain during treatment. Expected trial outcomes are changes in interictal spikes and decrease seizure frequency.

**Lay Summary (MUST be limited to 200 words, anything beyond 200 words will be truncated for print). Please keep in mind - Discover Brigham is open to the public, this lay summary needs to be appropriate for lay audiences with NO scientific background.**

The platform included in this project is a machine that sends small vibrations into people’s brains that have lots of seizures. Epilepsy is when someone has abnormal electrical activity in their brain, which results in recurring seizures. Most seizures include convulsions when your body shakes uncontrollably or causes unconsciousness and sometimes people have a seizure and no one notices. Some seizures last longer than others and the number of seizures are different for each person with epilepsy. People with epilepsy can be treated with medication or surgery. However, many people cannot handle surgery based on health reasons or the medication does not help. For this group, physicians have tried exposing parts of their brains to low-powered magnetic or electric fields for several hours spread out over weeks to decrease or stop the amount of seizures. Unfortunately, these treatments have not worked. Sending vibrations into the brain may be an alternative way to help stop seizures. The machine built in this project works similar to how ultrasound imaging takes pictures of a woman’s fetus. Sound will instead be pointed to places in the brain where the abnormal electrical activity is causing the seizures and will hopefully help stop them.

**Clinical Implications (MUST be limited to 40 words and accessible to a lay audience) - please describe the clinical implications of your research.**

The focused ultrasound platform provides novel instrumentation for investigating a potentially new treatment option for refractory epilepsy.

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Title*
A 5-YEAR ANALYSIS OF THE VIOLENCE RECOVERY PROGRAM AT BRIGHAM AND WOMEN’S HOSPITAL

Authors* Elizabeth A Bryant MPH, Manuel Castillo-Angeles, MD, MPH
Deepika Nehra Marta Chadwick Ramsis Ramsis Leo Andrew Benedict Reza Askari, MD Ali Salim, MD

PI* Ali Salim, MD
Abstract Body (MUST be limited to 200 words, anything beyond 200 words will be truncated for print)*

Objectives: Our hospital established a violence recovery program (VRP) in 2012 to provide in-hospital and community case management for victims of violence. Our aim was to assess the short term performance of VRP and to describe the patients who utilized the offered resources. Methods: This single-center retrospective study includes patients admitted from 2012 to 2016. Data was obtained from VRP’s database and BWH’s Trauma Registry. Participants approached by VRP but refused further interventions were classified as non-users; those with a minimum of 3 encounters were considered high-users. Demographics and injury characteristics were compared between non-users and high-users. Services utilized by high-users were examined. Results: 447 patients were included; 134 (30%) were high-users. High-users compared to non-users were younger (p=0.0005), more likely to be black (p<0.001), more likely to have sustained a gunshot wound (p<0.001) and had longer hospital lengths of stay (p<0.001). High-users most commonly used housing assistance (63%), employment assistance (59%), and safety planning (41%). Conclusion: Over five years, our VRP provided extensive assistance to 30% of eligible patients. We did not identify any modifiable factors differentiating high-users from non-users. Further work is ongoing to identify barriers to utilization of VRP services to improve utilization and evaluate longer-term outcomes.

Lay Summary (MUST be limited to 200 words, anything beyond 200 words will be truncated for print). Please keep in mind - Discover Brigham is open to the public, this lay summary needs to be appropriate for lay audiences with NO scientific background. *

In 2012, Brigham and Women’s Hospital created a program called the Violence Recovery Program (VRP) to assist patients injured by stabbing or guns with challenges they may face after they leave the hospital. An example would be to help feel safe when they go home or find accessible housing. We wanted to see which patients used VRP the most and which services they used. We looked at patients who were seen by VRP between 2012 and 2016. We decided that patients who refused VRP services would be called non-users and patients who saw VRP three or more times would be called high-users. We included 447 patients. Almost one third were high users. The high users were young, more likely to be black, more likely to have been injured by a gun, and stayed in the hospital longer than non-users. High users used housing assistance, employment assistance, and safety planning the most. Our VRP provided extensive assistance to 30% of patients who could have been seen by them. This suggests that patients may have challenges seeing VRP, especially if they are not in the hospital for a long time. Our next steps will be to determine what these challenges are.

Clinical Implications (MUST be limited to 40 words and accessible to a lay audience) - please describe the clinical implications of your research.*

Understanding which patients are most likely to use VRP and which services are most commonly used by patients is essential to ensuring VRP is meeting patients' needs.
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- Patient-Centered Outcomes/Comparative Effectiveness
- Regenerative Medicine
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If you selected 'other' please specify your research area:

Title*
Interleukin-1 Blockade Improves Left Ventricular Contractility in Acute Heart Failure without Increasing Myocardial Work

Authors*
Leo Buckley, Salvatore Carbone, Cory Trankle, Justin Canada, Claudia Oddi Erdle, Jessica Regan, Michele Viscusi, Dinesh Kadariya, Hayley Billingsley, Ross Arena, Antonio Abbate, Benjamin Van Tassell

PI*
Leo Buckley
Inflammation correlates with poor outcomes in acute heart failure (AHF). Interleukin-1 (IL-1) is a cytokine that drives inflammation in AHF. IL-1 acts as a direct cardiosuppressant and blunts the response to isoproterenol stress testing in mice. We hypothesized that, in patients with acute HF, IL-1 blockade improves left ventricular (LV) contractility. Data were pooled from two clinical trials. AHF patients were randomized to IL-1 blockade with IL-1 receptor antagonist (anakinra) or placebo for 14 days starting in hospital (n=13) or within 2 weeks post-discharge (n=40). LV contractility was measured as LV end-systolic elastance (Ees) and LV ejection fraction (LVEF). Myocardial work was calculated as a myocardial oxygen consumption surrogate. There were no baseline differences between both groups regarding Ees (1.04 vs. 0.93 for anakinra vs. placebo) or LVEF (30% vs. 30%) (P>0.90 for both). Ees and LVEF increased significantly in anakinra (∆Ees=0.13 and ∆LVEF=4%; P=0.03 vs. baseline for both), but not placebo patients (P>0.22 for both). Pressure-volume area did not change in either group (p>0.19 for both groups). These pilot data suggest that anakinra increases LV contractility in AHF. Most important, anakinra did not affect myocardial work, marking an important distinction from positive inotropes.

Lay Summary: In patients who are hospitalized for acute heart failure, high levels of inflammation are associated with worse outcomes. Inflammation weakens the heart’s ability to squeeze and eject blood. The medication anakinra has strong anti-inflammatory effects by activating one of the body’s natural defenses against abnormally high inflammation levels. However, it is unknown whether blocking inflammation in acute heart failure will affect the heart’s squeezing capacity. We tested whether anakinra can improve the heart’s squeezing function in patients with acute heart failure. Patients were assigned randomly to receive either anakinra or a placebo dummy medication for 2 weeks. We measured the heart’s squeezing function with end-systolic elastance and with ejection fraction. In patients who received anakinra, both measures of heart squeeze increased. In placebo patients, there was no change. Importantly, the heart did not need to increase its energy usage in order to increase squeezing function. These data are important as they improve our understanding of anakinra and indicate that larger clinical trials of anakinra are needed.

Clinical Implications: Anakinra improves contractility without increasing myocardial oxygen consumption - an important distinction from positive inotropes. IL-1 blockade with anakinra has shown promising results in phase 2 heart failure clinical trials.
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- Women's Health & Gender Biology

If you selected 'other' please specify your research area:

Title*
A Monoclonal anti- aP2 Antibody treats type 2 diabetes and Fatty Liver Disease

Authors*
M. Furkan Burak, Karen Inouye, Ariel White, Alexander Lee, Amir Tirosh, Ediz Calay, Gurol Tuncman, Kosei Eguchi, Adrian Moore, Gokhan Hotamisligil

PI*
Gokhan Hotamisligil
The lipid chaperone aP2/FABP4 has been implicated in the pathology of many immunometabolic diseases, including diabetes in humans, but aP2 has not yet been targeted for therapeutic applications. aP2 is not only an intracellular protein but also an active adipokine that contributes to hyperglycemia by promoting hepatic gluconeogenesis and interfering with peripheral insulin action. Serum aP2 levels are markedly elevated in mouse and human obesity and strongly correlate with metabolic complications. These observations raise the possibility of a new strategy to treat metabolic disease by targeting serum aP2 with a monoclonal antibody (mAb) to aP2. We evaluated mAbs to aP2 and identified one, CA33, that lowered fasting blood glucose, improved systemic glucose metabolism, increased systemic insulin sensitivity, and reduced fat mass and liver steatosis in obese mouse models. We examined the structure of the aP2-CA33 complex and resolved the target epitope by crystallographic studies in comparison to another mAb that lacked efficacy in vivo. In hyperinsulinemic-euglycemic clamp studies, we found that the antidiabetic effect of CA33 was predominantly linked to the regulation of hepatic glucose output and peripheral glucose utilization. The antibody had no effect in aP2-deficient mice, demonstrating its target specificity. We conclude that an aP2 mAb-mediated therapeutic constitutes a feasible approach for the treatment of diabetes.

Lay Summary: Obesity, diabetes and other related cardiovascular diseases have been tremendously threatening humanity around the world and became a huge out-of-control pandemic-public health problem. These diseases caused not only higher rates of early death (mortality) and injury (morbidity) in the world, but also economic burden that has been amounted to trillions of dollars per year. Today, there are more than 400 million diabetics around the world, and furthermore, one of every two patients are unaware of his/her disease. Thereby, if we include the obese and overweight risk groups, this problem directly affects more than one billion people in the world and threatens the world economy. aP2 is an active adipokine that releases by fat cells and increases glucose production in liver, hence contributes to high blood sugars in diabetes. Also, aP2 levels increase in human obesity and therefore plays a significant role in the development of obesity related diabetes. We accomplished to block this harmful hormone in blood circulation by a monoclonal antibody coded as CA33, which we developed through the technology of vaccination. This novel drug decreased fasting blood glucose and cholesterol levels, improved insulin sensitivity, and decreased fat accumulation in the liver despite severe obesity.

Clinical Implications: An anti-aP2 monoclonal antibody could treat obesity related metabolic alterations such as type 2 diabetes, fatty liver disease and dyslipidemia.
First Name*  
Lee-Shing

Last Name*  
Chang

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Clinical/Research Fellow

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Outcomes Research

Title*  
A weighty issue: Gender disparities in bariatric surgery counseling

Authors*  
Lee-Shing Chang, Shervin Malmasi, Naoshi Hosomura, Huabing Zhang, Victor J. Lei, Alexa Rubin, Clara Ting, Kimhouy Tong, Alexander Turchin

PI*  
Alexander Turchin
Bariatric surgery (BS) achieves superior weight loss and reduction in morbidity/mortality in patients with obesity compared with lifestyle/medical interventions. Despite these benefits, few patients with obesity undergo BS. Importantly, little systematic data exist on how frequently providers discuss BS with patients. We developed and validated a natural language processing program to identify documentation of BS discussion in narrative provider notes (sensitivity 83.3%, PPV 100% in detecting BS counseling). We utilized this program to study rates of BS counseling in patients with moderate to severe obesity who had not previously undergone BS. Analysis of 1,466,051 notes from 66,263 patients with obesity seen at BWH over the past 20 years showed that women with BMI >=35 kg/m² were significantly less likely than men with comparable BMI to receive BS counseling (1.5% of notes for women versus 1.7% of notes for men; p <0.0001). This gender disparity was most pronounced among patients with highest BMI (3.7% of notes for women versus 6.2% of notes for men with BMI>=45 kg/m², p <0.0001). Few patients with obesity receive BS counseling; women receive even less counseling than men. Further investigation is needed to improve awareness of this effective treatment and reduce gender disparities in obesity management.

Few patients with obesity receive counseling on bariatric surgery as a treatment option. Women receive even less counseling than men. Further investigation is needed to improve awareness of this effective treatment and reduce gender disparities in obesity management.
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- Regenerative Medicine
- Trauma
- Women’s Health & Gender Biology
- Other

If you selected 'other' please specify your research area:

Title*
SEQaBOO (SEQUencing a Baby for an Optimal Outcome)

Authors*
Yvonne I. Chekaluk1, Anne B.S. Giersch1,4, Jun Shen1,4, Margaret R. Toro1, Linda B. Johnson1, Margaret A. Kenna2,4, Juliana Manganella2, Michael S. Cohen3,4, Patricia Levesque3, Jennifer Hochschuld5, Kathryn Gregory1,4, and Cynthia C. Morton1,4
1Brigham and Women’s Hospital, 2Boston Children’s Hospital, 3Massachusetts Eye and Ear, 4Harvard Medical School, 5Harvard University

Abstract Body (MUST be limited to 200 words, anything beyond 200 words will be truncated for print)*
Hearing loss is the most common sensory deficit in humans. One in 500 newborns has hearing loss and the frequency increases to one in 100 by school age. Congenital hearing loss can present as syndromic (accompanied by pathology in other organ systems), or nonsyndromic (where deafness is the only finding), with the latter accounting for approximately 70% of congenital hereditary deafness. Over 150 genetic loci have been discovered for nonsyndromic hearing loss, but causative genes have been identified for only about half. There is a critical need for clinical genomics applications to identify genetic and molecular etiologies of hearing loss. Through genomic sequencing of DNA from newborns who do not pass hearing screening, SEQaBOO will integrate high-throughput genomic approaches into routine newborn screening for hearing loss, to facilitate early and more precise diagnosis, more effective management, and better potential therapeutic interventions. We will analyze and assemble genomic data and, perform annual surveys of the cohort of children to ascertain general health, including speech and language development in addition to hearing status, and parental attitudes and implications of genomic sequencing in newborns.

Lay Summary (MUST be limited to 200 words, anything beyond 200 words will be truncated for print). Please keep in mind - Discover Brigham is open to the public, this lay summary needs to be appropriate for lay audiences with NO scientific background.
Hearing loss is the most common sensory deficit in humans. One in 500 newborns has permanent hearing loss and that number increases to 1 in 100 children by school age. Early detection and intervention of hearing loss before the critical period of speech and language acquisition translate into improved social skills, academics, and quality of life. Universal newborn hearing screening was adopted in the U.S. since the 1990s. Massachusetts requires that all newborns be offered hearing screening prior to hospital discharge. Newborns who do not pass this initial screen are scheduled at approximately 1 month of age for a follow-up diagnostic hearing test. However, clinical diagnosis often does not distinguish among different types of hearing loss. SEQaBOO will investigate how genomic information may benefit and assist in providing care and management of newborns with hearing loss. Through genomic sequencing of DNA from newborns who do not pass hearing screening, we hope to provide the earliest possible diagnosis of any genetic cause of hearing loss, to guide optimal clinical management and avoid unnecessary diagnostic tests. In addition, through this project, we will ascertain the impact on the child's development through annual surveys regarding general health, hearing, and speech and language development.

**Clinical Implications (MUST be limited to 40 words and accessible to a lay audience) - please describe the clinical implications of your research.**

The SEQaBOO project is designed to elucidate possible genetic causes of hearing loss in newborns, to provide a better avenue for personalized medicine and more precise early diagnosis, better management, and more optimal targeted therapeutics for hearing loss.
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<td>Cirelli</td>
<td>MSN, ACNS-BC</td>
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<td>Clinical Nurse Educator</td>
</tr>
</tbody>
</table>

**Twitter Handle (if applicable)**

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If you selected 'other' please specify your research area:

Nursing Quality Improvement

**Title**

Staff Perceptions of the BWH Phlebotomy Program

**Authors**

Anne Brogan, MS, RN; Elizabeth Cirelli MSN, RN, ACNS-BC; Joyce Johnson PhDc, RN, Elizabeth Jan McGrath, BSN, RN, MHA; Sarah Thompson, MSN, RN, CCNS

**PI**

Anne Brogan
In December 2016, as part of an innovative way of providing care for patients, BWH decided to start a unit based phlebotomy program. The Patient Care Assistants (PCAs) were trained to provide phlebotomy service for patients. Identified concerns with the centralized program included delayed lab collection and results affecting the timing of clinical decision making and patient discharge. The program was piloted on a few units before the hospital wide training began. The roll out on 15ABCD was managed with assistance from a Program Manager, two unit Clinical Educators, and two Nursing Directors. The PCAs were given a choice to participate in the program. Those who said yes received additional compensation, a 4-hour educational class, an online tutorial, instruction on the patient identification and label verification process, and 16-24 hours of skills practice with a phlebotomist who deemed them competent. Fifty-five percent of the 15abcd unit based PCAs were trained to perform phlebotomy. To evaluate staff’s perception of the success of the program, an online survey was utilized. A response rate of 43% was obtained. Of the respondents, 54% believe labs are being collected in a timely manner. Overall, PCAs answered questions more favorably than the RN staff.

Quality improvement initiatives occur every day in the healthcare field. Results are often determined by comparing various data points. This study looked at the success of one such program through the eyes and the lived experiences of its participants. Tower 15ABCD began on a quality improvement initiative: unit based phlebotomy. Patient Care Assistants (PCA) who volunteered received a 4-hour educational class, an online tutorial, instruction on the use of the clinical application utilized for phlebotomy, and 16-24 hours of skills practice with a phlebotomist. In the first nine months, 55% of the unit based PCAs were trained. With the support of the hospital based phlebotomy service, the program has been effective. To assist future units when implementing this program and to improve the current system on 15ABCD, the leadership team on the unit decided to evaluate the clinical staff's perception of the initiative. An 8-question online survey was designed. The questionnaire was administered to both registered nurses and the PCA staff. A response rate of 43% was obtained. 54% of respondents believe labs are being collected in a timely manner. Overall, PCAs answered questions more favorably than the RN staff.

Quality improvements projects that have the support of staff tend to be more successful. The opinions of the end users can identify areas for improvement, motivate change, and ensure the long-term success of the project.
First Name*  Laila
Last Name*  Cochon
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If you selected 'other' please specify your research area:
Patient Safety

Title*
Safety Events in Diagnostic Imaging from an Electronic Safety Reporting System

Authors*  Laila Cochon, Ronilda Lacson, Aijia Wang, Ramin Khorasani
PI*  Ronilda Lacson

Abstract Body (MUST be limited to 200 words, anything beyond 200 words will be truncated for print)*
Background: Although diagnostic imaging is predominantly non-invasive, it carries safety risks that could potentially harm patients. Identifying safety events in diagnostic imaging is of utmost importance. Purpose: Measure the incidence of reported safety events that are related to diagnostic imaging from safety reports submitted in the Electronic Safety Reporting System (ESRS), and assess contributing factors to these safety events. We evaluated safety events that were attributed to person factors compared to non-person factors and compared the proportion of events that led to patient harm. Methods: From all safety events reported in the institutional ESRS at the Brigham and Women’s Hospital between January 01 2015 and December 31, 2015, safety reports related to diagnostic imaging were obtained. • reports were manually assessed by two independent reviewers, including 10% of reports that were reviewed by both reviewers, for human factors that contributed to the safety event. • SEIPS 2.0 human factor framework was used to classify human factors into the following: person, organization, task, tools/technologies and environment. Inter-reviewer agreement was measured. • Kappa agreement between reviewers was reported • chi-square was used to compare proportion of events that led to patient harm among events attributed to person factors compared to non-person factors. Results: A total of 11,570 safety reports were retrieved from the ESRS, 854 of which were classified under the general event type "Imaging" or occurred at an imaging site. 71% of events were attributed to 'person' factors (606/854). Using the SEIPS framework, events were classified as follows: 606 events from the safety reports were attributed to 'person' factors, of which 107 (17.7%) led to harm, 550 events were attributed to other non-person factors, of which 150 (27.3%) resulted in harm (chi-square analysis, p<0.0001). Kappa measurement for inter-annotator agreement revealed kappa=0.79 (95% CI, 0.598-0.987). Conclusion: Most safety events in the ESRS were attributed to 'person' factors. However, events attributed to person factors resulted in significantly less patient harm, compared to all other factors. Most events with reported harm were attributed to task and environment factors, which can be addressed in future institutional initiatives.

Lay Summary (MUST be limited to 200 words, anything beyond 200 words will be truncated for print). Please keep in mind - Discover Brigham is open to the public, this lay summary needs to be appropriate for lay audiences with NO scientific background.*

This projects purpose was to identify potential patient safety events within diagnostic imaging. For this, we used data from our internal safety reporting system, limited to diagnostic imaging events or happening in a radiology facility. In order to correctly characterize and identify contributing factors, an ergonomics scheme by Carayon et. al was used.

Clinical Implications (MUST be limited to 40 words and accessible to a lay audience) - please describe the clinical implications of your research.*

Patient safety is of the utmost importance for our institution, this research sought to identify and characterize patient safety events within diagnostic imaging. Conclusions and further research can help improve quality and patient safety.
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- Trauma
- Other

If you selected 'other' please specify your research area:

Title*
Protein Biomarker Detection Using Single Molecule Arrays for Early Detection of Cancer and Monitoring Response to Therapy

Authors*
Limor Cohen, David R. Walt

PI*
David R. Walt

Abstract Body (MUST be limited to 200 words, anything beyond 200 words will be truncated for print)*
Biomarker measurements in blood are important for disease detection, monitoring, and treatment. Biomarkers are typically elevated in the affected organ but become diluted and decrease in concentration once they enter the bloodstream. The ability to detect low levels of blood biomarkers will enable early detection of disease and increased survival rates. The most commonly used biomarkers are nucleic acids and proteins. Sensitive nucleic acid detection is made possible by the polymerase chain reaction (PCR) and related technologies, which can amplify a single molecule. On the other hand, such amplification does not exist for protein detection and thus protein detection methods suffer from lack of analytical sensitivity. Therefore, tools capable of high sensitivity measurements are necessary for measuring protein biomarkers in blood. We have developed an ultra-sensitive protein detection method using Single Molecule Arrays, which is capable of measuring proteins in biological fluids at sub-ng/ml concentrations. Here, we describe the principles of this technology and clinical applications for measuring protein biomarkers in patient samples for early detection of breast cancer and monitoring response to immuno-therapy.

Lay Summary (MUST be limited to 200 words, anything beyond 200 words will be truncated for print). Please keep in mind - Discover Brigham is open to the public, this lay summary needs to be appropriate for lay audiences with NO scientific background. *

Blood tests are instrumental for diagnosing disease. A blood test to detect breast cancer early is a major goal of our research. Blood tests are less invasive than tissue biopsies and can be administered yearly at a regular check-up. Using this approach, we hope to be able to detect cancer early before it metastasizes and reaches a later stage. Another aspect of our research is to monitor response to therapy. Many cancers, even those affecting the same organ, are biologically different. Some patients may respond to a given drug, while others do not. We aim to identify responders to a drug shortly after drug administration, using a simple blood test, to improve disease treatment.

Clinical Implications (MUST be limited to 40 words and accessible to a lay audience) - please describe the clinical implications of your research.*

We are interested in identifying protein biomarkers in the blood for early detection of breast cancer and for monitoring response to cancer therapy. This will result in better disease prognosis and more effective therapy.

* 

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If you selected 'other' please specify your research area:

Title*
Probing the immunomodulatory potential of mesenchymal stromal cell-derived extracellular vesicles

Authors*

PI*
Jeff Karp

Abstract Body (MUST be limited to 200 words, anything beyond 200 words will be truncated for print)*
Mesenchymal stromal cells (MSC) are a promising cell source for cell-based therapies as they exhibit a potent immunomodulatory action in different diseases. The MSC secretome appears to be responsible for their immunomodulatory potential and MSC-derived extracellular vesicles (EVs) play a key role in mediating the immunomodulatory effects of MSCs. However, clinical translation of MSC-EV therapies requires optimized protocols for isolation, characterization and functional evaluation. This work aims to develop functional assays to assess the immunomodulatory potential of MSC-EV isolated from different MSC donors. Our
EV characterization analysis indicates consistent EV isolation and purity from different MSC donors. Monocyte and endothelial cell-based assays developed were able to distinguish between different MSC-EV donors based on their immunomodulatory properties. Active EV fractions also suppressed inflammation and loss of barrier function in a human Lung-on-a-Chip pulmonary inflammation model. These functional assays are useful tools that can be used to select potent MSC-EV donors towards the evaluation of their future therapeutic potential.

**Lay Summary (MUST be limited to 200 words, anything beyond 200 words will be truncated for print). Please keep in mind - Discover Brigham is open to the public, this lay summary needs to be appropriate for lay audiences with NO scientific background.**

Regenerative properties of mesenchymal stromal cells have been widely studied in several pre-clinical and clinical trials. Extracellular vesicles secreted by mesenchymal stromal cells play a key role as it has been shown that the extracellular vesicles replicate the mesenchymal stromal cell action and avoid the safety concerns associated with cell administration. Therefore, extracellular vesicles have great potential in regenerative medicine. This project focus on the development of therapies based on mesenchymal stromal cell-derived extracellular vesicles and on the establishment of tools to assess their immunomodulatory potential on reducing inflammation.

**Clinical Implications (MUST be limited to 40 words and accessible to a lay audience) - please describe the clinical implications of your research.**

Inflammation is a common state of many diseases including lung and cardiovascular diseases. The development of cell-based but cell-free therapies using mesenchymal stromal cell-derived extracellular vesicles have great potential on reducing inflammation and promoting regeneration of injured tissues.

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BWH Division (if applicable)  Ann Romney Center for Neurologic Diseases
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If you selected 'other' please specify your research area:

Title*  Complement activation is associated with microscopic pathology in the placentas of women with NMO


PI*  Tanuja Chitnis
Abstract Body (MUST be limited to 200 words, anything beyond 200 words will be truncated for print)*

Increased rate of preeclampsia and pregnancy loss has been reported in women with neuromyelitis optica (NMO) but mechanisms are unknown. To establish a placenta registry for women with NMO and explore complement binding pregnant women with NMO were prospectively enrolled in a longitudinal study registry. Placental specimens were obtained from 8 distinct states in the United States and in Europe. To date, 13 NMO pregnancies have been captured, with mean gestational age at enrollment of 31 weeks. At delivery, mean maternal age was 32.1 years, disease duration was 7 years, and gestational age was 38.1 weeks. One pregnancy resulted in preeclampsia and urgent delivery at 28 weeks, and one resulted in neonatal ventriculomegaly. There were no significant differences in gross or microscopic pathologic findings between the individuals with and without NMO. Immunofluorescence staining revealed an increase in C4b staining in NMO patients with placental microscopic pathology compared to those without (p=0.02). However, there was no compensatory rise in CD46 regulatory complement in these NMO placentas with pathology (P value >0.05). Overall, these results suggest that dysfunction in the regulation of complement activation in women with NMO could give rise to microscopic placental pathology, resulting in adverse maternal and fetal outcomes.

Lay Summary (MUST be limited to 200 words, anything beyond 200 words will be truncated for print). Please keep in mind - Discover Brigham is open to the public, this lay summary needs to be appropriate for lay audiences with NO scientific background. *

Neuromyelitis optica (NMO) is consisting of inflammation and demyelination of the optic nerve and spinal cord. Increased rate of pregnancy loss has been reported in women with NMO but mechanisms are unknown. To establish a placenta registry, pregnant women with NMO were prospectively enrolled in a longitudinal study registry. Placental specimens were obtained from 8 distinct states in the United States and in Europe. To date, 13 NMO pregnancies have been captured, with mean gestational age at enrollment of 31 weeks. At delivery, mean maternal age was 32.1 years, disease duration was 7 years, and gestational age was 38.1 weeks. One pregnancy resulted in preeclampsia and urgent delivery at 28 weeks, and one resulted in neonatal brain disease. There were no significant differences in pathologic findings between the individuals with and without NMO. Immunofluorescence staining revealed an increase in inflammatory complement in NMO patients with placental microscopic pathology compared to those without. However, there was no compensatory rise in regulatory complement in these NMO placentas with pathology. Overall, these results suggest that dysfunction in the regulation of complement activation in women with NMO could give rise to microscopic placental pathology, resulting in adverse maternal and fetal outcomes.

Clinical Implications (MUST be limited to 40 words and accessible to a lay audience) - please describe the clinical implications of your research.*

Overall, these results suggest that dysfunction in the regulation of complement activation in women with NMO could give rise to microscopic placental pathology, resulting in adverse maternal and fetal outcomes.

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Last Name*  de la Rosa

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BWH Title or HMS Rank (if relevant)*  Postdoctoral research fellow

Twitter Handle (if applicable)  

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- Neurosciences
- Patient-Centered Outcomes/Comparative Effectiveness
- Regenerative Medicine
- Women's Health & Gender Biology

If you selected 'other' please specify your research area:

Title*  Identification of novel Resolvin Conjugate in Tissue Regeneration 3 (RCTR3) in human tissues stimulates proresolving phagocyte functions

Authors*  Xavier de la Rosa, Paul C. Norris, Nan Chiang, Ana R. Rodriguez, Bernd W. Spur, Charles N. Serhan

PI*  Charles N. Serhan

Abstract Body (MUST be limited to 200 words, anything beyond 200 words will be truncated for print)*  

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Note: The abstract and its components are provided as an example and may not reflect the actual submission process.
Resolvin conjugates in tissue regeneration (RCTR) are a new group of chemical signals that coordinate host responses to accelerate resolution of inflammation and infection via enhancing efferocytosis, organ protection and tissue regeneration. Here, using LC-MS-MS-based-metabololipidomics we identified a new member denoted RCTR3, present in human brain, lymph node, bone marrow, and spleen. Spleen incubated with Staphylococcus aureus, endogenous RCTRs were increased and deuterium labeled-docosahexaenoic acid (d5-DHA) gave d5-17-hydroxy-DHA production, confirming pathway activation. RCTRs were matched with materials prepared by total organic synthesis. The complete stereochemical assignment and actions indicated that RCTR1 is 8R-glutathionyl,7S,17S-dihydroxy-4Z,9E,11E,13Z,15E,19Z-docosahexaenoic acid, RCTR2 is 8R-cysteinylglycinyl,7S,17S-dihydroxy-4Z,9E,11E,13Z,15E,19Z-docosahexaenoic acid, and RCTR3 is 8R-cysteinyl,7S,17S-dihydroxy-4Z,9E,11E,13Z,15E,19Z-docosahexaenoic acid. RCTRs confirmed their actions with macrophage stimulating phagocytosis and efferocytosis. Proteome profiling demonstrated that RCTRs regulated both pro-inflammatory/anti-inflammatory cytokines with macrophages challenged with serum-treated-zymosan. RCTRs limited PMN migration towards LTB4-gradient. In hind-limb-ischemia-reperfusion-initiated organ injury, both RCTR2 and RCTR3 significantly reduced PMN infiltration into lungs, and lowered LTB4. Also, each RCTR (1 nM) accelerated planaria tissue regeneration time ~0.5 days. Taken together these results identify a new bioactive RCTR, establish the complete stereochemistry and rank order potencies for three RCTRs. Moreover, RCTRs are produced in human tissues and exert potent anti-inflammatory and pro-resolving actions with human leukocytes.

**Lay Summary (MUST be limited to 200 words, anything beyond 200 words will be truncated for print). Please keep in mind - Discover Brigham is open to the public, this lay summary needs to be appropriate for lay audiences with NO scientific background.**

New frontline drugs are urgently required to fight infectious diseases. Staphylococcus aureus is a significant cause of a wide range of infectious diseases in humans and can cause life-threatening infection. Despite advances in diagnosis and treatment, S. aureus remains a troubling pathogen with increasing prevalence throughout the world. In the present report, we describe a new molecule derived from omega3 fatty acid, namely Resolvin Conjugate of Tissue Regeneration 3 (RCTR3); also we determined the structures of RCTR 1, 2, and 3. These molecules were produced in human brain, lymph nodes, bone marrow, spleen, and they were along as their precursors levels increased with S. aureus infection. These indicate that the biosynthesis machinery were present in lymphoid organs, and were activated by bacteria infection to initiate RCTRs biosynthesis in order to fight infections. Using RCTRs, we demonstrated their potent actions fighting bacteria, reducing tissue damage, diminishing inflammation and promoting wound healing. In addition, we established the rank order potencies among these three molecules, and their importance in fighting bacterial infection. Thus, our findings provide new targets pathways to actively stimulate resolution of inflammation, clear infection and enhance tissue regeneration after infection, surgery or injury.

**Clinical Implications (MUST be limited to 40 words and accessible to a lay audience) - please describe the clinical implications of your research.**

New therapies are urgently required to fight infectious diseases, trauma or surgery injury. Here, we describe a new molecule derived from omega3 fatty acid that provide new targets pathways to treat infections diseases, inflammation or injury.

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- Women's Health & Gender Biology
- Trauma
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If you selected 'other' please specify your research area:

Title*
Evaluating the Impact of a Blood Pressure Remote Telemonitoring Program (BP Connect)

Authors*

PI*
Kamal Jethwani, M.D., M.P.H.
Hypertension affects 30-45% of the population globally. Remote monitoring of blood pressure (BP) has shown improvement in drug compliance and increased achievement of target BP. Our study aimed to increase patient engagement using a telemonitoring platform. We recruited 288 adult patients from primary care (n=149) and specialty clinics (n=139) within the Partners Healthcare network (Faulkner Hospital, BWH Renal, Endocrinology, and Cardiology departments, and MGH’s Women’s Health Association). The primary outcome examined “controlled BP” (<140/90 mmHg), and secondary outcomes observed changes in systolic and diastolic blood pressure (SBP, DBP). Of the patients from primary care clinics, 64.0% had uncontrolled BP (>140/90 mmHg) at baseline vs. 48.0% of patients at 3 months (P = 0.01). There was a significant decline in both the mean DBP (-4.3, P= <0.01) and the mean SBP (-10.1, P= <0.01) in this patient population. Among patients from specialty clinics, BP was controlled in 43.2% of patients at 3 months vs. 11.2% at baseline (P = 0.01), with a decrease in mean SBP (-5.2, P <0.00) and DBP (-2.5, P= 0.01). BP Connect provides an opportunity for participants to remotely track their BP, fostering patient-provider disease management that may improve clinical outcomes and decrease burden of disease.

Lay Summary (MUST be limited to 200 words, anything beyond 200 words will be truncated for print). Please keep in mind - Discover Brigham is open to the public, this lay summary needs to be appropriate for lay audiences with NO scientific background.

Hypertension, or abnormally high blood pressure, affects one third of the global population. Our study, BP Connect, uses a remote, online platform where patients can work to manage their blood pressure (BP) outside of the clinic. Our study recruited 288 patients: 149 from primary care clinics, and 139 from specialty clinics at BWH and MGH. BP is expressed as the ratio of systolic (SBP), how much pressure the blood exerts on the arterial wall when the heart beats, over diastolic (DBP), how much pressure the blood exerts on the arterial wall between heart beats. Using our remote BP monitoring platform, we tracked patients overall BP (SBP/DBP) to see if it was controlled (<140/90 mmHg) or uncontrolled (>140/90 mmHg). After three months of using the platform, 48.0% of patients at primary care clinics had uncontrolled BP compared with 64.0% at baseline. Specialty care clinic patients saw a similar result, with 43.2% of patients controlled vs. 11.2% controlled at baseline. Additionally, we observed significant drops in both SBP and DBP in both clinic populations. BP Connect provides an opportunity for patients to track their BP remotely, fostering patient-physician disease management that may significantly reduce the number of deaths linked to hypertension-related diseases.

Clinical Implications (MUST be limited to 40 words and accessible to a lay audience) - please describe the clinical implications of your research.

Our remote-monitoring study showed significant increased achievement of target controlled blood pressure. These programs have great potential to increase patient engagement, fostering patient-physician disease management that may significantly reduce the number of deaths linked to hypertension-related diseases.

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- Regenerative Medicine
- Women's Health & Gender Biology

If you selected 'other' please specify your research area:

Title*  Baseline Characteristics of the VITamin D and OmegA-3 TriaL (VITAL): Effects on Bone Structure and Architecture

Authors*  Catherine Donlon; Sharon Chou, MD; Cindy Yu; Trisha Copeland; Nancy Cook, ScD; JoAnn Manson, MD, DrPH; Julie Buring, DSc; Meryl LeBoff, MD

PI*  Meryl LeBoff, MD
Abstract Body (MUST be limited to 200 words, anything beyond 200 words will be truncated for print)*

Vitamin D is widely used to support bone health, although effects of supplemental vitamin D alone on bone are inconsistent. This ancillary study to the large, randomized controlled VITamin D and OmegA-3 Trial (VITAL) aims to determine whether vitamin D3 (2000 IU/day) improves musculoskeletal outcomes. VITAL has a median treatment of 5-years in 25,874 men ≥50 years and women ≥55 years from 50 states. In our ancillary study, in-person assessments were completed at baseline and 2-years post-randomization in a subcohort of 773 participants (46.8% women, 53.2% men). Medical histories were obtained by annual questionnaires. Body composition and bone mineral density (BMD) were determined by dual-energy X-ray absorptiometry. Physical performance was tested using grip strength, walking speed, standing balance, and chair stands. At baseline, participants had a mean age of 63.8±6.1 years and body mass index (BMI) of 28.31±5.14 kg/m2; 30% were obese. Mean BMD was greater in men than women, and 25% of participants had low muscle mass by appendicular lean mass/BMI. Baseline characteristics were evenly distributed among treatment groups, suggesting that unidentified confounders will be similarly distributed. Final VITAL analyses will help advance clinical and public health recommendations regarding the role of supplemental vitamin D3 on musculoskeletal outcomes.

Lay Summary (MUST be limited to 200 words, anything beyond 200 words will be truncated for print). Please keep in mind - Discover Brigham is open to the public, this lay summary needs to be appropriate for lay audiences with NO scientific background. *

Vitamin D is widely used to support bone health, but effects of supplemental vitamin D alone on bone are inconsistent. The VITamin D and OmegA-3 Trial (VITAL) is investigating in 25,874 U.S. men and women in all 50 states whether supplemental vitamin D3 and/or omega (ω)-3 fatty acids reduces the risk of developing cancer, cardiovascular disease, and stroke. Participants are assigned to vitamin D3 (2000 IU/day) and ω-3 fatty acids (1 gram/day), vitamin D3 and placebo, ω-3 fatty acids and placebo, or double placebo for 5-years of treatment. We are studying whether high-dose vitamin D3 has positive effects on fractures, bone structure and architecture, as well as body composition (fat and lean tissue). A total of 773 participants completed in-person assessments in Boston at baseline and 2-years later. Assessments included tests of bone mineral density (BMD), bone structure, body composition, and physical performance. The baseline characteristics show that variables were evenly distributed among the four treatment groups. Therefore, the 2-year follow-up data analyses will help to advance clinical and public health recommendations regarding the effects of supplemental vitamin D3 and/or ω-3 fatty acids on musculoskeletal outcomes.

Clinical Implications (MUST be limited to 40 words and accessible to a lay audience) - please describe the clinical implications of your research.*

Findings from the VITAL: Bone Health ancillary studies will elucidate the role of high-dose supplemental vitamin D on bone health and body composition in women and men and will inform clinical practice and public health recommendations.

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**First Name**
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**BWH Department**
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**BWH Division (if applicable)**

**BWH ID Number**

**Email Address**
hdu2@bwh.harvard.edu

**BWH Title or HMS Rank (if relevant)**
Postdoctoral fellow

**Twitter Handle (if applicable)**

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- Women's Health & Gender Biology

**If you selected 'other' please specify your research area:**

#### Title*
Pre- and early post-natal loss of Tsc2 induces kidney Hybrid Oncocytic/Chromophobe Tumors (HOCT) via c-JUN

#### Authors*
Heng Du, Heng-Jia Liu, Mahsa Zarei, John R. Dreier, Damir Khabibullin, Nicola Alesi

#### PI*
Elizabeth P. Henske, David J. Kwiatkowski

**Abstract Body (MUST be limited to 200 words, anything beyond 200 words will be truncated for print)**
Renal cell carcinoma occurs in up to 4% of Tuberous Sclerosis Complex (TSC) patients, often affecting children and young adults. We explored the pathogenesis
of TSC-associated RCC using two mouse models. First, loss of Tsc2 was induced by i.p.
tamoxifen injection at E17.5 in Tsc2flox/floxROSA26-CreER+ mice (n=24),
examined at age 6 m. Second, loss of Tsc1 was induced by injecting Cre-encoding
adenovirus directly into the left kidney of TSC1flox/flox mice at P1 (n=19),
examined at age 1 year. Extensive TSC-associated kidney papillary RCC (PRCC)
(all mice) and hybrid oncocytic/chromophobe tumors (HOCT) (54%, 58%) were
seen in both models. PRCC showed strong and diffuse expression of phospho-S6-
S240/244 (pS6), CK7, carbonic anhydrase-IX but negative vimentin staining;
while the HOCT were positive for pS6, S-100 and vimentin. A phospho-RTK screen
and immunoblotting showed high levels of p-AXL and total AXL in kidney tumor
lysates. c-Jun was also highly expressed by immunoblotting, and is predicted to
drive AXL expression. Immunoblot analysis of a cell line established from the
kidney tumors showed TSC-dependent c-Jun and AXL expression. These novel
mouse models of TSC-related PRCC and HOCT elucidate novel mechanisms of
disease development and potential therapeutic targets for TSC-associated PRCC
and HOCT.

Lay Summary (MUST be limited to 200 words, anything beyond 200 words will be truncated for
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be appropriate for lay audiences with NO scientific background. *

Tuberous sclerosis complex (TSC) is a genetic disease caused by mutations in
either TSC1 or TSC2, and is characterized by formation of tumors in multiple
organs. Kidney cancer occurs in up to 4% of TSC patients. We generated novel
mouse models of human TSC-associated kidney cancer. We discovered that two
genes, not previously known to be involved in TSC kidney cancer, were very
active in these mouse cancers: AXL and c-Jun.

Clinical Implications (MUST be limited to 40 words and accessible to a lay audience) - please
describe the clinical implications of your research.*

These findings provide new insight into how kidney cancer develops in TSC
patients, and provide new opportunities for potential therapies.

*  

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- Trauma
- Women's Health & Gender Biology
- Other

If you selected 'other' please specify your research area:

Title*
Comparing Efficacy of Stages of Automation of Fall Prevention Protocols as Measured by Patient EngagementFall

Authors*
Megan Duckworth, BA, Srijesa Khasnabish, BS, Patricia Dykes, RN PhD

PI*
Patricia Dykes, RN PhD

Abstract Body (MUST be limited to 200 words, anything beyond 200 words will be truncated for print)*
The development of Fall T.I.P.S. (Tailoring Interventions for Patient Safety), a fall prevention toolkit integrated into the electronic health record with clinical decision
support, reduced falls by 25% in an acute care hospital by leveraging health information technology to 1) conduct fall risk assessments, 2) develop tailored fall prevention plans with the evidence-based interventions and 3) consistently implement the plan along with universal fall precautions1. A laminated version of the Fall T.I.P.S. toolkit has reduced falls and falls with injury rates2. The purpose of this study is to examine differences in patient engagement (as defined by patient knowledge of personalized fall risk factors and prevention plan) and model efficacy as related to the different stages of Fall TIPS automation embodied by four different fall prevention protocols. Our previous work suggests that patient and family engagement is associated with improved efficacy. To assess efficacy of the different stages of automation with respect to patient/family member engagement, random audits are conducted and include interviews of patients and family members. The main outcome measured is the percentage of patients and family members who reported engagement in the three-step fall prevention process across the four levels of automation.

Lay Summary (MUST be limited to 200 words, anything beyond 200 words will be truncated for print). Please keep in mind - Discover Brigham is open to the public, this lay summary needs to be appropriate for lay audiences with NO scientific background. *

At Brigham and Women’s Hospital, we made a tool that helps nurses, patients and family members create personalized plans to prevent the patient from falling. It reduced fall rates by 25%. There are four different versions of the tool. Some are all electronic, and others don’t require a computer. These display the personalized fall prevention plan on a laminated poster. We are studying whether one version of the tool is better than any other. We are measuring if the automation of the tool is good or bad by interviewing patients and family members. It is important for patients and families to know about the patient’s risk factors for falling and the ways to stop a fall from happening. We want to make sure that patients and families are still engaged in fall prevention no matter which tool is used.

Clinical Implications (MUST be limited to 40 words and accessible to a lay audience) - please describe the clinical implications of your research.*

The goal of this project is to improve patient safety by reducing the number of patients who fall while they are in the hospital. Our research shows that if patients and families are aware of their fall risk factors and fall prevention plan, the patient is less likely to fall. If patients and families are more aware of the plan with one version of the tool, we will know how to improve the care we provide our patients.

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If you selected 'other' please specify your research area:

Title*
Patient Safety Learning Lab (PSLL) - Suite of Tools and Use Reports

Authors*
Jenzel Espares, Theresa Fuller, Anuj Dalal, Robert Boxer, Jeffrey Schnipper

PI*
Jeffrey Schnipper, MD

Abstract Body (MUST be limited to 200 words, anything beyond 200 words will be truncated for print)*
The Patient Safety Learning Lab study has released a suite of health IT tools that are aimed to uphold patient safety and promote patient-centered care at Brigham and Women’s Hospital. Among the suite of health IT tools are an inpatient portal containing personalized safety information, MySafeCare – an application that allows patients and family members to submit either concerns or compliments about their hospital stay, the Patient Safety Dashboard which compiles data from various sources in Epic and places them in one visual display, and Fall TIPS – a fall prevention initiative that aims to reduce the frequency of falls in the inpatient setting. This study has gone live on multiple units in the Brigham since December 2016, and we have reached the point in the study where we have generated a protocol to communicate the impact of these tools to clinical staff. Usage reports are now sent out on a weekly basis, which are expected to increase awareness of the tools and simultaneously promote its continued use.

Lay Summary (MUST be limited to 200 words, anything beyond 200 words will be truncated for print). Please keep in mind - Discover Brigham is open to the public, this lay summary needs to be appropriate for lay audiences with NO scientific background. *

The Patient Safety Learning Lab, a research study at Brigham and Women’s Hospital, has released health IT tools that can help keep patients safe. While some of these tools are meant for use by hospital staff, there are also tools that patients and family members can interact with – such as an inpatient portal where they can see their own personalized health information, and an application where they can submit feedback about their hospital stay. This study has been going on in the hospital since December 2016, and we now send out weekly reports to staff on how often these tools are being used. These reports help to remind doctors, nurses, and others to use these tools regularly, and we believe that the patient will receive an overall higher level of care.

Clinical Implications (MUST be limited to 40 words and accessible to a lay audience) - please describe the clinical implications of your research.*

With consistent use of all tools by both clinical staff and patients, it is expected that safety risks and other preventable medical harms will be decreased in BWH units that have this suite of tools available to them.

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