

Voices Lead | Lives Change | Hope Endures



A LETTER FROM MARY BETH...

The Voices of Hope Advisory Committee met with researchers in early August for the annual update of all Voices of Hope research projects currently being conducted.

The only word to describe the research team's progress on all of the hunches is EXTRAORDINARY!!

We hope you will take the time to read the update of each of the hunches. Of significance is the information concerning the clinical trial for Hunch #4 and animal trial for Hunch #8.

The fact that your Voice has contributed to research that will lead to a clinical trial with the potential for advancing treatment for Metastatic Breast Cancer is significant!

I would like to welcome Susanna Scott to the 100 Voices of Hope team. Susanna is the new Assistant Director of Development at the IUSCC. One of her primary responsibilities is 100 Voices of Hope, and during her short time on the board she has already proven to be one of our greatest assets! Please do not hesitate to contact her with any questions.

We have begun raising our Voices for the VOH 2015 Hunch Research Project. It is not too early to send in your Voice! Contact Susanna if you need information about where to send your check or if you'd like to make a stock transfer that she can help to coordinate.

Our annual meeting will be held November 19th at the Speak Easy at 5255 North Winthrop Avenue, from 6–8 p.m. A new format is in the works for this year. Past and current Voices and Whispers are invited, and we would like for you to extend an invite to anyone who may have interest in contributing to 100 Voices of Hope. Contact Susanna at sfscott@iu.edu or 317-278-2120.

Another upcoming event is our Zumba for the Cure event at Cesar's Group Fitness Studio at 9546 Allisonville Road, Suite 117, from 10–11:30 a.m. The minimum fee is \$10 per participant, and you can register by clicking [here](#).

With hope for cancer free tomorrows,

Mary Beth Gadus

HUNCH #8 (2014)



DRS. HARI NAKSHATRI AND HIROKI YOKOTA received approval from the Institutional Animal Care Approval Committee after our May update and are now beginning a pilot experiment of guanabenz, a drug shown to kill breast cancer cells and strengthen bone cells, on 15 animals. By October, they will have the first results of this trial. 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 also received 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.

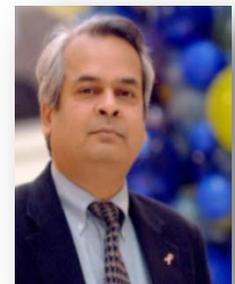
This hunch proposes to validate guanabenz's anti-cancer and bone-strengthening effects in a formalized laboratory study. The team's goal is to develop data to compliment clinical studies with this drug to demonstrate prevention and treatment of bone metastases and to rebuild bones damaged by cancer.

KEY ACCOMPLISHMENTS

- 100 Voices of Hope funding has allowed for an animal trial of guanabenz, a drug that kills breast cancer cells and strengthens bone cells.
- Dr. Kathy Miller received a \$200,000 grant from the [Breast Cancer Research Foundation](#), \$70,000 of which will supplement this research with a clinical trial of guanabenz that is underway.

HUNCH #7 (2014)

DR. SUNIL BADVE is studying a group of metastasis suppressor genes (MSGs) that are thought to play an important role in preventing the development of metastases. In experimental models, turning off the MSGs increases the frequency and size of metastasis, and human tumors that have turned off the MSGs have a worse prognosis. Unlike some other cancer genes, the MSGs are not "mutated," they are just turned off. Since the last update in May, the logistics of the projects have been mapped with a start date of September anticipated. The main question this research is trying to answer is: How do cancer cells turn off MSGs?



Until recently it has been hard to study the regulators (called long non-coding RNA, or lncRNA for short) of these genes, but new technology makes this possible. First, Dr. Badve will use data from the [Cancer Genome Atlas](#), an NCI-sponsored project including genomic data from almost a 1,000 breast cancer patients, to identify lncRNAs associated with metastasis.

After confirming those leads in tumors from the IUSCC breast tissue bank, it will be determined if those same lncRNAs turn off MSGs and increase metastasis in mouse models. The goal is to identify and analyze FDA-approved drugs that turn the MSGs back on and prevent the development of the metastasis.

KEY ACCOMPLISHMENTS

- To target drug treatment for a breast cancer tumor, it is critical to identify how cancer cells work and metastasize. This research focuses on how cancer cells turn off genes that prevent metastasis.
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HUNCH #6 (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. Since the last update in May, he has submitted his findings to be published in the [American Chemical Society Chemical Biology Journal](#), a highly influential journal. He has also collected enough data from 100 Voices of Hope Funding to submit a new NIH proposal to continue his research.

He is following a chemical method to develop a targeted drug that kills malignant tumor cells and spares healthy cells. A new compound named IPR1110– discovered in his laboratory– targets a protein called uPAR that is only present in malignant cells. His is the only lab in the world that has developed a small molecule than can attach to uPAR. The lab is working to chemically link IPR1110 to a chemotherapeutic so that when the molecule attaches to uPAR, it delivers the drug to malignant cells. The main question his research is trying to answer is whether IPR1110 can attach to uPAR successfully and deliver the chemotherapeutic to destroy malignant cells while excluding healthy cells.

Dr. Meroueh anticipates that the molecule IPR1110 may also act as a stand-alone agent for the treatment of metastasis. His recent data verifies that IPR1110 can be used as both a homing agent to deliver a chemotherapeutic and may be useful as a therapeutic agent. With 100 Voices of Hope funding, he has been able to make the targeting agent as effective as the drug to which he is linking. His next steps include animal testing in December and January to assess the effectiveness of the compound.

KEY ACCOMPLISHMENTS

- Dr. Meroueh used 100 VOH funding to develop data that was submitted to the [American Chemical Society Chemical Biology Journal](#), the second most influential journal in chemical biology.
- With the data collected from 100 VOH funding, he also plans to submit a new NIH proposal to expound his research.
- He developed a new compound, the only one of its kind in the world, that may be used to deliver chemotherapy to malignant cells without harming normal cells.
- The compound he developed may also be able to treat metastasis in addition to delivering chemotherapy.

HUNCH #5 AND #4 (2011/12)

#5 - DR. MILAN RADOVICH sequenced the genomes of 135 patients with triple negative tumors being treated with a new drug combination and presented his finding at the 2014 annual meeting of the [American Society of Clinical Oncology](#) (ASCO). Those results demonstrated a druggable pathway and RNA biomarkers that mediate chemotherapy resistance in triple negative tumors. Dr. Radovich is currently sequencing the plasma from the trial which allows for sensitive detection of treatment response and relapse in patients.



In collaboration with industry, Dr. Radovich has early access to a diagnostic tool that will allow his lab to detect circulating tumor DNA with an extremely high sensitivity. They are also in the early phases of developing a new analysis method for circulating RNA biomarkers in anticipation of submitting an NIH proposal specifically for RNA biomarkers for early cancer detection. This work has identified novel mechanisms of why triple-negative breast cancers can become resistant to chemotherapy in newly diagnosed patients. Patients who have residual tumor after chemotherapy have a high recurrence rate. Further, the data is informing the laboratory of new therapeutic interventions for those patients who develop resistance.

KEY ACCOMPLISHMENTS

- 100 VOH funding led to a presentation by Dr. Radovich of his research at the [American Society of Clinical Oncology](#) in June.
- He is preparing to use the data collected to submit an NIH proposal to research RNA biomarkers for the early detection of recurrent triple-negative breast cancer.

#4 - DR. MILAN RADOVICH is in the final phase of completing the mouse studies in collaboration with [Novartis](#) using a novel drug combination for triple-negative breast cancer. The two-drug combination has been so successful that treatment to mice had to stop so that researchers would have residual tumor to analyze. A final anti-tumor efficacy study of the combination is being tested in mice with implanted human tumors to see if the response to treatment remains effective. Dr. Radovich has been invited by Novartis to submit an Investigator Initiated Trial grant request with the hopes of opening a Phase I trial in metastatic triple negative breast cancer within six months.

KEY ACCOMPLISHMENTS

- Dr. Radovich's lab found a new drug combination that significantly reduced triple negative breast cancer tumors in animals. In collaboration with industry, this 100 VOH funded research will be moving into a clinical trial within six months.
- He presented research at the [Annual San Antonio Breast Cancer Symposium](#) in December, 2013.

HUNCH #3 (2011)

DRS. SUNIL BADVE AND YESIM GÖKMEN-POLARS' 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 in remission and taking hormonal therapies at five and 10 years out to learn which genes are being expressed.

The first part of the research focuses on the biomarker ESRP1 and its 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 primary 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

- Research related to identifying gene markers that indicate endocrine resistance in ER positive breast cancer was recently accepted to be published in [Modern Pathology](#), a highly ranked and influential international journal.
- Drs. Badve and Gökmen- Polar presented findings at the 2013 [Annual San Antonio Breast Cancer Symposium](#) and at the 2014 [American Association of Cancer Research](#) annual meeting.

HUNCHES #1 & #2 (2009/10)

DR. HARI NAKSHATRI has 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 is seeking grant funding. 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

- Dr. Nakshatri's research and 100 VOH funding resulted in a \$400,000 [National Cancer Institute](#)-funded grant.
- His work was published in both [Breast Cancer Research](#) and [Cancer Research](#), the most highly cited cancer research journal in the world.



100 VOICES OF HOPE INVITES YOU TO BECOME AN ADVOCATE FOR WOMEN LIVING WITH BREAST CANCER BY SUPPORTING LABORATORY RESEARCH. FOR MORE INFORMATION PLEASE CONTACT:

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