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Summer 2015 Newsletter

Indiana University
Melvin and Bren Simon Cancer Center
2014 Year in Review

In 2014, we raised $117,850.29 from 145 whispers, voices and shouts!

Events

Our advisory board graciously hosted a personal dinner and a night at Forrest Formsmma Art Gallery. We also partnered with Cesar’s Group Fitness Studio and raised over $2,000 with a fun morning of dancing. To end the year, we held our annual meeting at the SpeakEasy and feasted on delicious catered food from Keith Little.

Research

We had a record number of hunch submissions from the IU Simon Cancer Center. Two proposals focused on muscle wasting and combining Avastin with another treatment. Investigators from the winning hunch will develop a nanomachine to remove cancer cells from the bloodstream. This is in partnership with Purdue University.

Since 2008, we’ve raised over $850,000 for metastatic breast cancer research at the IU Simon Cancer Center and fully funded 9 hunches.

You’ve made this possible.
Dear friends,

2014 was a big year for us, and we are so thankful for your support in raising over $117,000 and funding a ninth hunch!

We are looking to the future of 100 Voices, and our goal this year is to reach $1 million cumulatively for metastatic breast cancer research at the IU Simon Cancer Center. With your help, we can achieve our goal!

Our advisory board will be meeting with 100 Voices of Hope researchers in July. This newsletter includes the latest updates on their hunches and features information about our winning hunch for 2015.

Here are some exciting numbers from 2014:

- Our current hunches have resulted in 5 published articles and one is in the process of being submitted.

- Our researchers have submitted or presented 8 presentations at national and local conferences for breast cancer research.

- We’ve received $1.6 million in direct grant funding from 100 Voices of Hope hunches.

- 100 Voices of Hope has generated data that has helped secure over $3 million of additional grant funding.

- There are a total of 9 grants in different stages of submission as a result of our donations.

This year, we will be hosting a few events around the city that we’d love for you to attend. We will keep you updated in our e-blasts and on our Facebook page with dates and times.

On behalf of the advisory board, thank you from the bottom of our hearts for making this possible. We look forward to record-breaking 2015!!

Mary Beth Gadus

Founder 100 Voices of Hope
The winning hunch for 2015 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.

We’ll keep you updated on this project throughout the year, and the team is incredibly grateful for your support!
Goals for 2015

In 2015, we have 3 simple goals.

Raise $150,000 and reach $1 Million Dollars in grassroots funding for Metastatic Breast Cancer Research.

Celebrate your 100 Voices, whispers and shouts.

Fund a 10th Hunch.

To become involved, e-mail Susanna Scott at sfscott@iu.edu.
Drs. Hari Nakshatri and Hiroki Yokota have progressed in the past six months and are in the process of **conducting two pre-clinical animal trials on mice**. Their pilot experiment focuses on guanabenz, a drug traditionally used to treat high blood pressure. Its shown promise in killing breast cancer cells and strengthening bone cells. In addition to the animal trial, 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**

- Began two mouse studies and now testing the effects of guanabenz in spontaneous lung metastasis models. The first trial that tested guanabenz with or without taxol in the treatment of bone metastasis was unsuccessful at arresting the spread of cancer.
- 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*
DR. SUNIL BADVE studies metastasis suppressor genes (MSGs) that are thought to play a role in preventing metastasis. When these suppressor genes are turned off in experimental models, both frequency and size of metastasis increase. 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.

**Since August of 2014, Dr. Badve has identified an IncRNA that plays a major role in ER+ breast cancer.** To prove his theory, Dr. Badve will determine if this IncRNA turns off MSGs and increases metastasis in mouse models. Finally, a large number of FDA-approved drugs that may turn the MSGs back on and prevent the development of metastasis will be analyzed.

**KEY ACCOMPLISHMENTS**

- Prepared and submitted journal manuscript from research findings on June 1, 2015.
- Submitting data from this research to present at the San Antonio Breast Symposium.
- Planning an NCI grant and submitted a DoD grant
- Awarded $3 million grant for ethnicity-determined immune factors and DCIS outcomes using data from this hunch

“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*
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.

Since August of 2014, his lab has had several updates. They’ve discovered a new small molecule that binds to a site on uPAR that is more effective for delivering a chemotherapeutic. His is the only lab in the world that has developed a molecule that can attach to uPAR. He is also making progress in developing the necessary chemistry to link the drug to the tumor.

Second, Dr. Meroueh has found a new compound that inhibits a kinase that is overexpressed in triple negative breast cancer and is highly druggable. He and his colleagues are currently developing this compound into therapeutic agents. A therapeutic could stop the kinase and thus stop tumor growth in triple negative breast cancer.

Third, his lab has found a new compound that could have significant implications for treating Ras-driven tumors. Ras was one of the first oncogenes to be discovered and is found in many types of tumors including non-small cell lung cancer and pancreatic adenocarcinoma.

KEY ACCOMPLISHMENTS
- Published article in Methods in Molecular Biology
- Published article in the American Chemical Society Chemical Biology Journal, the second most influential journal in chemical biology
- Presented at the University of Kansas Center for Computational Biology and Department of Biomolecular Sciences
- Presented at the Indiana University Chemical Biology Retreat

“This funding is critical to pursue high-risk high-reward projects that may not be funded by the NIH or DoD. My inspiration for research is to find a cure for cancer and other diseases.”

Dr. Samy Meroueh
Hunch Updates

Triple-Negative Breast Cancer Precision Medicine &
Triple-Negative Breast Cancer Drug Development
HUNCH #5 AND #4 (2011/12)

#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.

Moving forward, Dr. Radovich has identified a novel set of long noncoding RNAs that are breast cancer specific and can be detected in the bloodstream. In collaboration with Purdue and University of Texas, his lab is developing a device to detect these biomarkers in order to make a low-cost and portable method for breast cancer detection.

KEY ACCOMPLISHMENTS
- Presented at the American Society of Clinical Oncology in June of 2014
- Submission of NIH grant

#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 in vivo preclinical data is complete, demonstrating excellent activity of the drug combination. Their pharmaceutical partner has approved preclinical data and they are designing the Phase I/II clinical trial for metastatic triple-negative breast cancer patients.

KEY ACCOMPLISHMENTS
- Presented at the American Society of Human Genetics Annual Meeting
- Presented at the San Antonio Breast Cancer Symposium
- Received funding from IU Simon Cancer Center Core Pilot Grant
- Submitted DoD Breakthrough Award grant which is currently under review
- Submitted NIH 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
Genes Predicting Late Recurrence of Breast Cancer  
HUNCH #3 (2010)

Drs. Sunil Badve and Yesim Gökmen-Polar’s project is progressing along two fronts. The 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. **Since August of 2014, Sunil and Yesim have made major progress in documenting the role of ESRP1 in breast cancer.**

ESRP1 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.

**KEY ACCOMPLISHMENTS**
- Submitted abstract to American Association of Cancer Research and San Antonio Breast Cancer Symposium
- Awarded $3 million grant for ethnicity-determined immune factors and DCIS outcomes using data from this hunch

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.
Get 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.

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 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. Contact Susanna Scott at sfscott@iu.edu or 317-278-2120 to learn more.