

*An extraordinary group of ordinary people funding  
research to stop metastatic breast cancer.*



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**100 Voices  
of  
HOPE**

In 2015, we raised a record **\$225,421** from **193** whispers, voices, and shouts.

We broke the \$1 million mark in cumulative fundraising for research.

### Match

Last year, part of our success came from donors like you that offered generous matching gifts. If you are interested in becoming a match donor at the **\$5,000** or **\$10,000** level, please e-mail us at [sfscott@iu.edu](mailto:sfscott@iu.edu). Every dollar makes a difference, and this can magnify the impact of your giving!

### Events

This **August**, we are partnering with the **Carmel Racquet Club** for a tennis and pickleball round robin. Be on the lookout for other events throughout the year including a night at Bubs and our annual meeting on our Facebook page and in e-mails. If you are interested in partnering for an event please contact us.

Since 2008, we've raised over **\$1,051,780** for metastatic breast cancer research at the IU Simon Cancer Center and fully funded **11 hunches**.

**You've made this possible.**

## From the Desk of Mary Beth Gadus

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*Dear Friends,*

As we kick off 2016, our new advisory board has been working hard to envision the future of 100 Voices of Hope and plan strategically for the next 3-5 years. With this in mind, we are eager for any input and ideas from you, the inspiration and reason for what we do!

We are incredibly thrilled to have broken through the \$1 million mark in funding, which enabled us to fully support two promising hunches, named in memory of the dear Anne Abernethy and Mary Corbett. Many of you have supported us for years, and we are so thankful that you have made this dream a reality.

As I think about where we've come and where we're going I feel hopeful. In 2008, we started as a grassroots group raising money for innovative research. \$1 million later, we are still that group, but we've welcomed many new faces and ideas. We've also gotten to know our local researchers better and had the opportunity to follow their journeys as they make research discoveries. Now, we turn to how to grow strategically while keeping you, the voices, at the center of what we do.

As you read through the following pages, here are some important numbers to remember and proof of our success.

- Our current hunches have resulted in **5 published articles** and **4 more** are in the process of being submitted.
- Our researchers have submitted or presented **10 presentations** at national and local conferences for breast cancer research.
  - We've received **\$4.6 million** in grant funding from 100 Voices of Hope hunches.
  - We have **6 grants** in the process of submission or under review.
- We have **1** hunch in the final stage of being approved for a Phase II clinical trial with patients.

With 100% of our funding going to local research, it's hard to imagine a more worthy way to invest in breast cancer investigations right here in Indiana. I encourage you to share your own personal story with friends and family and help us grow 100 Voices of Hope across the state.

On behalf of the advisory board, thank you from the bottom of our hearts for all that you do.

*Mary Beth Gadus*

Founder, 100 Voices of Hope

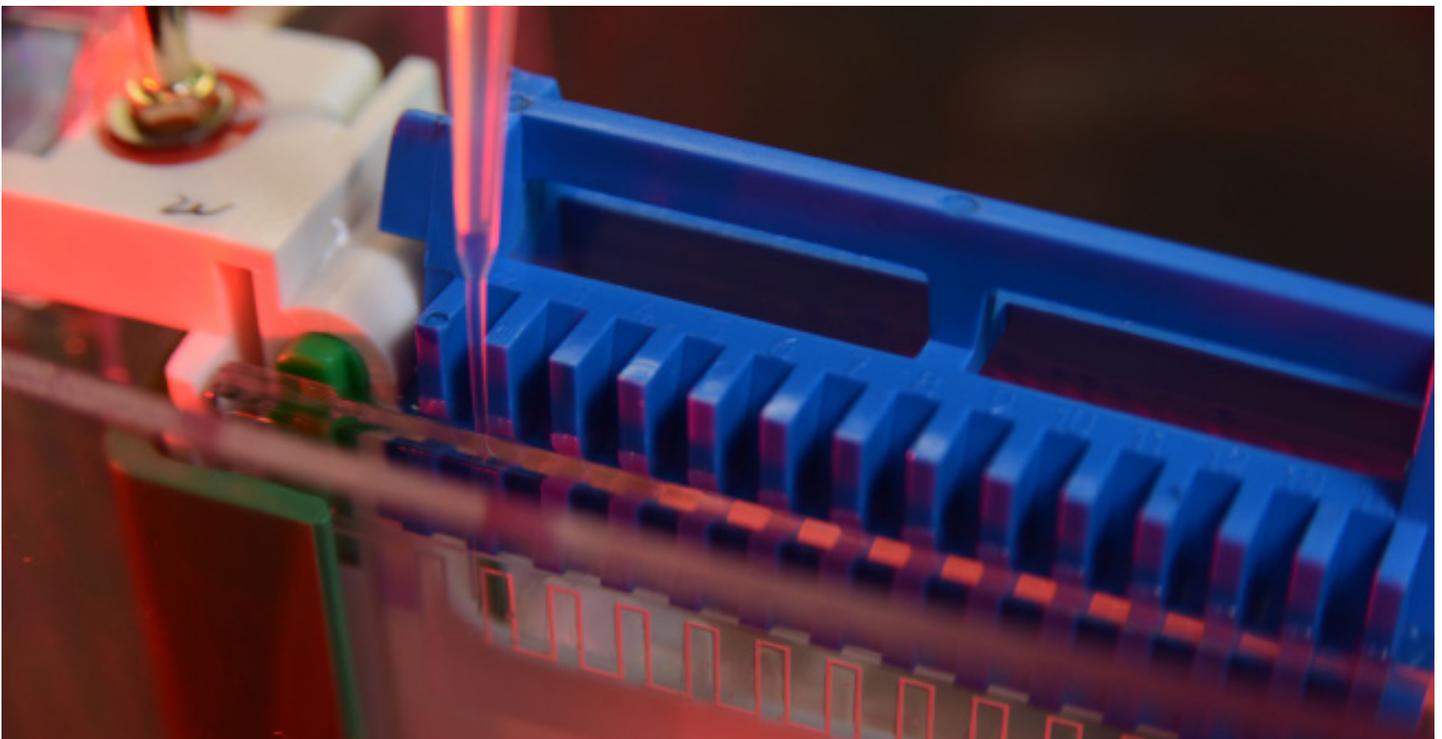
In 2015, we raised \$225,421 from 193 whispers, voices and shouts. We far surpassed our \$1 million goal and have now raised a cumulative \$1,051,780 for metastatic breast cancer research at the IU Simon Cancer Center. This year we are able to fully fund two hunches in memory of two very special women, Mary Corbett and Anne Abernethy. We will strive to continue to honor their lives by tirelessly pursuing research for better treatments for this disease that has personally affected so many of us.

### **Hunch 10 in memory of Mary Corbett**

Hunch #10 is spearheaded by Drs. Jian-Ting Zhang, Jing-Yuan Lui and Hal Broxmeyer. It focuses on triple negative breast cancer and immunotherapy, a very promising area in cancer research where drugs are used to train our own bodies to attack aggressive tumors. The team is working on finding an alternative to a very effective immunotherapy drug – pembrolizumab – that Jimmy Carter received recently. Finding an alternative is key because the cost of pembrolizumab exceeds \$1 million a year. Dr. Jian-Ting Zhang and his team will screen a library of FDA-approved drugs to look for matches, with the goal of identifying an alternative that is easy to make and has already been demonstrated as safe in humans. They hope to close in on a drug within the funding period and move it to clinical trial as quickly as possible. With so few effective options for treating triple negative breast cancer, these studies are extremely important to find solutions that can move to clinical trial more quickly.

### **Hunch 11 in memory of Anne Abernethy**

Hunch #11 was proposed by Dr. Milan Radovich and focuses on triple negative breast cancer. He and his team plan to test two FDA-approved drugs in mice with triple negative tumors that have shown great potential for being an effective combination. If they receive positive results, this hunch would be used to support the launch of Phase I/II clinical trials. Dr. Radovich's hope is that this combination will provide a new "precision medicine" based drug combination for triple negative breast cancer.



## Hunch #9 – Novel Diagnostics and Treatment of Bone Metastasis (2015)

Hunch #9 is innovative in two ways. It is the first collaborative project we've funded with a team of Purdue biomedical engineers. Second, this hunch applies to all types of metastasis and focuses on developing a microfluid device that can circulate in the bloodstream and destroy metastatic cancer cells as they migrate.

The team of researchers includes Dr. Hiroki Yokota, biomedical engineer; Dr. Likhun Zhu, mechanical engineer; Dr. Sungsoo Na, biomedical engineer; Dr Jong Eun Ryu, mechanical engineer; and Dr. Mangilal Agarwal, Associate Director of Research Development. Dr. Yokota also works with Dr. Hari Nakshatri on Hunch #8.

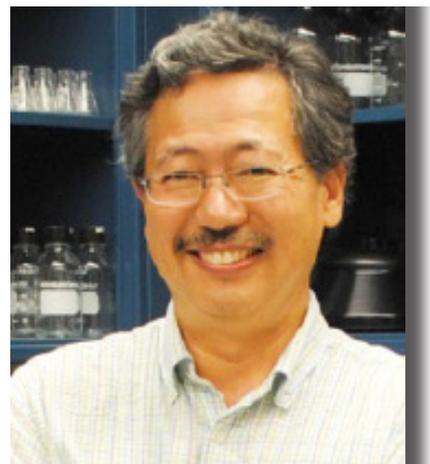
The purpose of the project is to create a microfluidic device that senses metastatic cancer cells in the bloodstream and destroys them. Specifically, the device will detect cell wall stiffness, which is different in cancer cells versus normal cells. This is proof-of-concept funding, meaning that we are funding the idea at its beginning stages – the hardest time to attract support. As we move forward in cancer research, more collaboration between the physical sciences including engineering and the biological sciences including chemistry is pivotal. Both sides offer unique perspectives in how we can treat and stop metastasis, which is the primary reason people lose their lives to cancer.

### Key Accomplishments

- Developed a device that can differentiate between cancer cells and normal cells and adding a gate to sort cancer and normal cells in the next 6 months
- Preparing a journal article for submission
- Presented at the 2016 Amelia Project Meeting in Kokomo, IN
- Received two grants from IUPUI totaling \$30,000 to grow this research

*"100 Voices of Hope allows us to form a research team of five investigators at Purdue School of Engineering and Technology, and conduct a proof-of-concept experiment. Four of five are in the area of fluid dynamics, biomechanics, microfabrication, and nanotechnology, and they have no previous experience in breast cancer research. We appreciate this research opportunity to develop a novel device that can assist in treatment of breast cancer and bone metastasis."*

**Dr. Hiroki Yokota**



### HUNCH #8 – GUANABENZ AND ITS ANALOG FOR TREATMENT OF BONE METASTASIS (2014)

DRS. HARI NAKSHATRI AND HIROKI YOKOTA are working together to study guanabenz, a drug traditionally used to treat high blood pressure. Its shown promise in killing breast cancer cells and strengthening bone cells. Specifically, Dr. Yokota's group is researching guanabenz at a cellular level to see if it and other chemical agents can prevent bone metastasis by blocking kinase activity. Blocking kinase activity in malignant cells helps stop bone metastasis in breast cancer. Dr. Kathy Miller is also working on a grant from the Breast Cancer Research Foundation to study guanabenz with patients.

The drug – guanabenz – has been shown to kill breast cancer cells and stop the spread of breast cancer cells to bone in the laboratory. However, persistent bone pain experienced by patients with bone metastasis is largely due to bone loss. Guanabenz is also shown to prevent bone degradation and promote new bone formation, which will help to alleviate pain.

The purpose of this hunch is to discover the mechanism that enables guanabenz's anti-cancer and bone-strengthening effects in a formalized laboratory study. The team's goal is to develop data to initiate clinical studies with this drug to demonstrate prevention and treatment of bone metastasis and to rebuild bones damaged by cancer.

#### Key Accomplishments

- Completed two mouse studies. The first tested if guanabenz could reduce lung metastasis in mice and found it did not. The second tested a guanabenz analog (drug much like guanabenz) using two mouse models and found that this analog can reduce tumor size in mammary and bone tumors.
- Identified a few other guanabenz analogs that might be more potent for stopping the spread of cancer.
- Developing strategy to deliver these drugs directly to bone.
- Received a \$200,000 grant from the Breast Cancer Research Foundation, \$70,000 of which is being used to supplement research on guanabenz



*"100 Voices of Hope allows us to establish a new collaboration between a cancer scientist and bone biologist for developing novel treatment for bone metastasis from breast cancer. It also allows unhindered testing of a hypothesis without the fear of being a complete failure. Even if 10% of what we do with 100 Voice of Hope funding is successful, that is a huge achievement."*

**Dr. Hari Nakshatri**

## HUNCH #7 – LncRNAs AND METASTASES (2014)

DR. SUNIL BADVE studies metastasis suppressor genes (MSGs) that are thought to play a role in stopping cancer from spreading. When these suppressor genes are turned off in experimental models, cancer spreads faster and the tumors are larger. Human tumors with inactive MSGs are known to have a worse prognosis.

Until recently, it has been hard to study what turns these MSGs on and off. We do know that regulators (called long non-coding RNA or lncRNA for short) are responsible for flipping the switch on MSGs. Using new technology, Dr. Badve has been using data from the Cancer Genome Atlas, a national genome bank, to study almost 1,000 breast cancer patients and identify these regulators or lncRNAs associated with metastasis.

### KEY ACCOMPLISHMENTS

- Identified a regulator that plays a major role in ER+ breast cancer and re-named it DEEBC. Designed probes for clinical marker development to identify this regulator in women with ER+ breast cancer. DEEBC's presence helps prevent breast cancer and metastasis.
- Submitted article about DEEBC that is under review to be published in Scientific Reports – a member of Science journal group
- Presented at the 2016 United States and Canadian Academy of Pathology Conference
- Identified an FDA-approved drug that can be repurposed for ER+ cancers and is under review for approval
- Presented at the 2015 San Antonio Breast Cancer Symposium
- Awarded \$3 million grant for ethnicity-determined immune factors and DCIS outcomes using data from this hunch
- Planning an NCI grant and submitted a DoD grant



*"100 Voices of Hope provides avenues for new idea development and pilot research. I am inspired to do research to help better the lives of patients and translate basic science into clinical practice."*

**Dr. Sunil Badve**

### HUNCH #6 – CREATION OF NOVEL UPAR CONJUGATED THERAPY FOR TREATMENT OF BREAST CANCER (2013)

DR. SAMY MEROUEH is developing drugs for the prevention and treatment of metastatic disease by targeting a protein that is exclusively expressed by malignant tumors called uPAR. His goal is to develop a drug that links to the protein to invade and kill malignant tumor cells.

Dr. Meroueh has completed funding for this project and is using his findings from our donations to feed into future research endeavors. Below are some of the key accomplishments from his work that donors like you made possible.

#### KEY ACCOMPLISHMENTS

- Discovered a novel small molecule that inhibits invasion and colonization of bone by breast cancer cells. These compounds inhibit ex vivo bone colonization with the same efficacy as the FDA-approved drug zoledronic acid in a study done by a bone metastasis expert, Dr. John Chirgwin. Unlike zoledronic acid, our compounds target the cancer cells directly. Dr. Meroueh is currently pursuing these novel compounds in animal studies and plans on publishing the results, submitting a patent application, and a grant application to the NIH to develop therapeutic agents to prevent and reverse bone metastasis.
- Submitted an R21 grant application to the NCI to pursue his drug-linking strategy to deliver chemotherapeutics and recruit the immune system to destroy malignant cells. The R21 obtained a very competitive score. Based on this promising score, he was invited to resubmit the grant to a special 5-year R21-R33 mechanism at the NCI that was developed for technology development projects.
- Awarded a 5-year 3-million dollars National Cancer Institute (NCI) grant to pursue novel compounds that were discovered in his laboratory. These compounds inhibit a protein that plays a key role in cancer invasion and metastasis. These compounds have been patented and licensed by a pharmaceutical company.
- Developed novel and promising kinase inhibitors that inhibit networks associated with triple-negative breast cancer growth and metastasis. This project was started in collaboration with Dr. George Sledge. He has submitted a patent for these compounds and is pursuing them in animal models with collaborators at MD Anderson and the University of Chicago.
- Submitted 5 publications and one provisional patent this year. Two of the manuscripts have been accepted for publication at the Journal of Chemical Information and Modeling and Molecular Biosystems.



*"This funding from 100 Voices is critical to pursue high-risk high-reward projects. My inspiration for research is to develop non-toxic drugs that prevent and reverse cancer metastasis in breast and other tumors."*

**Dr. Sammy Meroueh**

## HUNCH #5 AND #4 – TRIPLE-NEGATIVE BREAST CANCER PRECISION MEDICINE & TRIPLE-NEGATIVE BREAST CANCER DRUG DEVELOPMENT (2011/2012)

#5 - DR. MILAN RADOVICH is sequencing tumors from a Phase II clinical trial led by Dr. Kathy Miller. These tumors are from patients with triple negative breast cancer who have residual disease after neoadjuvant chemotherapy. All genomic sequencing of this trial is now complete. From this work, his lab has begun to understand mediators of chemotherapy resistance, biomarkers of response/prognosis, and circulating biomarkers of relapse both DNA and RNA based.

### KEY ACCOMPLISHMENTS

- Developing a device to detect biomarkers in order to make a low-cost and portable method for breast cancer detection
- Submitted a National Institute of Health grant to join this research with a newly launched Phase III breast imaging clinical trial to see if this test will detect breast cancer in women with negative mammograms but who will develop breast cancer prior to their next screening
- Presented and won award at 2015 San Antonio Breast Cancer Symposium
- Presented at 2015 ECOG-ACRIN Young Investigator Symposium
- Presented at the American Society of Clinical Oncology in June of 2014

#4 - DR. MILAN RADOVICH is developing therapeutic targets for metastatic triple-negative breast cancer with funding for this hunch. His lab has been maturing a synergistic dual drug combination that targets two important cancer pathways. The final preclinical data is complete, demonstrating excellent activity of the drug combination.

### KEY ACCOMPLISHMENTS

- Completed all pre-clinical experiments to lead to a first-in-human trial
- Designed a Phase II clinical trial that is currently under review for approval
- Submitted paper that is currently under review to be published in scholarly journal
- Presented at the American Society of Human Genetics Annual Meeting
- Presented at the 2013 and 2015 San Antonio Breast Cancer Symposium
- Presented at the 2015 American Association for Cancer Research Annual Meeting
- Received funding from IU Simon Cancer Center Core Pilot Grant
- Submitted DoD Breakthrough Award grant which is currently under review
- Submitted a National Institute of Health grant which is under review



*"100 Voices of Hopes enables researchers to pursue innovative ideas that are geared to have maximal impact for breast cancer patients. There is nothing more enjoyable than making new discoveries that can be used to help others."*  
**Dr. Milan Radovich**

### **HUNCH #3 – GENES PREDICTING LATE RECURRENCE OF BREAST CANCER (2010)**

DRS. SUNIL BADVE'S AND YESIM GÖKMEN-POLAR'S project goal is to determine genes that are involved in the late recurrence of breast cancer, particularly estrogen receptor (ER) positive breast cancer. Breast tissue taken at the time of diagnosis is being compared with tissue from women who are taking hormonal therapies at five and ten years out to learn which genes are being expressed.

ESPR1 is a biomarker that plays a role in endocrine resistance. Endocrine therapy is an important part of ER positive breast cancer treatment, and patients sometimes develop resistance leading to late recurrence. It has been found that in patients with endocrine resistance, there is a higher expression of ESRP1, resulting in poor outcomes. Drs. Badve and Gökmen-Polar are drilling further down into the gene sequencing to identify a druggable target to overcome endocrine resistance.

The second part of the research involves a genetic analysis of tumors from 2,000 patients with ER positive breast cancer. This provides a very thorough breakdown of genetic differences between tumor types. Knowing the gene pathways in tumors that lead to late recurrence will give Drs. Badve and Gökmen-Polar a picture of genes that can be targeted for therapeutics.

Drs. Badve and Gökmen-Polar have spent the funding from 100 Voices of Hope and are continuing to use this research. See below for accomplishments from funding made possible by donors like you.

#### **KEY ACCOMPLISHMENTS**

- Documented the role of ESPR1 in breast cancer and submitted a patent for alternative splicing in endocrine resistance
- Awarded \$3 million grant for ethnicity-determined immune factors and DCIS outcomes using data from this hunch
- Working on NIH grant for 2016

### **HUNCHES #1 AND #2 (2008/09)**

DR. HARI NAKSHATRI identified a potential biomarker for recurrent breast cancer in circulating blood; he patented his biomarker and secured a \$400,000 National Cancer Institute-funded grant to expand the project. While this project has been successfully completed, his research continues and is focusing on how to improve cardiac function in breast cancer patients. He recently secured a \$1.2 million grant from the Department of Defense for his work in this area. In addition, his initial work on this biomarker was published in *Breast Cancer Research* (2011 13: R86) and additional studies in *Cancer Research* (2014 74:4270-81).

#### **KEY ACCOMPLISHMENTS**

- Awarded \$400,000 National Cancer Institute-funded grant.
- Published articles in *Breast Cancer Research* and *Cancer Research*, the most highly cited cancer research journal in the world.
- Secured a \$1.2 million Department of Defense grant for continuing research in this area

## How to Become Involved

### GIVE

#### WHISPERS

Gifts of any level are welcomed and can be made in honor or memory of a loved one

#### VOICES

Gifts of \$1,000 can be made by a single donor or multiple whispers

#### SHOUTS

Gifts of greater magnitude are gratefully accepted

#### MATCHES

Use your gift to grow others!

### ADVOCATE

#### RAISE

\$1,000 through email or letter campaigns

#### HOST

a fundraising event

#### CELEBRATE

special events by inviting friends and family to donate to 100 Voices of Hope

#### ORGANIZE

10 friends to donate \$100 each to fund a voice in someone's honor.

### PARTICIPATE

Meet with fellow advocates. Connect directly with our research team at events. Be a voice in choosing which research hunch is funded.

### TO MAKE A GIFT

Gifts are made payable to  
IUF/100 Voices of Hope and mailed to:

IU Foundation | PO Box 7072 | Indianapolis, IN 46207-7072

Or online at [cancer.iu.edu/100voices](http://cancer.iu.edu/100voices). Contact Susanna Scott at [sfscott@iu.edu](mailto:sfscott@iu.edu) or 317-278-2120 to learn more.