Greetings!

This newsletter is full of exciting information — reflecting enthusiasm and momentum on every front. The progress is thanks to you! Your participation and contribution of time and resources simply make our research possible.

This has been a very productive year. There is tremendous energy at the core of the longitudinal project, thanks to our many study participants, like Jennifer who shares her experiences on page 2. There is unprecedented hope because scientists are truly narrowing in on discoveries in the biological mechanisms underlying bipolar disorder. There is the anticipation that we will be able to use technology and computational modeling to predict illness risks and outcome patterns. Read on!

The stem cell research led by Sue O’Shea is expanding and continues developing functional models based on neurons and support cells (astrocytes) showing fundamental differences in activity between bipolar and non-bipolar derived cells (page 5). We can now measure the effect of medicines in cells and we will soon use these models to test new medicines to treat bipolar disorder.

Paul Jenkins (page 3) leads a lab focused on genetic mechanisms, and is narrowing in on the mechanism of action of one of the bipolar associated genes (ANK3). Rachel Bergmans (page 4) has taken on the microbiome project to determine the effect of the gut biology on the brain. She has engaged experts in microbiology and public health, bringing bipolar research into new fields of inquiry.

Identifying and predicting patterns of bipolar is a core element of our program. Emily Mower Provost and I continue with the PRIORI project (page 5) to determine the behavioral and acoustic patterns that associate with mood states and changes. There will soon be a time when a person can utilize mobile technology to monitor health and identify risks of impending mood changes.

Continued on next page
Jennifer is one of 1,252 research participant collaborators who have volunteered to help advance bipolar research. The entire Prechter research team is grateful to every participant for their time and dedication. We are also extremely pleased that the experience is a positive, even therapeutic, addition to the lives of our participants.

Please tell us a little bit about yourself!

I went to the University of Michigan to study voice. I was very accomplished academically and still study with abandon anything I can get my hands on, which is one reason I LOVE working with the Prechter researchers!

I am a rapid cycling, bipolar I with mixed episode states typified by crying spells. What that all means is that I can be both manic and depressed at the same time and that I can flip back and forth multiple times.

I was diagnosed at the age of 24 but I have had all the signs and symptoms since I was six years old. Thanks to the fantastic work of my doctor, I have been stable since 2004!

How did you first hear about the Prechter Program?

I first heard about the research program when my mom found an article in a paper. She thought I would enjoy giving back and I have been doing it ever since. I am going on my 9th year with the program and have done every study I qualify for. I figure God gave me this illness for a reason and I had better use it to the best of my ability to help others.

What do you do in your free time?

I trained my dog Maya to be a therapy dog and we spend a good portion of every day visiting with the people in my neighborhood. I also crochet stuffed animals. I have an Etsy shop where I have hundreds of my creations. I am hoping to get enough traffic that I can donate a portion of the proceeds to the Prechter Program. To take a look, please visit www.MayasSoftFriends.com

By participating in the Prechter research, it is my passion, hope and mission to help other people. I have been through a lot, I have been suicidal and in fact spent most of my adolescence and teen years debating suicide attempts. I don’t want others to feel the way I’d felt.

What motives you to stick with it and collaborate with the research team?

I participate in the research with the hope that one day we will find a way to make a simple diagnosis and create a successful treatment plan in a matter of weeks rather than years.

Mathematicians are analyzing illness patterns from individuals with bipolar and generating models to describe the course of illness, much in the same manner that financial analysts create models of the stock market. Joel Peterman (page 4) is searching for clues in conditions common in bipolar disorder such as obesity and the metabolic syndrome, asking how these comorbidities contribute to the outcomes and difficulties in people’s lives.

Innovative methods of managing bipolar disorder are being tested. Cynthia Burton (page 3) proposed that direct current stimulation in combination with a form of cognitive therapy will be effective in treatment of the disorder. We have a team focused on clinical trials that collaborates nationally, testing medications and their effectiveness for people with bipolar disorder.

We are privileged to work with wonderful people in the fertile academic environment of the University of Michigan and you meet some of them in these pages. U-M is simply the best place to be, bounding with opportunity and fueled by the brilliance of creative scientists.

Big ideas spawn ‘big data.’ Your valued support not only generates the BIG — it generates a legacy of ideas and data, an expanding base for research in bipolar disorder for years to come. Your gift to the Heinz C. Prechter Bipolar Research Program will go twice as far — the World Heritage Foundation – Prechter Family Fund will match every dollar given our research up to $5 million. Thank you for your support, your passion and your commitment. We are now closer than ever to life-changing discovery, because of you. And we will get there, together.

Why I participate in research » Q&A with Jennifer F.

Jennifer is one of 1,252 research participant collaborators who have volunteered to help advance bipolar research. The entire Prechter research team is grateful to every participant for their time and dedication. We are also extremely pleased that the experience is a positive, even therapeutic, addition to the lives of our participants.
**Neuromodulation plus cognitive training** to improve working memory among individuals with serious mental illness

People with serious mental health conditions (bipolar disorder and schizophrenia/schizoaffective disorder) often have impaired neurocognition, leading to difficulties with attention, learning, and problem-solving. In particular, working memory, the ability to hold information very briefly in short-term memory, can be a problem.

Novel non-pharmacological treatments such as cognitive remediation have been shown to have a positive impact on neurocognitive abilities such as attention, working memory, and cognitive flexibility.

Researchers are focusing on potential “cognitive enhancers” to boost the effects of cognitive training. Transcranial direct current stimulation (tDCS) is one potential treatment that is considered exceptionally safe and cost-effective.

This study, led by Cynthia Burton, Ph.D. (pictured), will investigate the impact of a combined computerized cognitive training and tDCS intervention, studying individuals with serious mental illness who also have problems with working memory. This research is a critical step in advancing knowledge of neurocognitive treatments that will improve the everyday functioning of individuals affected by mental illness.

**Collaborating with the Department of Pharmacology — A BIPOLAR GENE STUDY**

The Jenkins lab, led by Paul Jenkins, Ph.D., is a new research group in the U-M Department of Pharmacology that began collaborating with the Prechter Program in 2015. The group studies the basic cellular and molecular mechanisms underlying complex neuropsychiatric diseases, such as bipolar disorder, using confocal microscopy, molecular and cell biology, transgenic mouse models, and biochemistry.

**Bipolar disorder is a highly heritable disorder, which means that it is strongly linked to the patient’s genetic background.** Because of this strong genetic component, there has been a great deal of effort to understand the genes that underlie susceptibility to this disorder.

Genetics analyses use genome-wide association studies (GWAS), large multi-center studies in which U-M participates, to identify risk genes. One of the strongest and most-replicated leads from these studies is the ANK3 gene, which encodes the protein ankyrin-G, a gene that is fundamental in facilitating communication between neurons and their targets.

The Jenkins lab research focuses on the role of ankyrin in forming the myelin sheaths that surround neuronal axons to protect them and to allow electrical communication between neurons to occur rapidly.

In searching the Prechter Genetics Repository, our team identified a human iPSC (stem cell) line with the very mutation that the Jenkins lab is studying in an animal model. Not only did we have stem cell lines from the individuals, but Emily Martinez, a research associate in the O’Shea stem cell lab, had developed neural progenitor cells from this line. We are now differentiating those progenitor cells from the volunteer with the ANK3 gene mutation to neurons for electrophysiological analysis.

Our goals are to determine the basic cell biology of ankyrin in myelination, the role of this particular abnormality, and how it may contribute to bipolar disorder. This will lead to new pharmacological targets and may lead to the development of more effective medicines.

Ankyrin-G (red) is responsible for building synapses, or connections between neurons, in the brain. Synapses are marked with a transporter of neurotransmitters (green).
Rachel Bergmans, Ph.D. & the microbiome sub-study

Dr. Bergmans is a postdoctoral research fellow and joined the Prechter Program in July 2017. She received her doctoral degree in epidemiology from the University of Wisconsin-Madison in 2017, after completing training in public health (M.P.H.) at the University of Michigan in 2013. Her graduate work focused on environmental determinants of health and health disparities, especially regarding the impact of food insecurity and nutrition on mental health.

As part of the Prechter research team, Dr. Bergmans studies the gut microbiome, the billions of microorganisms that live in our digestive system. This research is designed to determine whether targeting the human gut microbiome may provide a novel strategy for easing the burden of disease within bipolar patients.

The makeup of our gut microbiome reflects many things — like the foods we eat, the environment we live in and the drugs we take. It is becoming increasingly clear that our gut microbiome can influence mood state and potential risk of psychiatric illness. 

Surprisingly, little is known about our gut microbiome and the influence it has on our daily lives. Dr. Bergmans’ research specifically explores how living with bipolar disorder can be improved by what we eat.

Gut Microbiome

Joel Peterman, Ph.D., Postdoctoral Neuropsychology Fellow

Dr. Peterman is a postdoctoral neuropsychology fellow who joined the Prechter team in September 2016. He received his doctoral degree in clinical psychology from Vanderbilt University in 2016. His graduate work focused on the role social cognitive deficits play in the social functioning deficits associated with schizophrenia.

Dr. Peterman is interested in exploring the effects medical co-morbidities, specifically obesity and metabolic syndrome, have on cognitive functioning in individuals with bipolar disorder.

By evaluating cognitive functioning and the proliferation of medical co-morbidities across a period of time, the contributions co-morbidities play in cognitive functioning across the lifespan may be able to be teased apart.

Understanding how other conditions exacerbate the manifestation of bipolar disorder may provide an in-road into adjusting clinical approaches when providing psychiatric care to individuals living with bipolar disorder.

Neuropsych Testing
Ann Laszczyk, Ph.D., Postdoctoral Research Fellow

Dr. Laszczyk is a postdoctoral research fellow in the Department of Cell and Developmental Biology, having joined the Prechter Program in July 2017. She is a native Michigander, and received her B.S. from Central Michigan University, followed by a doctoral degree in neurobiology from the University of Alabama at Birmingham in 2017.

Dr. Laszczyk’s research builds on her experience with neural stem cells to examine the characteristics of forebrain GABAergic interneurons from individuals with bipolar disorder. GABAergic interneurons are inhibitory neurons of the nervous system that play a vital role in neural circuitry and activity. They are so named due to their release of the neurotransmitter gamma-aminobutyric acid (GABA).

In the lab, Dr. Laszczyk is deriving new induced pluripotent stem cell lines, differentiating them into GABAergic neurons, then characterizing their behaviors. These interneurons may be particularly important in neuropsychiatric conditions that have a developmental component. Abnormalities in GABAergic neurotransmission have been implicated in bipolar disorder. These neurons are unique in that early in development, they are excitatory neurons, later inhibitory, so that an imbalance or a delay or malfunction in this switch may be involved in bipolar disorder.

Meet the team — PRIORI
(Predicting Individual Outcomes for Rapid Intervention)

The Prechter Program collaborates with the U-M College of Engineering on the development of computational methods for predicting mood swings in bipolar patients based on understanding the specific voice patterns that accompany transitions from healthy euthymic states to either mania or depression. Investigations suggest that manic and depressive mood states can be recognized from speech data collected via our smart phone app, PRIORI.

One prominent symptom of bipolar disorder is changes in speech patterns. During mania, speech increases in rate, rhythm, and volume. During depression, the opposite occurs. The purpose of the PRIORI study is to design new computational approaches to detect these meaningful changes early in a mood episode, possibly even before depression or mania occurs. The ability to predict mood changes with time to intervene may mitigate the episodes of mania and depression and prevent serious outcomes such as suicide.

In 2016, a multidisciplinary team from Care New England’s Butler Hospital, Brown University and the University of Michigan embarked on a project to advance screening capabilities for suicide risk. The group received a grant from the National Institute of Mental Health to conduct a five-year research study utilizing the PRIORI technology.

Researchers will record and analyze changes in speech patterns to identify how they relate to changes in suicide risk. It is the research team’s hope that results of this study will have implications for both prevention and early intervention of suicide, and that the smartphone technology will provide methods for monitoring patients’ suicide risk over time. Participants in the study will be recruited in a psychiatric inpatient setting, an important population given the elevated suicide rates in the weeks and months following hospital discharge.

FROM LEFT: Erica Vest, Bethany Navis, Soheil Khorram, and Zhaoxian Hu
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 Prechter Program’s goal to advance breakthrough medical research to develop cures for the illness.

Dear Friends:
This year again has been a remarkable one for the Prechter Program.

Our family foundation has made a matching gift commitment of up to $5 million to endow the work of the Heinz C. Prechter Longitudinal Study and Bipolar Genetics Repository at the University of Michigan. Our renewed commitment has two objectives: 1) to maintain and operate this collection of data in perpetuity and 2) to increase the momentum of important research into bipolar disorder. We are pleased that both current and new donors are rising to our challenge.

The longitudinal study and genetic repository make up the largest study of its kind in the country, providing critical data for major research into bipolar disorder around the world. Importantly, the data stimulates studies into existing treatments as well as testing of completely new ideas.

Donors may take advantage of the match by contributing to either the endowment fund or to another fund within the overall Prechter Bipolar Research Program. The Prechter name, I am honored and humbled to say, has become synonymous with bipolar research.

Please consider making a matching gift to help us transform understanding and treatment of bipolar disorder.

Very sincerely,

Waltraud E. Prechter
Founder, Heinz C. Prechter Bipolar Research Program

A conversation with bestselling author
Marya Hornbacher
Marya is the 11th Annual Prechter Lecture keynote speaker. See the back cover for details on this event.

Please tell us a little bit about the books you’ve authored.
I’ve been lucky enough to have the opportunity to write in a diverse range of genres and on a diverse range of subjects, though many of my books return to questions about mental health, culture, and the relationship between the two. I’ve written two memoirs, one on eating disorders and on bipolar disorder, as well as a book that addresses treatment of the co-occurring disorders of mental illness and addiction. The books that are closest to my heart, actually, are a novel, The Center of Winter, which is about a young family rebuilding itself after a father’s suicide, and a book about humanist ethics and the Twelve Step programs, called Waiting: A Nonbeliever’s Higher Power.

What motivates you to write?
At a very fundamental level, I love to work with language, with story, and with the ways the written word allows us to connect with one another; like painters who really love paint, I love the materials I get to work with every day. At a more conceptual level, I find myself constantly fascinated by the stories people tell themselves, the way we make sense of our world, the beliefs we hold, and the lengths to which people will go to survive. The stories I write — both fiction and nonfiction — have that in common: they look at what it takes for us, as humans, to survive, and even more, to find meaning and purpose in our lives.

How do you think stigma and society’s view of mental illness has changed since your youth?
I think that there’s been a modicum of change in the popular perception of mental illness. Certainly now people who have access to care are more likely to be diagnosed, and helped, more quickly. But we continue to battle the same egregious care gap — people who need care most are still least likely to receive care; the care available is often limited and not always skilled; professionals do not have the resources they need; and the community of people who live with mental health disorders continues to remain on the margins of society, removed from positions of social or political influence. I feel that it’s time to stop worrying about stigma — essentially, worrying about what “people” think of “us” — and start putting our efforts toward creating a political shift that would make care available, and creating a shift in the healthcare industry that would improve care. I do not feel the campaigns to end stigma are negative in any way: I simply want to know what the end goal of those campaigns will be, and what practical impact lower stigma might have in our day to day lives.

What do you do in your free time?
I don’t have much free time, but I treasure it when I do. I live quite a ways from an urban center, so I’m able to do a lot of hiking. I love cooking for friends. I read voraciously. And I travel a good deal.
Meet our new development director Lisa Fabian

My name is Lisa Fabian and I am the new Associate Director of Development for the Prechter Program. I just reached my six-month employment anniversary and I can report that I simply love my job.

Being a part of the University of Michigan and Ann Arbor community is an honor. Ann Arbor has felt like home ever since I arrived as a freshman, which explains the “I’d rather be in Ann Arbor” bumper sticker that has been with me since I graduated from the College of LSA in 1984. I’ve lived in several other places, but nowhere else has the combination of intellectual stimulation, diversity, and lack of pretense that permeates Ann Arbor.

As much as I love Ann Arbor, you are the main reason I love my job. Every day I talk to you — people who care about mental health and often have firsthand knowledge of the havoc that bipolar illness wreaks. In far too many cases, you have lost a loved one to “bipolar suicide.” Yet, day after day, you are shining examples of forward-looking qualities like resilience, compassion and generosity. Of course there is pain, but you choose to push on, to partner with the Prechter Program, and to improve outcomes for your loved ones and people you will never meet.

Next year, it will be 30 years since my dad died by bipolar suicide. There is no place that offers the hope and promise of a better future for those with bipolar illness than the Heinz C. Prechter Bipolar Research Program. So, each day, I pay tribute to my dad, guided by the lessons and love I learned from him, and the resilience of my amazing mother who held things together through it all.

I am delighted to have been given the opportunity to work with this team. Thank you for all you do to advance our work. If I haven’t met you yet, I look forward to it.

Kindly,

Lisa Fabian
734-763-4895, fabianl@umich.edu

1984 with my dad at my graduation from the University of Michigan.
FEATURING: Marya Hornbacher

AUTHOR OF: Madness
A Bipolar Life

» Featured speaker; panel discussion about the present and future of research in bipolar disorder; reception
» This event is free and open to the public. Please RSVP at www.prechterprogram.org/lecture
» If you are unable to attend, join via webcast: michmed.org/Erapv (case sensitive)
» Local bookstore Crazy Wisdom will be selling the book at the event.

“The Hornbacher is a virtuoso writer.”
— New York Times

“Hooks readers from the start ... [As Hornbacher] whips around this rollercoaster ride, her unflinching style keeps us firmly seated beside her.”
— USA Today

The 11th Annual Prechter Lecture is sponsored by the Bruce C. Abrams Foundation & Holbrook’s Roofing

The mission of the Heinz C. Prechter Bipolar Research Program 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.

The vision of the Heinz C. Prechter Bipolar Research Program is to personalize treatment of bipolar disorder and prevent recurrences to enable those with bipolar disorder to lead healthy and productive lives.

To sign up to receive our yearly printed newsletter or our quarterly E-newsletter, please contact Kat at kbergman@umich.edu or 734-232-0456.