



DEPRESSION CENTER

**HEINZ C. PRECHTER BIPOLAR RESEARCH FUND**  
 UNIVERSITY OF MICHIGAN

## PRECHTER FUND *MOMENTUM*

FROM THE PRINCIPAL INVESTIGATOR

***What makes a person bipolar, prone to manic highs and deep, depressed lows? Why is it so hard to find new treatments for a condition that affects millions of people worldwide?***

*Bipolar disorder affects individuals across their lifespan and therefore must be studied in a longitudinal fashion.*



**Melvin G. McInnis, M.D., FRCPsych**

Thomas B. and Nancy Upjohn Woodworth  
 Professor of Bipolar Disorder and Depression  
 Professor of Psychiatry  
 Principal Investigator,  
 Heinz C. Prechter Bipolar Research Fund

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### **What does the Prechter logo mean?**

*The blue ribbon “P” is surrounded by a white circle. It represents the cycle of the illness. Always in search for balance and wellness in life, patients with bipolar disorder alternate between the poles of “mania” and “depression.” The blue ribbon breaking through the circle signifies the Fund’s goal to advance breakthrough medical research to develop cures for the illness.*

Enormous progress has been made toward finding the answers to these fundamental questions in the field of neuroscience. Researchers at the Heinz C. Prechter Bipolar Research Fund are at the vanguard of the science of bipolar disorder. These physician-scientists work tirelessly **to develop personalized treatments for bipolar disorder and to prevent recurrences to enable those with bipolar disorder to lead healthy and productive lives.**

### CURRENT RESEARCH

The goals of the Prechter Fund are to discover the fundamental biological changes that cause bipolar disorder and develop new interventions to treat and prevent the illness. Researchers do this through the study of the longitudinal course in people who are diagnosed with bipolar. Research involves biology (including genetics), clinical, and environmental features. The illness has a biological foundation, and is influenced by personal, social and environmental surroundings. It is recognized

that an integrated approach is needed in order to understand the individual with the disease.

Bipolar disorder is an illness that has been with mankind since recorded history. Research is essential to both treat and prevent bipolar disorder in future generations. **Our research emphasizes strategies to identify the illness at earlier stages of development; and among people with established bipolar disorder to test methods to predict emerging episodes of mania and depression.** People with bipolar disorder do live productive lives, yet many suffer unnecessarily.

### RESEARCH ANCHORS

**Our research programs are anchored in the “Longitudinal Study of Bipolar Disorder” and the Heinz C. Prechter Bipolar Repository.**

CONTINUED ON NEXT PAGE



These studies enroll participants in clinical research and provide a base for the storage of the biological samples and related clinical and environmental data. Thus far, the Longitudinal Study, entering its 10th year in 2016, has enrolled over 1100 individuals. From these participants, billions of data points have been generated through biological samples (DNA), neuropsychological testing, clinical interviews, bimonthly follow-up, and innovative monitoring using mobile devices.

Participants also collaborate with the research team in additional studies that have resulted in the acquisition of several more big data sets in cell biology, sleep, nutrition, physiology, and genetics. Participants generously offer their personal time and information in the search for new treatment strategies. All of the data is stored in the Prechter Bipolar Repository.

*Philanthropic gifts support almost 60 percent of the total resources allocated to bipolar research.*

**iPSC: CELLULAR AND MOLECULAR NEUROBIOLOGY OF BRAIN DISORDERS**

In March 2014, a team of researchers led by Sue O’Shea, Ph.D., and myself published a report of the first stem cell lines (iPSC) generated from patients with bipolar disorder. This is a powerful model to study cell function, and stimulates the discovery of new molecules that will create and test new medications. The Prechter Fund is a strong leader of biomedical research in bipolar disorder.

**PRIORI: PREDICTING INDIVIDUAL OUTCOMES FOR RAPID INTERVENTION**

Predicting and preventing episodes in bipolar disorder is a priority and part of our vision. We are using smartphone technology to capture data in a non-obtrusive, in-the-moment manner. The software application runs in the background of the mobile device and gathers the acoustic patterns of speech that are sent to a secure server for computational analysis.

We have acoustic data from over 40,000 calls from people participating in this project. Our data indicate that we can identify acoustic features

from speech gathered on a mobile smartphone that predict depressed and manic states of bipolar disorder.

We are actively developing the next phases of this program, which include large multi-site clinical trials to test the efficiency of predicting episodes in sufficient time to intervene.

**THE FUTURE OF BIPOLAR RESEARCH: 2016 AND BEYOND**

We are looking at and learning about bipolar disorder from across a broad spectrum of scientific and technological disciplines.

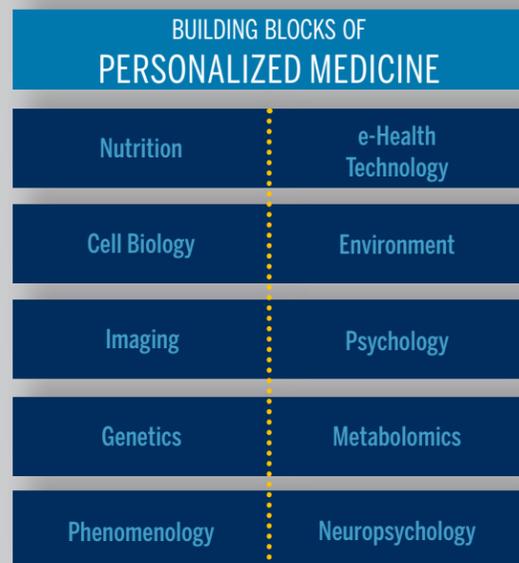
It is clear from the research trajectory of the past decades that there is no one specific approach that will lead to the fundamental knowledge of bipolar disorder and provide specialized treatments and prevention for bipolar disorder. Rather, it is this combined, multidisciplinary, dynamic approach that we believe will be successful.

I invite you to visit our website [www.prechterfund.org](http://www.prechterfund.org) for up-to-date information on all our research projects and to contact me with any questions.

Live well,



[mmcinnis@umich.edu](mailto:mmcinnis@umich.edu)



Dear Friends:

Thank you so much for your continued support of our research. Over the past years, under the direction of Dr. McInnis, the Prechter Fund has thrived and grown as a unique model of scientific collaboration and medical research focused exclusively on the intricacies of bipolar illness.

Our ultimate goal is to achieve personalized treatments for the patient and to become the number one place in the nation regarding all research into bipolar — a place of hope, a place where research turns into results for patients. As we mark the close of 2015, we can reflect on the many significant accomplishments achieved by the research team.

Your contributions have made it possible for the Prechter Fund to come this far. Thank you so very much.

Very Sincerely,

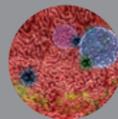



The Prechter Fund is supporting critical projects across several research areas

Clinical Translational Research



Microbiome



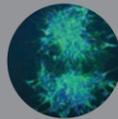
Neuropsychology



PRIORI Smartphone app



Stem Cells: iPSC



Our research director, **Melvin McInnis, M.D.**, regularly pens an “Ask the Doctor” column for *bp Magazine*. This article is copied with permission from *bp Magazine’s* Spring 2014 edition. To subscribe to *bp Magazine*: [www.bphope.com](http://www.bphope.com) or 877-575-4673.

**ASK THE DOCTOR: FEELING BETTER ABOUT SAD**

**What is seasonal affective disorder (SAD), or “winter depression,” and how does it affect people with bp?**

Seasonal affective disorder (SAD) refers to a pattern of symptoms that appear to align with the seasons. SAD is not a diagnosis on its own, just the description of a pattern; for example, getting depressed in the fall or winter two seasons in a row would constitute a pattern.

Anyone can experience changes in mood that are affected by the season. We associate these phases with variations in sunlight: Most of us feel more cheerful on a warm, bright, sunny day than on a cold, cloudy, dim winter afternoon. In people with bipolar disorder, SAD is more commonly found in individuals with bp II, who often report a slow malaise setting in during the fall that remits in early spring with a bounding relief and a surge of impulsive energy. While the symptoms may be sufficient to qualify for a depressive or hypomanic episode, often they are “subthreshold” in frequency and intensity. But for the bearer of such symptoms, the misery of the dark, dreary winter is barely tolerable and the exuberance of spring is colorful and intense.

**What treatments are available for bipolar that follows a seasonal pattern?**

The best treatment for bipolar disorder involves a good relationship with a care provider who is familiar with your

symptom pattern and able to recognize emerging problems and risk factors. Any mood changes you may experience during the seasons are important data for your provider, so it is important that you stay in close communication with him or her during such times of change.

For depressive symptoms in the fall, your provider may suggest the use of a light box and regular exercise in addition to the medical and psychological management of bipolar disorder. Spring mania can be very tricky: When is an upswing in mood an emerging manic episode as opposed to normal joy and delight at the return of warm, sunny days?

The critical problem with mania is that as your mood begins to escalate, your self-perception and insight begin to dissipate. You can very rapidly become convinced that you are just fine, and that your actions — actions that others may consider to be indiscreet or risky — are perfectly reasonable. It is helpful to enlist a family member or friend to provide ongoing feedback on your health and stability. Ask them to be honest and direct with you if they note any worrisome changes in your mood or behavior that might be suggestive of mania. A manic episode can have profound personal, social, and vocational implications — early intervention is crucial and life-saving.

Whether your bipolar disorder is affected by the seasons or not, the importance of maintaining a healthy lifestyle year-round cannot be overstated. Recognize your risks, and work out a plan with your care provider to minimize them.

## Microbiome Sub-Study Added to the Longitudinal Study of Bipolar Disorder



We all have billions of microorganisms and microbes that live in our digestive system, called our microbiome. Some of these resident bugs are beneficial and some are not. The makeup of our microbiome reflects many things — like the foods we eat, the environment we live in, the drugs we take, and many factors we don't even understand yet.

It is becoming increasingly clear that our microbiome can influence mood state and potentially risk of psychiatric illness.

Yet, this field is in its infancy and there is limited understanding of which microbes are important for mental health or how they influence psychiatric disorders.

We have a unique opportunity to study these issues in research participants who comprise the Prechter Longitudinal Study of Bipolar Disorder, which now has almost 1,200 people enrolled. The microbiome may be involved with both the physical and psychological components of bipolar disease burden. Bipolar individuals are at twice the risk of developing metabolic syndrome compared to the general population and, on average, have significantly higher Body Mass Indexes (BMIs). Prior studies link the composition of the microbiome to obesity, and this may be a factor in bipolar illness-related obesity as well. Studies also suggest that the microbiome plays a role in mood and anxiety behavior.



Simon Evans, Ph.D.

The microbiome is a largely unexplored area as a diagnostic or prognostic tool for psychiatry disorders, even though there is emerging data highlighting its potential importance. However, nearly all of the work to date has focused on animal models, extrapolating to potential clinical applications in human psychiatric and neurological disorders.

In this sub-study, via collection of fecal samples, we will survey the microbiome of well-characterized bipolar and control subjects to investigate potential differences associated with several factors, including severity of disease state, medication exposure, early life stress exposure, personality factors (e.g. neuroticism), and rapidity of mania/depression cycling.

— by Simon Evans, Ph.D.



Kelly Ryan, Ph.D.

## MEET OUR TEAM

**Kelly Ryan, Ph.D.**, Clinical Assistant Professor, Neuropsychology Section, University of Michigan Department of Psychiatry

Dr. Ryan has always been fascinated with how **changes in the brain can manifest as problematic behaviors, and specifically, how they can have devastating effects on one's daily life.** This led her to pursue a career in clinical neuropsychology. Her early research looked at how executive functioning (one's ability to make decisions, solve problems, and plan and organize — all skills that are associated with the frontal region of the brain) created problems in everyday situations, such as driving a car or interacting with others, in patients with neurological illness.

Since joining the Prechter Bipolar Research Team in 2009, she has been exploring the role of executive functioning on important areas of life functioning, such as work, among individuals with bipolar disorder. While she recognizes that there need to be research efforts looking for risk factors, causes, and more effective treatment of symptoms in bipolar disorder, **she finds that it is also crucial to understand what specific aspects of the disease — which can include psychological, cognitive, and biological aspects — interfere with leading a normal life.** She is using mobile technology (smartphones) to capture real-time measurements of mood, cognition, and daily functioning to help identify individuals at future risk for disability and develop personalized and preventative strategies.

## “Fuzzy Thinking” in Depression & Bipolar Disorder: New Research Finds Effect is Real

In 2015, **Dr. Ryan** was the lead author of a paper published in the prestigious journal *BRAIN* that received a lot of media attention. People with depression or bipolar disorder often feel their thinking ability has gotten “fuzzy,” or less sharp than before their symptoms began. Now, the researchers have shown in a very large study that effect is indeed real — and rooted in brain activity differences that show up on advanced brain scans.

What's more, the results add to the mounting evidence that these conditions both fall on a spectrum of mood disorders, rather than being completely unrelated. That could transform the way doctors and patients think about, diagnose and treat them.

In the paper, the researchers report the results of tests they gave to 612 women — more than two-thirds of whom had experienced either major depression or bipolar disorder. The researchers also present data from detailed brain scans of 52 of the women, who took tests while brain scans were conducted.

Seen as groups, women with depression or bipolar disorder did equally badly on the test, which required sustained concentration. The test asked them to react rapidly when certain letters flashed briefly on a screen, amid a random sequence of other letters. Compared with the group with no mental health conditions, the groups with either diagnosis lagged noticeably on this standard test of cognitive control.

Very large study adds to evidence that mood disorders are points on a spectrum, not completely separate — and could lead to better diagnostic tests

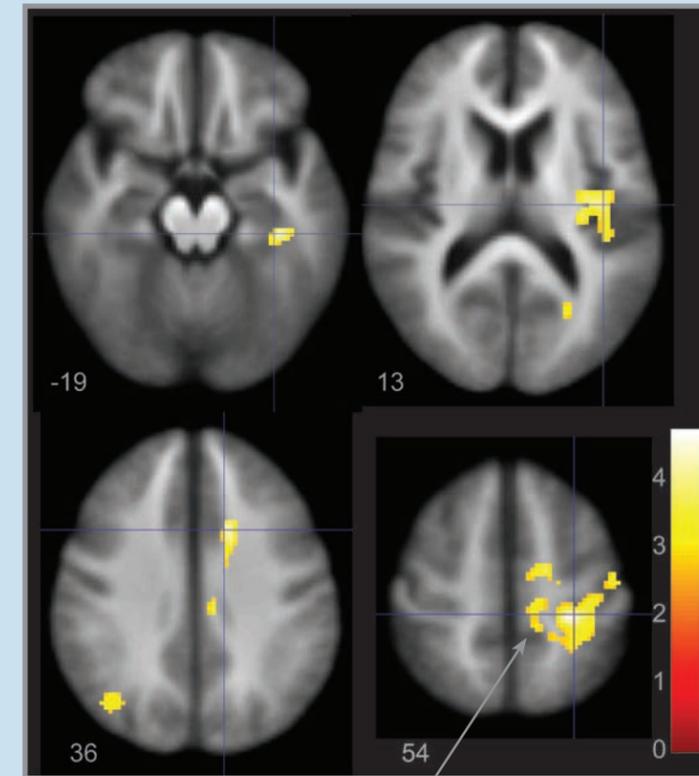
And while many individual women with depression or bipolar scored as well on the test as healthy participants, nearly all the test-takers in the bottom 5 percent of performers had one of the two mood disorders.

On the brain scans, the researchers found that the women with depression or bipolar disorder had different levels of activity than healthy women in a particular area of the brain called the right posterior parietal cortex. In those with depression, the activity in this area was higher than in healthy individuals, while in those with bipolar disorder it was lower. The area where the differences were seen helps control “executive function” — activities such as working memory, problem solving and reasoning.

“In all, we show a shared cognitive dysfunction in women with

mood disorders, which were pronounced in the cognitive control tests and more nuanced in scans,” says Dr. Ryan. “These findings support the idea of seeing mood disorders dimensionally, as a continuum of function to dysfunction across illnesses that are more alike than distinct,” adds Ryan. “Traditionally in psychiatry we look at a specific diagnosis, or category. But the neurobiology is not categorical — we're not finding huge differences between what clinicians see as categories of disease. This raises questions about traditional diagnoses.”

— by Kara Gavin



These regions of the brain were most associated with poor performance on the “fast thinking” test, both among women with depression and women with bipolar disorder.

## ELIZABETH GUZ — *Link by Link, Helping Us Find a Cure for Bipolar Disorder*

Liz Guz's middle child, Michael, would have been 23 years old in March 2015.

"He had been anxious and depressed for a long time," Liz said. "I knew something was wrong, and it became worse as an adolescent. He had been to a therapist and psychologist, and it was very frustrating. He started self-medicating, and ended up overdosing."

To honor the life of their son, his family established a memorial fund at the University of Michigan Depression Center. Gifts to the Michael Guz Memorial Fund directly support the Prechter Bipolar Research Fund.

"I felt I had a choice," Guz said about moving forward and transforming her grief into something more positive. "I talked with others who lost children. I realized I can't change the past, but I can change the future and how I handle this. I wanted to make a decision for my kids to overcome this, and to take a more proactive approach."

"I started looking into charities, and found the Prechter Fund. My mother-in-law suffered from mental illness, so there is a genetic link in the family. I wanted to prevent it from happening to my other children, and future grandchildren."

To further raise awareness and funds for bipolar research, Liz and her daughter Lauren launched **ELLA Designs Original Jewelry**. 50% of all proceeds of their business are donated to the Prechter Fund in memory of Michael.

"I look for things that I like, and then I usually try to find pendants or something and put my own twist on it," Guz said of the jewelry designs. "There are different chains, and beautiful magnetic clasps that can be attached. It's very versatile, like modular jewelry."

The pieces run between \$35 and \$475. Liz sells the pieces at various shows and house parties throughout the year. She also has a website where orders can be placed.

"It's amazing to me when selling at a show, everyone has a story," she said. "People are starting to talk more about it. There's still a stigma, but people are realizing it's a legitimate illness, and I do have hope that there will be more attention given to it."

"The Prechter Fund is doing amazing things and more groundbreaking research to make treatment more tailored for the individual by testing stem cells and finding what medications will work best. Eventually, I think it will save lives."

To date, Liz's efforts, including donations from family and friends and jewelry proceeds, have resulted in more than \$200,000 in support for bipolar research.

On September 3, 2015, Liz Guz was honored by the National Council of Jewish Women, Greater Detroit Section. She received the **Woman of Vision Award**. The award "honors a woman who contributes her knowledge, resources and skills for the betterment of the community."

The Heinz C. Prechter Bipolar Research Fund is proud to congratulate and thank Liz for her unwavering dedication to our mission.



Michael Guz

**ELLA**  
DESIGNS  
Original Jewelry



Liz Guz and daughter Lauren



Visit [www.elladesignsjewelry.com](http://www.elladesignsjewelry.com) to check out Liz's jewelry and contact her directly if you'd like to host a party at your home.



## STEM CELLS AS FASHION ACCESSORIES

Spice up your wardrobe while supporting our research! Next May, during mental health awareness month, the Prechter Fund will once again **celebrate our donors with special silk scarves and ties**.

The first design in 2015 was a hit, with many donations coming in to support our research and many people complimenting the limited-edition scarves and ties.

The images they featured were the cells that are taken from research participants as part of our stem cell study. This study is using stem cells derived from simple human skin cells. In this exciting project, we take skin cell samples from adults both with and without bipolar disorder, turn them back to their embryonic state, and ultimately grow them into nerve cells that look and behave like brain cells. This allows us to understand — in a laboratory — how individuals might react to different treatments; it is truly the heart of "personalized medicine."

It wasn't just donors out in the community who took note — Prechter Bipolar Research Fund staff members also made gifts to invest in our mission.

Says Marisa Kelly, Research Technician Associate:

*"I made a donation to my place of work because I feel so inspired by the research team that I am fortunate enough to work with. The work that we do here has the potential to really make an impact on people's lives for the better. I feel passionate about helping to be a part of the solution for those who struggle with bipolar disorder, as it is such a pervasive and often times invisible condition. I found the scarves/ties to be such a creative way to make mental illness a little more visible in the public eye. The pattern used is a brilliant combination of science and art and is a nice conversation starter. This rewarding experience has made me more likely to donate again in the future; it feels good to support a cause that I, myself, pour much passion and energy into. I found it important to support our research enterprise monetarily because I see every day how even a little bit has the potential to make a big difference."*



Pictured above are Marisa Kelly, Brent Doil, Holli Bertram, and Kat Bergman from the Prechter team wearing their scarves and ties.



Dr. Melvin McInnis wears one of the ties and displays one of the scarves that bear images of human stem cells.

Photo: Robin Erb, Detroit Free Press



Look for the unveiling of 2016's scarves and ties on our website and in our e-newsletter this spring. You can subscribe to it here: [prechterfund.org/news-and-events/enews](http://prechterfund.org/news-and-events/enews)

## Become a Victor for Bipolar Disorder

Philanthropic support offers scientists the opportunity to think boldly as they collaborate, pursue unconventional hypotheses, and make progress on treatments that will improve the lives of individuals and families facing bipolar disorder.

The ability for researchers to work without interruption is a critical component in moving the science forward. Donations can raise awareness by elevating the profile of disease and the need for more research. This is particularly true for research in bipolar disorder and depression, which receives just one-fourth of national funding for cancer research.

The support and generosity of individuals and family foundations have provided essential funding for the Prechter Longitudinal Study, stem cell research and PRIORI project. Since 2004, the Prechter family's investments over the years have inspired more than \$5 million in additional philanthropy from other individuals and



**VICTORS FOR MICHIGAN**

family foundations to support bipolar research. These investments have leveraged millions more in grant funding.

We encourage you to join us in sharing the news of the Prechter bipolar research with others. Please

help us create a community of individuals that share our vision for seeking progress in bipolar treatments and change the face of bipolar for families and the world. You can help by volunteering, hosting events, donating and inspiring others to make a commitment to the cause.



Go to [prechterfund.org](http://prechterfund.org) to make your gift today, or call Stephanie Peterson at 734-647-0616 to discuss other ways you can support this important work.

# 9th Annual Prechter Lecture

The 9th Annual Prechter Lecture took place on November 2, 2015. Our keynote speaker was **Leroy E. Hood, M.D., Ph.D.**

A pillar in the biotechnology field, Dr. Hood is among the most accomplished scientists world-wide. He is president and co-founder of the Institute for Systems Biology in Seattle, WA, which aims to study human life in all its stages to predict, prevent, or diminish the effect of human disease. Dr. Hood led the teams that developed the DNA gene sequencer and synthesizer, and the protein synthesizer and sequencer – four instruments that paved the way for the successful mapping and understanding of the human genome. He is the recipient of several prestigious international awards and in 2013, he received the National Medal of Science from President Obama.



Dr. McInnis and Dr. Hood

Dr. Hood addressed a full auditorium with his talk titled **“Systems Medicine and Proactive P4 Medicine: Medicine at a Tipping Point – Bipolar Disease and Scientific Wellness.”** He focused on the tipping points related to the challenges of biology and medicine.

He emphasized that it is an integrated, cross-disciplinary, systems approach that will lead to precision medicine (predictive, preventive, personalized, and participatory). Dr. Hood pointed out that there is a shift in the health industry from studying disease to studying wellness. The bipolar research team can use Dr. Hood’s systems approach by inclusively analyzing these various data types and following the wellness-to-disease transitions.



To view a video of the event:  
[prechterfund.org/lecture/2015](http://prechterfund.org/lecture/2015)



Thank you to our lecture series sponsors: Comerica, Dearborn Sausage Company, Fritz Enterprises, Holbrook’s Roofing, and Scott Snow Financial Advisors

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**f** PRECHTERBIPOLARRESEARCH

**MISSION** ›› The mission of the Heinz C. Prechter Bipolar Research Fund is to provide a repository of longitudinal clinical, genetic, and biological data to investigators worldwide for collaborative research on the causes, prevention, and treatment of bipolar disorder.

**VISION** ›› To personalize treatment of bipolar disorder and prevent recurrences to enable those with bipolar disorder to lead healthy and productive lives.

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