

# **Women in Medicine and Science Symposium**

September 26, 2016

3:00-6:00 pm

Bornstein Family Amphitheater & PBB Rotunda  
Brigham and Women's Hospital



## About the Photographs

The cover of this Abstract Book is meant to represent the vibrant history of women physicians, scientists, nurses, other healthcare workers and staff at Brigham and Women's Hospital. In addition to sharing photos from past WMMS, we highlight the diverse medical and science careers of several Brigham women featured in the photo collage:



### **Mary Ellen Avery, MD (1927- 2011)**

Dr. Avery graduated from the John Hopkins University School of Medicine in 1952. Following her internship and residency at Hopkins, she came to Harvard Medical School in 1957 to undertake a research fellowship in pediatrics. Avery went on to become the first woman named Physician-in-Chief at Boston Children's Hospital, a position which she held from 1974-1985. During these years, she established a Joint Program in Neonatology at Boston Children's Hospital, Brigham and Women's Hospital and Beth Israel Hospital. In 1991, Avery received the National Medal of Science for her outstanding research, which resulted in lifesaving efforts for premature infants.



### **Sara Danziger (1900-1985)**

Ms. Danziger worked in the Department of Pathology at the Free Hospital for Women and the Boston Lying-In Hospital, which were later amalgamated with other hospitals to form the present-day Brigham and Women's Hospital. She collaborated on pioneering research leading to publications in the *American Journal of Obstetrics & Gynecology*, *Obstetrics & Gynecology* and *The Anatomical Record*.



### **Nina E. Scarito, MD (1917-1994)**

Dr. Scarito received her AB, Honors in Bio-Chemistry, from Radcliffe College in 1937, where she wrote a thesis on 'The chemistry and metabolism of uric acid and related compounds.' After graduating from the Women's Medical College of Pennsylvania, she was among the first female physicians accepted for training at the Free Hospital for Women, and she taught at Harvard Medical School during World War II. She later moved to Lawrence, Massachusetts, where she practiced as an Obstetrician for nearly half a decade (delivering over 20,000 babies in the process!). In 2006, the city of Lawrence built and dedicated a park in her honor, just blocks from the site where her office had stood for many years.

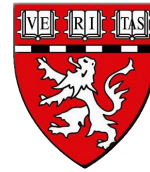
### **Photo Credits**

Throughout this booklet, current photos are supplied by the BWH Center for Faculty Development & Diversity. Historical photos are presented courtesy of the Brigham and Women's Hospital Archives at the Center for the History of Medicine in Francis A. Countway Library of Medicine, Harvard Medical School.

*With thanks and appreciation to **Catherine Pate**, Brigham and Women's Hospital Archivist at the Center for the History of Medicine, Francis A. Countway Library of Medicine, HMS.*



## What BWH Women say about WMSS...



'I value the opportunity to **affirm women's contributions** to my field and to science.'



'It is important to participate in the Women in Medicine and Science Symposium because even as more women are deciding to pursue careers in medicine and science than ever before, they are still underrepresented in leadership positions. With events like this to promote **academic growth, collaboration and mentorship** from current physician women leaders, I'm certain that with time, this gap will narrow and, ultimately, close.'

'Nowadays, **exposure** is a key to scientific success, especially for **women**.'

'In 1993, the NIH first mandated that women be included in all NIH funded clinical trials. Two decades later, the gender gap persists, but the conversation has dulled. That is precisely why the **WMSS is so vitally important**. Each year, **it is a reminder** to our medical and scientific community that we must continue the conversation and that we cannot become complacent in our endeavors to erase this disparity.'

'The Symposium provides **encouragement and support** to women scientists, many of whom, like me, have had to overcome obstacles and make tough choices as they strive to **balance their responsibilities as a mother/spouse/daughter** etc. with the rigorous focus and commitment required to build a successful research career.'

'It is my obligation as a woman in science to **build my network** along with other women driving scientific discovery and innovation to remain competitive in the field and continue to enable myself to reach the highest level of scientific research.'



## Women in Medicine and Science Symposium From the President

Dear Colleagues,

I'm delighted to welcome you to the 2016 Women in Medicine & Science Symposium, which marks the Brigham's fifth anniversary of celebrating the outstanding achievements in research made by women at our organization.

September is the American Medical Association's Women in Medicine Month, and it presents a welcome opportunity to highlight the exciting, cross-disciplinary work being conducted by our women scientists and physicians.

My hope is that today's symposium will energize you and generate new ideas and collaborative opportunities among our faculty and trainees.



I encourage you to engage with the many Brigham resources available to support your personal and professional development, including the Center for Faculty Development & Diversity (CFDD), the Office for Women's Careers (OWC), the Office for Research Careers (ORC), the Brigham Research Institute (BRI), the Center for Clinical Investigation (CCI) and the Mary Horrigan Connors Center for Women's Health & Gender Biology, all of which are co-sponsors of today's event.

Please enjoy the outstanding diversity of research presented during today's program – and thank you for your own contributions to medicine, science and our health care community.

With warm regards,



Elizabeth G. Nabel, MD  
President, Brigham and Women's Health Care



**Women in Medicine and Science Symposium**  
From the OWC Director

Dear Colleagues,

On behalf of the Center for Faculty Development & Diversity (CFDD) and its member offices, I would like to welcome you to the fifth annual Women in Medicine & Science Symposium, as we observe Women in Medicine and Science Month this September. I want to personally acknowledge the contributions of our women clinicians, scientists and researchers. You are all part of a group of exemplary individuals that reflects the great diversity of science, extraordinary range of talents, and wonderful collaborative spirit at the Brigham and Women's Hospital.

The goal of the Women in Medicine & Science Symposium is to celebrate the success and highlight the contributions of women researchers and scientists in scientific discovery and clinical innovation. BWH is proud to support and advance some of the most important basic, translational, epidemiological and clinical research studies in the world, and to continue to support the advancement of women.

I would like to thank the CFDD, the Office for Women's Careers, the Office for Research Careers, the Brigham Research Institute, the Center for Clinical Investigation and the Mary Horigan Connors Center for Women's Health & Gender Biology for their support.

Your efforts are critical to our mission and success, and I am honored to be able to celebrate your research accomplishments, and most importantly, the energy and commitment that you bring to your work every day.

Sincerely,



Kathryn Rexrode, MD, MPH  
Director, Office for Women's Careers  
Center for Faculty Development & Diversity

**Women in Medicine and Science Symposium**  
From BWH History



Heidi Booth at Brigham and Women's Hospital (1978)



Postgraduate Class of Nurses at the Free Hospital for Women (1906)



**Women in Medicine and Science Symposium  
From BWH History**



Student nurses at Peter Bent Brigham Hospital School of Nursing (1966)



Sara Danziger working in a Brigham Pathology Lab (c1939)

## Women in Medicine and Science Symposium From the Event Chairs

### Why is this event significant to you?



**Elena Aikawa, MD, PhD, FAHA**

*Director, Vascular Biology Program, CICS, BWH  
Associate Professor of Medicine, HMS*

This year we celebrate the 5<sup>th</sup> Women in Medicine and Science Symposium (WMSS). Since our inaugural meeting in 2012, WMSS has provided a platform to celebrate scientific discoveries and innovation at Brigham and Women's Hospital. Each year we recognize female clinical and research scientists from different departments and of varying academic ranks, who then present their research to participants of the Symposium. WMSS has also fostered the initiation of numerous cross-departmental collaborations and the establishment of many mentor-mentee relationships. Finally, the Symposium has allowed participants to share innovative discoveries with the entire Brigham community.



We would like to thank our reviewers for taking the time to ensure that each submitted abstract received fair consideration. We also would like to thank the members of CFDD and OWC for their tremendous effort in organizing these meetings. In particular, we wish to acknowledge Dr. Betsy Nabel, this year's keynote speaker, for her support of women's leadership and innovation. Please join us today in celebrating the clinical and research achievements of women trainees and faculty at BWH, all of whom have worked to bridge the gender gap in academic medicine.



**Kathryn M. Rexrode, MD, MPH**

*Director, Office for Women's Careers,  
Center for Faculty Development and Diversity  
Associate Professor of Medicine, HMS*

The Women in Medicine and Science Symposium allows us to recognize the many contributions that our women scientists, researchers, clinicians and trainees are making in scientific discovery, innovation and clinical collaboration. We hope to advance collaboration by creating a forum to share and celebrate the scientific and clinical achievements of our talented women faculty.



## Women in Medicine and Science Symposium Celebrating 5 Years

### *Previous Presenters*

#### **2015**

##### *Keynote:*

Paula Johnson, MD, MPH; Ingrid Katz, MD, MHSc

##### *Presenters*

Hildur Arnardottir, PhD; Bindu Chamarthi, MD; Tracy Doyle, MD, MPH; Roopali Gandhi, PhD; Pamela Ghosh, PhD; Katherine Gregory, PhD, RN; Michalina Janiszewska, PhD; Emily Lau, MD; Angeliki Pantazi, MD, PhD; Lauren Ritterhouse, MD, PhD

#### **2014**

##### *Keynote*

Terrie Inder, MD, MBChB

##### *Presenters*

Bindu Chamarthi, MD, MMSc; Lauren Gilstrap, MD; Anna Greka, MD; Bin Liu, PhD; Dongdong Ma, MD, PhD; Zehra Ordulu, MD, PhD

##### *Additional Remarks*

Cynthia Morton, PhD

#### **2013**

##### *Keynote*

Jill Goldstein, PhD; Reisa Sperling, MD

##### *Presenters*

Tara Deelman, MD, MSc; Seoyoung Kim, MD, MSCE; Claudia Goettsch, PhD; Laura Holsen, PhD; Ana Paula Abreu, MD, PhD; Farzaneh Sorond, MD, PhD



#### **2012**

##### *Keynote*

Julie Glowacki, PhD; Meryl S. LeBoff, MD

##### *Presenters*

Julia Charles, MD, PhD; Nicole Joller, PhD; Linda Lee, MD; Cecilia Lezcano, MD; Zehra Ordulu, MD; Sabina Signoretti, MD





# 2016 Program

## Welcome and Opening Remarks

### **Kathryn Rexrode, MD, MPH**

Director, Office for Women's Careers, CFDD, BWH  
Associate Professor of Medicine, HMS

### **Elena Aikawa, MD, PhD, FAHA**

Director, Vascular Biology Program, CICS, BWH  
Associate Professor of Medicine, HMS

## Keynote Speaker

### **Elizabeth G. Nabel, MD**

President, Brigham and Women's Health Care  
Professor of Medicine, HMS

## Featured Oral Presentations

### **Marta Fay, PhD**

Research Fellow, HMS  
Division of Rheumatology, Immunology and Allergy  
Department of Medicine, BWH

### **Nadine Palermo, DO**

Instructor, HMS  
Division of Endocrinology, Diabetes and Hypertension  
Department of Medicine, BWH

### **Maria Carmela Speranza, PhD**

Research Fellow, HMS  
Department of Neurosurgery, BWH

### **Viviany R. Taqueti, MD, MPH**

Assistant Professor, HMS  
Division of Cardiovascular Medicine  
Department of Medicine, BWH

## Featured Poster Presentations

### **Agnieszka Bronisz, PhD**

Instructor, HMS  
Department of Neurosurgery, BWH

### **Mandovi Chatterjee, PhD**

Research Fellow, HMS  
Division of Genetics  
Department of Medicine, BWH

### **Helen Christou, MD**

Assistant Professor, HMS  
Department of Pediatric Newborn Medicine, BWH

### **Kathryn Hall, PhD, MPH**

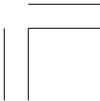
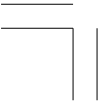
Instructor, HMS  
Division of Preventive Medicine  
Department of Medicine, BWH

### **Nina Paynter, PhD**

Assistant Professor, HMS  
Division of Preventive Medicine  
Department of Medicine, BWH

### **Jing Yan, PhD**

Research Fellow, HMS  
Division of Rheumatology, Immunology and Allergy  
Department of Medicine, BWH



## Women in Medicine and Science Symposium Keynote Speaker



**Elizabeth G. Nabel, MD**, brings a unique perspective to health care based on her experience as a physician, research scientist, academic medicine leader, and wellness advocate. At BWHC, she led development of a comprehensive strategic plan that defines a new model of medicine characterized by seven strategic commitments focused on innovation in care redesign toward population health management, in research and discovery through multiple life sciences collaborations, and in personalized therapies and precision medicine. Initiatives include a new translational research and clinical facility, and a \$1 billion campaign to advance innovation, patient care and community health.

Building on her lifelong commitment to improving health through science, in 2015 Nabel was appointed chief health and medical advisor to the National Football League. In this newly created advisory role, Nabel provides strategic input to the NFL's medical, health and scientific efforts; participates as an ex-officio member on each of the NFL's medical advisory committees; and identifies areas for the NFL to enhance player safety, care and treatment.

Nabel has a long record of advocacy for health and broadening access to care. As director of the National Heart, Lung, and Blood Institute from 2005-2009, Nabel leveraged the \$3 billion research portfolio to establish pioneering scientific programs in genomics, stem cells, and translational research. Nabel's work on the molecular genetics of cardiovascular diseases has produced 17 patents and more than 250 scientific publications.

Nabel has been named one of the nation's top leaders in medicine by Modern Healthcare and Becker's Hospital Review, and one of Boston's 50 most powerful people by Boston Magazine. Her honors include the Distinguished Bostonian Award from the Greater Boston Chamber of Commerce, the Kober Medal from the Association of American Physicians, the Champion in Health Care award from the Boston Business Journal, the Willem Einthoven Award from Leiden University in the Netherlands, the Amgen-Scientific Achievement Award, two Distinguished Achievement Awards and the Eugene Braunwald Academic Mentorship Award from the American Heart Association, and six honorary doctorates.

**Women in Medicine and Science Symposium**  
**Featured Oral Presenters**



**Marta Fay, PhD**  
Research Fellow, HMS  
Division of Rheumatology, Immunology  
and Allergy  
Department of Medicine, BWH



**Nadine Palermo, DO**  
Instructor, HMS  
Division of Endocrinology, Diabetes and  
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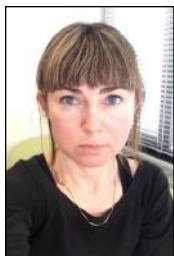


**Maria Carmela Speranza, PhD**  
Research Fellow, HMS  
Department of Neurosurgery, BWH



**Viviany R. Taqueti, MD, MPH**  
Assistant Professor, HMS  
Division of Cardiovascular Medicine  
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**Featured Poster Presenters**



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**Kathryn Hall, PhD, MPH**  
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Division of Preventive Medicine  
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Assistant Professor, HMS  
Division of Preventive Medicine  
Department of Medicine, BWH



**Jing Yan, PhD**  
Research Fellow, HMS  
Division of Rheumatology, Immunology and Allergy  
Department of Medicine, BWH



## GGGGCC expansion promotes *in vitro* and *in vivo* RNA granule formation

*Submitted by:* Marta Fay, PhD

*Mentor:* Paul Anderson, MD, PhD


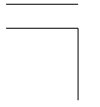
*Authors:* Fay M, PhD, Ivanov P, PhD, Anderson P, MD, PhD

**Background:** A hexanucleotide expansion, GGGGCC (G4C2), within the first intron of C9ORF72 is the most common mutation associated with amyotrophic lateral sclerosis (ALS) and frontal temporal dementia (FTD). Work from other groups suggests the G4C2 expansion itself, rather than the protein encoded by the C9ORF72 gene, promotes cytotoxicity. It is unclear whether G4C2 RNA (rG4C2) or the abnormal proteins produced cause neurodegeneration.


**Methods:** rG4C2 biophysical properties were assessed by fluorescence microscopy and live imaging, and the protein composition was assessed with multiplex proteomics and confirmed using immunoblotting.

**Results:** We discovered that rG4C2 promotes an *in vitro* phase transition that recapitulate RNA granules that form in cells. RNA granules are non-membranous compartments that are hypothesized to be gel-like due to high concentrations of RNA and protein. Examples include the nucleolus, neuronal granules and stress granules. In addition to forming granules *in vitro*, rG4C2 causes RNA granule formation in cells. Lastly, rG4C2 granule formation is length dependent, whereby longer, pathological repeats promote more granule formation *in vitro* and in cells.

**Conclusion:** Our findings reveal a unique biophysical property of rG4C2, prompting the hypothesis that G4C2 ALS/FTD-associated expansion promotes aberrant RNA granules that modulate RNA metabolism, and increases sensitivity to stress triggering neurodegeneration.







## Open Access to Diabetes Center from the Emergency Center Department Reduces Hospitalizations in the Subsequent Year

*Submitted by:* Nadine Palermo, DO

*Mentor:* Marie McDonnell, MD

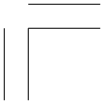

*Authors:* Palermo NE, DO, Modzelewski KL, MD, Farwell AP MD, Fosbroke J, MS, Shankar KN, MD, Alexanian SM, MD, Baker WE, MD, Simonson DC, MD, MPH, ScD, McDonnell ME, MD

**Background:** It is well known that patients with diabetes presenting to the Emergency Department (ED) for dysglycemia are at increased risk for unnecessary hospitalizations, often with longer length of stay and poor health outcomes. The Emergency Department Diabetes Rapid-referral Program (EDRP) was designed to capture patients who present to the ED for acute diabetes-related problems, but do not require inpatient admission and instead require rapid diabetes follow-up. This program provides ED staff with direct booking into a diabetes clinic within 24 business hours of ED discharge.

**Methods:** We conducted a single-center retrospective analysis of the EDRP cohort (N=420) and compared one year outcomes to a historical control group (N=791). We also compared EDRP patients who arrived (ARR) to the scheduled visit to those who did not show (NS). The primary outcome was hospitalization rate over one year. Secondary outcomes included ED recidivism rate, hemoglobin A1c (HbA1c) and health care expenditures.

**Results:** Compared with controls, EDRP patients were less likely to be hospitalized (27.1% vs. 41.5%,  $p < 0.001$ ) or return to the ED (52.2% vs. 62.3%,  $p = 0.001$ ) in the subsequent year. Total hospitalizations were also lower the EDRP patients ( $157 \pm 19$  vs.  $267 \pm 18$  per 1000 persons per year,  $p < 0.001$ ). The EDRP cohort had a greater reduction in HbA1c (-2.66% vs. -2.01%,  $p < 0.001$ ). The mean per patient health care expenditures were lower by \$5,461 in the EDRP cohort as compared with controls.

**Conclusions:** Eliminating barriers to scheduling diabetes focused ambulatory care for ED patients was associated with significant reductions in hospitalization rate, ED recidivism rate and HbA1c over the subsequent year.



# Preclinical Analysis of Combinatorial Glioblastoma Therapy with the Prodrug-Mediated Gene Therapy Vector AdV-tk and Immune Checkpoint Inhibition

*Submitted by:* Maria Carmela Speranza, PhD

*Mentor:* Sean Lawler, PhD, EA Chiocca, MD, PhD

*Authors:* Speranza M<sup>1</sup>, PhD, Kasai K<sup>1</sup>, PhD, Ricklefs F<sup>1,5</sup>, MD, Klein SR<sup>3</sup>, PhD, Passaro C<sup>1</sup>, PhD, Nakashima H<sup>1</sup>, PhD, Kaufmann J<sup>1</sup>, PhD, Bronisz A, PhD, Aguilar-Cordova E<sup>2</sup>, MD, PhD, Guzik BW<sup>2</sup>, PhD, Freeman GF<sup>3</sup>, PhD, Reardon DA<sup>4</sup>, MD, Wen P<sup>5</sup>, MD, Chiocca EA<sup>1</sup>, MD, PhD, FAANS, Lawler SE<sup>1</sup>, PhD

**Background:** AdV-tk is an immunostimulatory virus-based approach, known as Gene-Mediated Cytotoxic Immunotherapy(GMCI), that recently showed encouraging results in a Phase-II trial in glioblastoma. Given that virus-based cancer therapies can be immunostimulatory and immune-checkpoint inhibitors block tumor-induced T-cell exhaustion, the combination of these two approaches offers a potentially synergistic interaction. One of the molecular underpinnings of T-cell exhaustion is the expression of Programmed Death-1(PD1) and its ligand PD-L1.

**Methods:** We investigated PD-L1 expression after GMCI in human/mouse glioma cells in vitro through Western-blotting, flow-cytometry, qPCR, ELISA and immunohistochemistry. In vivo studies were performed using intracranial GL261 model and followed by BLI.

**Results:** Our experiments showed a consistent increase in cell surface PD-L1 levels and a type-I interferon response after GMCI that is at least partially responsible for autocrine/paracrine PD-L1 up-regulation. In vivo studies showed high levels of long-term survivors in the GMCI/PD1 combination(11/14), compared with GMCI(6/16), anti-PD1(5/12) and controls(0/11). In addition, tumor infiltrating lymphocytes after GMCI showed an increase in cytotoxic T-cell activation. However, there was also a significant increase in Tregs releasing immunosuppressive cytokines, and in PD1+/TIM3+ T-cells.

**Conclusions:** Our data show that GMCI/anti-PD1 combinatorial therapy is effective and strongly support clinical trials of GMCI/checkpoint inhibitor combinations in glioblastoma patients.

<sup>1</sup>Harvey Cushing Neurooncology Laboratories, Department of Neurosurgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA.

<sup>2</sup>Advantagene Inc. Auburndale, MA.

<sup>3</sup>Department of Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA

<sup>4</sup>Department of Neurooncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA.

<sup>5</sup>Department of Neurosurgery, University medical center Hamburg-Eppendorf, Hamburg, Germany.



## Excess Cardiovascular Risk in Women with Very Low Coronary Flow Reserve

*Submitted by:* Viviany R. Taqueti, MD, MPH

*Mentor:* Marcelo Di Carli



*Authors:* Taqueti VR, MD, MPH, Shaw LJ, PhD, Cook NR, ScD, Murthy VL, MD, PhD, Shah NR, MD, MPH, MD, Foster CR, MS, Hainer J, BS, Blankstein R, MD, Dorbala S, MD, MPH, Di Carli MF, MD


**Background:** Cardiovascular disease (CVD) fatality rates are similarly high for women as compared with men, yet obstructive CAD is less prevalent in women. Coronary flow reserve (CFR), an integrated measure of large and small vessel CAD and myocardial ischemia, identifies patients at risk for CVD death, but is not routinely measured in clinical practice.

**Methods:** Consecutive patients (N=329) referred for coronary angiography after stress testing with myocardial perfusion PET were followed (median 3.0 years) for cardiovascular death and hospitalization for MI or heart failure. Extent and severity of angiographic CAD were estimated using the CAD prognostic index, and CFR quantified using PET.

**Results:** Women relative to men had lower pretest scores and lower burden of angiographic CAD ( $p < 0.001$ ), but demonstrated greater risk of CVD events (adjusted HR 2.05,  $p = 0.03$ ). Impaired CFR ( $< 1.6$ ,  $n = 163$ ) was similarly present among women and men. When stratified by sex and CFR, only women with severely impaired CFR demonstrated increased adjusted risk of CVD events ( $p < 0.0001$ , interaction  $p = 0.04$ ).

**Conclusion:** Excess cardiovascular risk in women referred for angiography was independently associated with impaired CFR, representing a hidden biological risk. Impaired CFR, particularly absent severely obstructive CAD, may represent a novel target for CVD risk reduction.





## Long Non-Coding RNAs HIF1A-AS2 Modifies Response to Hypoxic Environment of Glioblastoma

*Submitted by:* Agnieszka Bronisz, PhD

*Mentor:* E Antonio Chiocca, MD, PhD

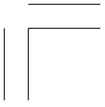

*Authors:* Mineo M, PhD, Chiocca EA, MD, PhD, Godlewski J, PhD, Bronisz A, PhD

**Background:** Long-non-coding RNAs (lncRNAs) have yet undefined role in the pathobiology of glioblastoma multiforme (GBM). These tumors are genetically and phenotypically heterogeneous with transcriptome subtype-specific GBM stem-like cells (GSCs) that adapt to the brain tumor environment, including hypoxic niches.

**Methods:** The GSCs with transcriptome characterized subtype were exposed to hypoxia. Expression of lncRNAs was characterized using Nanostring platform. RNA immunoprecipitation and mass-spectrometry were performed to map RNA-protein interaction. The knock-down strategy was used to characterize cellular and molecular phenotype in in vitro and in vivo GBM models.

**Results:** We identified hypoxia inducible factor 1 alpha-antisense RNA 2 (HIF1A-AS2) as a subtype-specific, hypoxia inducible lncRNA, up-regulated in mesenchymal (M) GSCs. Its deregulation affects growth, self-renewal and hypoxia-dependent molecular reprogramming in M GSCs in vitro. Amongst the HIF1A-AS2 protein interactome, IGF2BP2 and DHX9 were identified as direct partners. These associations were supported the maintenance of expression of their target genes. Knock-down of HIF1A-AS2 led to delayed growth of M GSC tumors and survival benefits. We identified hypoxia inducible factor 1 alpha-antisense RNA 2 (HIF1A-AS2) as a subtype-specific, hypoxia inducible lncRNA, up-regulated in mesenchymal (M) GSCs. Its deregulation affects growth, self-renewal and hypoxia-dependent molecular reprogramming in M GSCs in vitro. Amongst the HIF1A-AS2 protein interactome, IGF2BP2 and DHX9 were identified as direct partners. These associations were supported the maintenance of expression of their target genes. Knock-down of HIF1A-AS2 led to delayed growth of M GSC tumors and survival benefits.

**Conclusions:** Our data demonstrate that HIF1A-AS2 contributes to GSCs' speciation and adaptation to hypoxia within the tumor microenvironment, acting directly through its interactome and indirectly by modulating responses to hypoxic stress depending on the subtype-specific transcriptome context.





## The Mechanosensory Ion Channel Protein, Piezo, Regulates Cell Division during Skeletal Muscle Development

*Submitted by:* Mandovi Chatterjee, PhD

*Mentor:* Richard Maas, MD, PhD

*Authors:* Chatterjee M<sup>1</sup>, PhD, Miraoui H<sup>1</sup>, PhD, Xi QC<sup>1</sup>, David L<sup>2</sup>, PhD, Bennett A<sup>1</sup>, MS, Gupta V<sup>1</sup>, PhD, Maas R<sup>1</sup>, MD, PhD

**Background:** Mechanotransduction is a process by which mechanical stimuli are converted into biochemical signals in cells to elicit different physiological functions, including embryogenesis, hearing, touch and muscle contractility. Ion channels present in the cell membrane respond to such stimuli in the cellular environment. Piezo1 and 2 are transmembrane cation-selective ion channels that form mechanosensitive pores in cells. Gain-of-function mutations in *PIEZO1* and *2* cause congenital red cell and skeletal muscle disorders, respectively. Consistent with this, piezo2b-deficient zebrafish exhibit abnormal motility. Here we propose a mechanism by which Piezo might regulate skeletal muscle development.


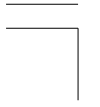
**Methods:** By immunofluorescence, we show that Piezo1 and 2 are present in the nuclear membrane of mouse myoblasts and also in mitochondria in zebrafish skeletal muscle.



**Results:** Mitochondrial integrity is also affected in the skeletal muscle of piezo2b-deficient zebrafish. Moreover, depletion of Piezo2 in C2C12 myoblast cells causes an M-phase cell cycle arrest.

**Conclusions:** The involvement of the cytoskeleton in transducing mechanical cues through its connections with the mechanosensitive ion channels is well established. We propose that Piezo proteins in the organelle membranes sense mechanical forces by directly interacting with the cytoskeleton to regulate crucial cellular functions such as mitosis during muscle development.

<sup>1</sup>*Division of Genetics, Department of Medicine, Brigham & Women's Hospital, Harvard Medical School*

<sup>2</sup>*Program in Cellular and Molecular Medicine, Boston Children's Hospital, Harvard Medical School*





## Acetazolamide treatment modulates the pulmonary inflammatory response and ameliorates severe experimental Pulmonary Hypertension.

*Submitted by:* Helen Christou, MD

*Authors:* Hudalla H<sup>1</sup>, MD, Michael Z<sup>1</sup>, MD, Kourembanas S<sup>1,2</sup>, MD, Christou H<sup>1,2</sup>, MD


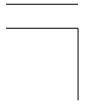
**Background:** Pulmonary inflammation contributes to pulmonary hypertension (PH). We previously reported that metabolic acidosis ameliorated experimental PH but the underlying mechanisms are unknown. We hypothesized that Acetazolamide (ACTZ) treatment will ameliorate Sugen/hypoxia-induced severe PH by modulating lung inflammation.

**Methods:** Adult male Sprague-Dawley rats injected with Sugen (20 mg/kg sc) or vehicle were exposed to hypoxia (9%O<sub>2</sub>) for 3 weeks followed by normoxia. ACTZ-treated animals received 1.7mg/ml in the drinking water either (1) Early (week 1 to 3) or (2) Late (week 4 to 7). We assessed hemodynamics and right ventricular hypertrophy (Fulton's Index, FI). Lungs and pulmonary arteries were isolated for RT-qPCR and morphometric analysis. Statistical analysis was by ANOVA.

**Results:** ACTZ-early treated animals had significantly lower RVSP and FI compared to Su/Hx animals. Late-treated animals showed a non-significant reduction of RVSP and a significant reduction in FI compared to untreated animals. Whole lung mRNA levels of TNF $\alpha$ , IL-6, and E-selectin were significantly higher in SU/Hx rats. This finding was associated with decreased smooth muscle cell contractile markers measured in isolated pulmonary arteries. These changes were ameliorated in ACTZ-treated animals.

**Conclusions:** Treatment with ACTZ ameliorates PH and RVH in the SU/Hx model of severe PH and this is associated with reduction in the lung inflammatory response.

*<sup>1</sup>Department of Pediatric Newborn Medicine, Brigham and Women's Hospital, and <sup>2</sup>Division of Newborn Medicine, Boston Children's Hospital; Harvard Medical School, Boston, Massachusetts*



## Pharmacogenomic effects of catechol-O-methyltransferase on aspirin and vitamin E cancer preventive treatment

*Submitted by:* Kathryn Hall, PhD, MPH

*Mentor:* Daniel Chasman, PhD

*Authors:* Hall KT<sup>1</sup>, PhD, MPH, Battinelli E<sup>2</sup>, MD, PhD, Passow D<sup>3</sup>, Kaptchuk TJ<sup>3,4</sup>, BA, Buring J<sup>1</sup>, DSc, Ridker P<sup>1</sup>, MD, Mukamal KJ<sup>4</sup>, MD, MPH, Chasman DI<sup>1</sup>, PhD

**Background:** Despite demonstrated effects of catechol-O-methyltransferase (COMT) on estrogen metabolism and cancer cell-proliferation, epidemiological studies of effects on cancer incidence are conflicting. We previously demonstrated interaction between *COMT* rs4680 and aspirin or vitamin E compared with placebo in cardiovascular disease and hypothesized such interactions may be relevant to cancer.

**Methods:** Association of common *COMT*rs4680 met/val polymorphism with incident cancer over 10-years among 23,294 initially cancer-free women from the Women's Health Study of aspirin and vitamin E was examined.

**Results:** Among placebo-allocated participants, the rs4680 val-allele was associated with lower total cancer incidence compared to the met-allele (per-allele HR=0.82[0.72-0.95], p=0.006). In contrast, the val-allele was associated with higher cancer rates among those allocated to vitamin E (1.14[1.01-1.30], p= 0.04), aspirin (HR=1.02[0.90-1.16], p=0.8) or both drugs (HR=1.15 [1.00-1.32], p=0.05). The interactions of genotype with treatment assignment were significant for both aspirin (p=0.03) and vitamin E (p=0.0006). Results were similar when controlling for hormone replacement therapy, BMI, smoking and alcohol use, for breast and colorectal but not lung cancer subtypes, and for rs4818, a *COMT* variant in LD with rs4680.

**Conclusions:** Together, these data support a role for *COMT* in cancer incidence and modification of its effects by commonly used drugs aspirin and vitamin E.

*1.Division of Preventative Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts*

*2.Division of Hematology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts*

*3.Program in Placebo Studies, Beth Israel Deaconess Medical Center, Boston, Massachusetts*

*4.Division of General Medicine and Primary Care, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts*



## Metabolomic precursors of coronary heart disease in women

*Submitted by:* Nina Paynter, PhD

*Mentor:* Kathryn Rexrode, MD


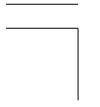
*Authors:* Paynter NP, PhD, Balasubramanian R, ScD, Gopal S, PhD, Giulianini F, PhD, Tinker LE, PhD, Manson JE, MD, DrPH, Cook NR, ScD, Albert CM, MD, MPH Clish C, PhD, Rexrode KM, MD, MPH

**Background:** Prior studies of metabolomic profiles and coronary heart disease (CHD) have had small case numbers and few women.

**Methods:** 371 metabolites were measured in a discovery dataset of 800 incident CHD cases and controls (matched on age, race/ethnicity, hysterectomy status and time of enrollment) in the Women's Health Initiative Observational Study (WHI-OS). Metabolites associated with CHD were identified adjusting for matching factors only and adjusting for matching plus use of aspirin, statins, anti-diabetics, anti-hypertensives, smoking, systolic blood pressure, diabetes, total and HDL cholesterol. All selected metabolites were validated in a separate set of 773 cases and controls from the placebo arms of the WHI Hormone Therapy trials and the WHI-OS.

**Results:** 67 metabolites were selected in the discovery data set. 25 validated adjusting for matching factors only and 11 validated after additionally adjusting for medications and CHD risk factors. These included glutamate and glutamine, which have been previously related to CHD, along with other amino acids, sugars, nucleosides, polyunsaturated phospholipids and highly saturated triglycerides. Novel metabolites were also identified, including plasmalogens and eicosanoids.

**Conclusions:** Multiple metabolites associated with CHD risk in women were identified and replicated, potentially illuminating biological mechanisms as well as markers of future risk.





## Gut Microbiota Induce IGF-1 and Promote Bone Formation and Growth

*Submitted by:* Jing Yan, PhD

*Mentor:* Julia F. Charles, MD, PhD

*Authors:* Yan J<sup>1</sup>, PhD, Herzog J<sup>2</sup>, BS, Tsang K<sup>1</sup>, BS, Bower M<sup>2</sup>, BS, Sartor RB<sup>2</sup>, MD, PhD, Aliprantis AO<sup>1</sup>, MD, PhD, Charles JF<sup>1</sup>, MD, PhD

**Background:** Appreciation of the role of the gut microbiome in regulating vertebrate metabolism has exploded recently. However, the effects of gut microbiota on skeletal growth and homeostasis have only recently been explored.



**Methods:** Germ-free (GF) mice were colonized with SPF gut microbiota for either 1 month or 8 month and bone phenotype were compared between GF and colonized mice.

**Results:** One-month colonization increased bone formation and widen growth plate. 8-month colonization resulted in increased longitudinal and radial bone growth. Serum levels of insulin like growth factor 1 (IGF-1), a hormone with known actions on skeletal growth, were substantially increased in response to colonization. Antibiotic treatment of SPF mice, in contrast, decreased serum IGF-1 and inhibited bone formation, suggesting that skeletal effects of microbiota are mediated by IGF-1. Treatment with vancomycin, a non-absorbable antibiotic that only targets Gram-positive bacteria, was sufficient to decrease serum IGF-1 and inhibit bone formation, indicating that Gram-positive commensals are sufficient for the regulation of bone formation by microbiota.

**Conclusions:** Our study demonstrates that colonization with microbiota provide a net anabolic stimulus to the skeleton, which is likely regulated by IGF-1. Manipulation of the microbiota may afford opportunities to optimize bone health and growth.

<sup>1</sup>Department of Medicine, Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital and Harvard Medical School, One Jimmy Fund Way, Boston, MA 02115

<sup>2</sup>National Gnotobiotic Rodent Resource Center, University of North Carolina at Chapel Hill, 120 Mason Farm Road, Chapel Hill, NC 27599



**Women in Medicine and Science Symposium  
Honorable Mentions**

**Utilizing human genetically modified cells to dissect stress responses**

Anaïs Aulas, PhD

*Division of Rheumatology, Immunology and Allergy, Department of  
Medicine, Research Fellow*

**Validation of a point-of-care human milk analyzer and opportunity for use in  
improving nutritional care of hospitalized preterm infants**

Mandy B. Belfort, MD, MPH

*Department of Pediatric Newborn Medicine, Assistant Professor*

**Benefit and Risk of Dual Antiplatelet Therapy in Females: DAPT Study  
Results**

Natalia Berry, MD, MBA

*Division of Cardiology, Department of Medicine, Clinical Fellow*

**Adaptive Design Clinical Trials in Medical Research and International  
Regulatory Assessment of New Therapies**

Laura Bothwell, MA, PhD

*Division of Pharmacoepidemiology and Pharmacoeconomics, Department  
of Medicine, Research Fellow*

**Proactive Psychiatric Consultation in the Medical ICU (MICU)**

Melissa Bui, MD

*Department of Psychiatry, Instructor*

**Appetite regulation in depression**



Hilal Cerit, MSc, PhD



*Women's Health Center of Excellence, Department of Medicine, Research  
Fellow*

**Increased Sensitivity to Angiotensin II in South Asians: A Potential  
Mechanism for the Increased Insulin Resistance and Cardiovascular Risk  
among South Asians**

Bindu Chamarthi, MD, MMSc

*Division of Endocrinology, Diabetes and Hypertension, Department of  
Medicine, Instructor*





**Women in Medicine and Science Symposium**  
**Honorable Mentions**

**Microbiota Regulate the Bacteria-Reactivity in The Primary Immunoglobulin Repertoire Early in Life**

Yuezhou Chen, MD, PhD

*Division of Rheumatology, Immunology and Allergy /Duane Wesemann Lab, Department of Medicine, Research Fellow*

**Prevalence and Predictive Value of BI-RADS 3, 4, and 5 Lesions Detected on Breast**

Sona Chikarmane, MD

*Breast Imaging and Diagnostic Center, Department of Radiology, Instructor*

**Rates of Lipid Testing and Statin Prescriptions among SLE and Diabetes Mellitus Patients in a Nationwide Medicaid Cohort**

Karen Costenbader, MD, MPH

*Division of Rheumatology, Immunology and Allergy, Department of Medicine, Associate Professor*

**How Women Education Leaders Make Critical Career Changing Decisions**

Susan Farrell, MD, EdM

*Department of Emergency Medicine, Assistant Professor*

**Eliciting the patient's experience – chronic pain in Latina women, implications for care in a community health center**

Barbara Gottlieb, MD, MPH

*Division of Primary Care and General Medicine, Department of Medicine, Assistant Professor*

**Susceptibility to exacerbations in asthma**

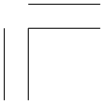

Nicole Grossman, MD



*Asthma Research Center, Department of Medicine, Research Fellow*

**Improving formal didactics for an internship in rural Australia**

Lisa Gruenberg, MD

*Division of Global Health Equity, Department of Medicine, Assistant Professor*





## Women in Medicine and Science Symposium Honorable Mentions

**Strategic Care Redesign Reduces Time to Diagnosis and Treatment of Lung Cancer in Vulnerable Patient Populations**

Sophie-Charlotte Hofferberth, MBBS

*Thoracic Surgery, Department of Surgery, Research Fellow*

**Television viewing time is associated with mortality in African Americans: the Jackson Heart Study**

Tasnim Imran, MD

*Division of Aging, Department of Medicine, Research Fellow*

**Individualized Faculty Coaching Improves Self Reported Teaching and Presentation Skills**

Jennifer Inra MD

*Division of Gastroenterology, Hepatology and Endoscopy, Department of Medicine, Instructor*

**Lysine Specific Demethylase-1- Deficiency Accelerates the Development of Renal Damage and Hypertension During Long Term Exposure to Dietary Sodium**

Isis Katayama, PhD

*Division Of Endocrinology, Diabetes And Hypertension, Department of Medicine, Research Fellow*

**VITamin D and Omega-3 Trial (VITAL) bone health study: Clinical factors associated with Trabecular Bone Score in women and men**

Seena Koshy, PhD

*Department of Radiation Oncology, Research Fellow*

**Silencing polycomb factor Bmi-1 enhances retinoic acid treatment effect by restoration of retinoic acid receptors in cutaneous squamous cell carcinoma**

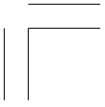

Christine Lian, MD



*Division of Surgical Pathology, Department of Pathology, Assistant Professor*

**Abnormal semantic emotional processing in post traumatic stress disorder**

Einat Liebenthal, DSc

*Department of Psychiatry, Lecturer*





**Women in Medicine and Science Symposium**  
**Honorable Mentions**

**Asthma Associates With Human Abdominal Aortic Aneurysm and Rupture**

Conglin Liu, MD, PhD

*Division of Cardiovascular Medicine, Department of Medicine, Research Fellow*

**Influence of Baseline Magnetic Resonance Imaging Features on Outcomes of Operative and Non-Operative treatment of Meniscal Tear in Patients  $\geq 45$**

Lindsey MacFarlane, MD

*Division of Rheumatology, Immunology and Allergy / Duane Wesemann Lab, Department of Medicine, Clinical Fellow*

**Identification of a novel mechanism of action of Fingolimod (FTY720) on human effector T cell function through TCF-1 upregulation**

Maria Antonietta Mazzola, MD

*Department of Neurology, Research Fellow*

**Peripheral Blood Minimal Residual Disease Analysis by Flow Cytometry has Diagnostic Utility for Adult Patients with Acute Lymphoblastic Leukemia**

Alissa Minkovsky, MD, PhD

*Division of Clinical Pathology, Department of Pathology, Clinical Fellow*

**Establishment of genetically-validated angiomyolipoma and lymphangiomyomatosis-derived cell cultures**

Barbara Ogórek, PhD

*Division of Pulmonary and Critical Care Medicine, Department of Medicine, Research Fellow*

**Toward a Glossary of Competency-Based Medical Education Terms**



Britlyn Orgill, MD



*Anesthesiology, Perioperative and Pain Medicine, Clinical Fellow*

**A Glycovariant of Human CD44 is Characteristically Expressed on Human Mesenchymal Stem Cells**

Olga Gisela Pachon Pena, PhD

*Program of Excellence in Glicobiology, Department of Dermatology, Research Fellow*





**Women in Medicine and Science Symposium**  
**Honorable Mentions**

**Analysis of Baseline Mental Health Data from the Sonya Slifka Multiple Sclerosis (MS) Study (Slifka Study)**

Laura Safar, MD

*Neuropsychiatry/ Sarah Minden's lab, Department of Psychiatry, Instructor*

**Expression profile of proinflammatory cytokines in memory T cells of pediatric demyelinating patients**

Shrishti Saxena

*Department of Neurology, Research Fellow*

**Finding genes for infertility: a balanced translocation in an oligospermic male uncovers SYCP2 overexpression**

Samantha Schilit, MA

*Department of Obstetrics & Gynecology*

**Altered NK Cell Transcription Factor Expression May Predispose to Infection After Trauma**

Anupamaa Seshadri, MD

*Department of Surgery, Research Fellow*

**Reduced Graphene Oxide/GelMA Hybrid Hydrogels as Scaffolds for Cardiac Tissue Engineering**

Su Ryon Shin, PhD

*Department of Medicine, Instructor*

**Myocardial Infarction Risk after Discontinuation of Thienopyridine Therapy in the Randomized DAPT Study**

Ada Stefanescu, MD



*Division of Cardiovascular Medicine, Department of Medicine, Research Fellow*

**hsa-miR-92a1\* in T cell function in Multiple Sclerosis**

Radhika Raheja Suresh, PhD

*Department of Neurology, Research Fellow*





**Women in Medicine and Science Symposium**  
**Honorable Mentions**

**Obesity is associated with increased risk for systemic lupus erythematosus in the Nurses' Health Studies**

Sara Tedeschi, MD, MPH

*Division of Rheumatology, Immunology and Allergy, Department of Medicine, Instructor*

**Metabolically unhealthy obesity and postmenopausal breast cancer risk in the Women's Health Study**

Deirdre Tobias, ScD

*Division of Preventive Medicine, Department of Medicine, Instructor*

**Using Graphene Oxide nano-flakes during Image-Guided Radiotherapy to minimize the potential of cancer recurrence or metastasis**

Dolla Toomeh, MS

*Department of Radiation Oncology, Research Fellow*

**The Standardized Outcomes in Reproductive Cardiovascular Care (STORCC) Trial**

Anne Marie Valente, MD

*Division of Cardiovascular Medicine, Department of Medicine, Associate Professor*

**The clinical impact of maternal cell contamination on prenatal next generation sequencing based testing**

Zena Wolf, PhD

*Laboratory for Molecular Medicine, Department of Pathology, Research Fellow*

**In silico prediction of positional effects of human balanced chromosome rearrangements**

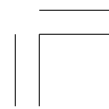
Cinthya J. Zepeda-Mendoza, PhD

*Morton lab, Department of Obstetrics & Gynecology, Research Fellow*

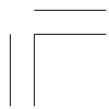




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