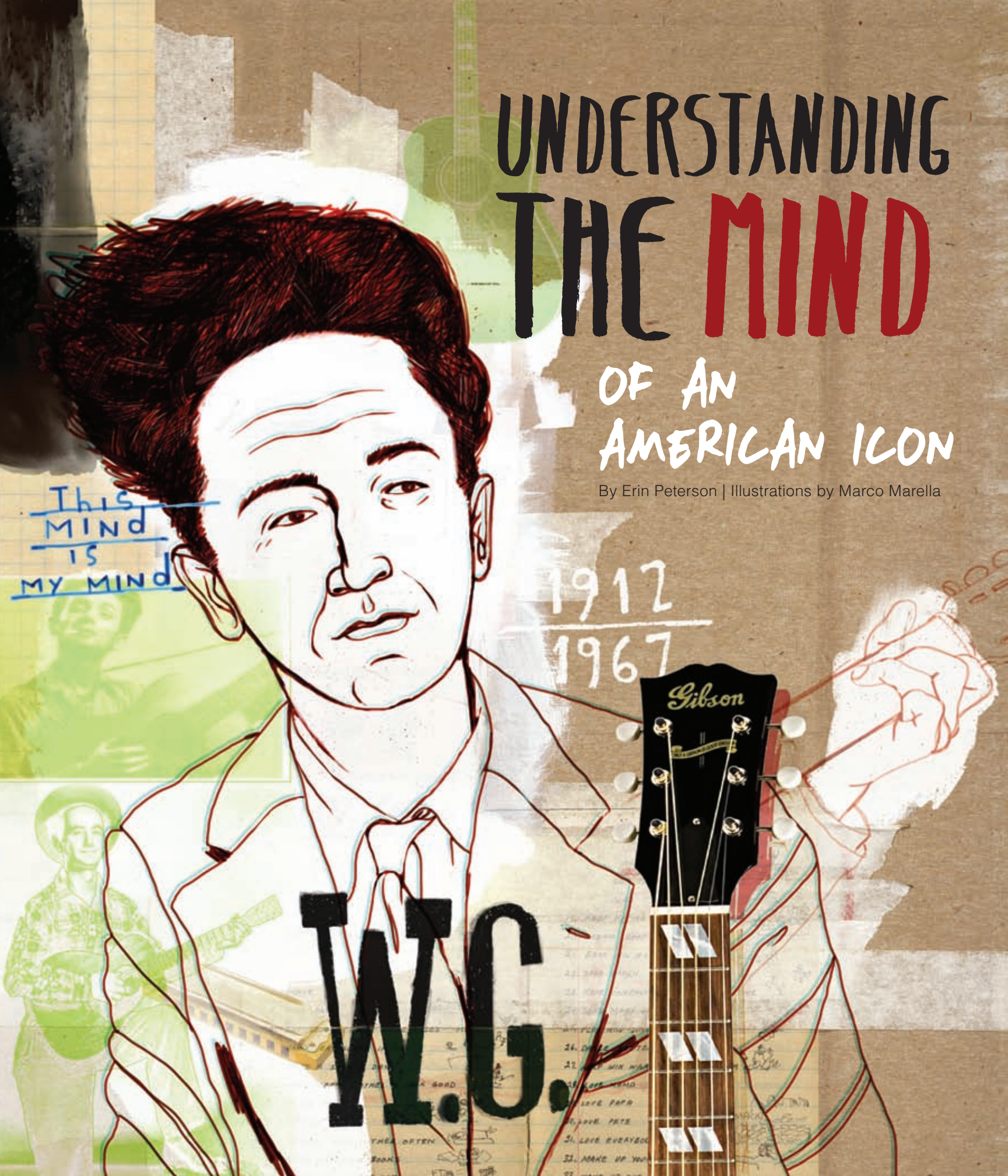
UNDERSTANDING
THE MIND
OF AN
AMERICAN ICON
By Erin Peterson | Illustrations by Marco Marella
This MIND IS MY MIND
1912
1967
Gibson
W.G.

Sixty years ago, folk legend Woody Guthrie was diagnosed with Huntington's disease. Now 100 years after his birth, scientific researchers and global health experts at St. Edward's and around the world are cracking the code of this destructive neurological disorder and bringing worldwide attention to the disease.

Few musicians have etched their way as deeply into the American DNA as Woody Guthrie. Known as the "Dust Bowl Troubadour," the prolific songwriter influenced musicians ranging from Bob Dylan to Bruce Springsteen to The Clash's Joe Strummer. Though Guthrie's left-leaning political views riled many, his songs about the Great Depression and World War II tapped into the fear and frustration of the times.

Guthrie had a sharp mind and a gift for words, but deep within his genetic code was a disease that unraveled him. In 1952, after years of erratic behavior, Guthrie was diagnosed with Huntington's disease. The inherited neurodegenerative disorder affects one in every 10,000 people, but symptoms often don't appear until well into adulthood. The devastating illness is marked by cognitive problems, depression and psychiatric issues. Those with the disease lose control of their movement, and they walk almost as though they are dancing. The disease's progression is slow but inexorable. Guthrie lived for 15 years after his diagnosis, finally succumbing to the disease in 1967 at age 55.

But the story does not end there. This year marks the centenary of Guthrie's birth. It also has been a time of breakthrough discoveries in our understanding of Huntington's and related diseases, including a project designed by Professor of Chemistry **Eamonn Healy**.

This October, experts from across the continent will gather at St. Edward's for the Global Health and Infectious Disease Symposium, sponsored by the Brother Lucian Blersch Endowment and the Kozmetsky Center of Excellence in Global Finance. They will celebrate Guthrie's legacy, highlight scientists' progress on diseases related to protein misfolding and discuss the broader issues surrounding global health policy. Healy says that the synergy that comes from pairing a beloved public figure with scientific research and policy issues will prove to be powerful. "This symposium is a way to look at the research not just in a narrow chemical or biological focus, but to put it in a larger social context," he says.

THE RED DEVILS

Several of Guthrie's family members, including his mother, suffered from Huntington's. His mother's unpredictable anger and depression were imprinted in his memory, though he rarely discussed it. Guthrie himself may have begun exhibiting symptoms of Huntington's more than a decade before his diagnosis. In 1942, just two years after writing "This Land is Your Land" and in the midst of penning his autobiography, he wrote a disquieting letter to Marjorie Mazia, the woman who would become his second wife. In it, he lamented the uncontrollable rage that boiled up in him, often from nowhere: "There really are quite a big bunch of little red devils with pitchforks poking around in me," he wrote. "[T]hat's just one of the wagon loads of wrong habits in me."

These early outbursts, which he attributed to alcohol and personal failings, likely had a deeply biological component. Huntington's disease, much like Alzheimer's and Parkinson's, belongs to a class of diseases caused by misfolded proteins. That makes them profoundly different from illnesses like chicken pox or Lyme disease, says Healy. "[Huntington's] isn't caused by a virus or a bacterium," he says. In other words, there's no rogue element to kill that will transform the individual from sick to well. The problem is burrowed within the body's cells themselves; the disease, even if unexpressed, has lived within the individual from the very beginning.

"THERE REALLY ARE QUITE A BIG BUNCH OF LITTLE RED DEVILS WITH PITCHFORKS POKING AROUND IN ME."

Misfolded proteins occur in all of us to some extent, and the body has developed a natural mechanism, called heat-shock response, to avoid the problems associated with this misfolding. Supercharging this heat-shock response may provide an exceptionally powerful tool against Huntington's, says Healy. While the heat-shock response is not equipped to deal with the substantial physiological changes associated with diseases like Huntington's, Healy and others believe it can serve as a road map for the development of novel treatments.

For now, the research isn't being done with beakers and microscopes but with powerful computers. Chemistry major **Carley Little '13** spent the summer working on the project. She and Healy used a computer simulation to mimic the behavior of the mutated proteins that misfold and collect to cause Huntington's. "Our hope is that by bonding amino-acid segments to this mutated protein, we can inhibit the activity that leads to neurodegenerative symptoms in Huntington's," Little says.

If the initial work continues to look promising, Healy will turn the project over to colleague **Peter King**, an associate professor of Biology, who will move the work from computer to laboratory. King and his students will isolate the mutated proteins to see if the effects predicted in the program actually occur in a real-world setting. The collaborative approach will ensure that the research moves forward from theory to practice. It also gives students a chance to watch scientific progress over time.

Even more importantly, the work has meaningful real-world implications. Although it is impossible to cure a genetic disease, new therapies may help prevent it from taking such a crushing toll.

THAT GONE FEELING

In 1952, as Guthrie's symptoms continued to worsen, he was admitted to Brooklyn State Hospital. Doctors hadn't yet homed in on the cause of his many problems, but Guthrie described his perplexing symptoms, from restlessness to depression, in another letter to Mazia: "Here's my funny feeling over me again. That lost feeling. That gone feeling. That old empty whipped feeling. Shaky. Bad control. Out of control. Jumpy. Jerky. High tension," he wrote. "No bodily (physical) pains; just like my arms and legs and feet and my whole body belong to someone else and not to me."

The acute burden of a disease like Huntington's is not simply that patients lose their health, says Simonetta Sipione, a Pharmacology professor at the University of Alberta, who will speak at the symposium. The most painful part is that Huntington's patients become, in a very real sense, different from who they once were. "With many diseases, you lose your health, but you don't lose yourself," she says. "With a neurodegenerative disease, you lose your ability to communicate with others. Your character itself is affected."

Sipione's research takes a different tack from Healy's, but it has already offered some promising results. Her lab is trying to understand the molecular mechanisms that underlie Huntington's. Specifically, her team is trying to understand why neurons become dysfunctional when they express the mutant protein known as "huntingtin."

The answer may lie, at least in part, in important lipid molecules known as gangliosides. Critical for healthy brain functioning, gangliosides help neurons communicate with each other and interpret signals sent from the surrounding environment. But for those with Huntington's, one of these crucial types of gangliosides, known as GM1, is produced at lower levels than normal, and this may be one of many factors that causes the dysfunction.

Sipione's research group began administering GM1 to live mice that had the mouse version of Huntington's. The hope was that boosting GM1 levels would show therapeutic effects. "Indeed, when we administered the GM1 to these mice, we were able to completely restore normal motor behavior in this specific mouse model," she says.

FROM WORDS TO ACTION

The upcoming Global Health and Infectious Disease Symposium will cover a vast swath of territory, from the life of Woody Guthrie to Huntington's disease research to global health policy. But perhaps even more ambitious than the topics themselves is the action symposium organizers hope to inspire.

Chemistry Professor **Eamonn Healy** hopes the discussions and speeches will help students see that the objectives set forth in the St. Edward's mission take life at events like these. "This symposium will show what it means to be involved in important issues," he says. "Certainly, it will show what it means to be a scientist and a public policymaker but also what it means to be a citizen and to be engaged in important issues in society."

Elisa Díaz Martínez, director of the Kozmetsky Center of Excellence in Global Finance, believes the symposium will inspire actions, both small and large, from those who attend. "Students, faculty, community members — they can volunteer, do surveys or do community work," she says. "There are so many huge problems, and the only way we'll find solutions is to collaborate. The message we hope to get across is that we can all be involved."

The results couldn't be more encouraging, but Sipione is quick to note the pitfalls: Mice are not humans, and many auspicious treatments never bridge that interspecies gap. There are years of work and clinical trials ahead. But she says there is real reason for optimism: "It's impossible to say right now, but our hope is our findings will eventually be successfully translated to humans."

A Real Perfect Kind of Chance

As Guthrie's disease progressed, doctors ultimately were able to connect the dots and diagnosed him with Huntington's. He reflected on the diagnosis with thoughtfulness and heartbreaking clarity in a 1956 letter to a friend: "My mother Nora Belle did have my very own [H]untington's," he wrote. "God is just giving me here my real perfect kind of a chance to just see and to just feel exactly how my own Mother saw and felt." Guthrie's struggle was a personal one that connected him to his family, but his fame helped bring a misunderstood disease to light.

With hundreds of thousands of people around the world carrying the gene for Huntington's, it's critical to look beyond the scientific questions to see the disease from a global health standpoint, says Kozmetsky Center of Excellence in Global Finance Director **Elisa Díaz Martínez**. "Huntington's can be found on every continent, but researchers who work on the disease are typically in the developed world," she says.

Because knowledge and resources are concentrated in wealthy countries, individuals with the disease in developing areas are far less likely to have significant knowledge of Huntington's, let alone treatment for its symptoms. Organizations such as the World Health Organization can have a major impact in ensuring greater access to medical treatment for the disease, but they must first be convinced of its critical importance.

Identifying Huntington's as a global health issue may also hasten the creation of treatments for the disease, says conference speaker Luiz Augusto Galvão, sustainable development manager at the Pan American Health Organization. "Building partnerships among countries and researchers can help develop a global health network that can lead to both new and innovative solutions," he says. "The more we are able to share scientific research globally, the faster we can upgrade our knowledge." Because Huntington's shares important characteristics with more widely known diseases such as Parkinson's and Alzheimer's, the work being done on one disease may influence the research approach for others, he notes.

Guthrie hoped to have an enduring impact through his music, not his illness, but he may do both. His life, scientific research and global health policy may not seem to have obvious links, but they are deeply connected. Stories like Guthrie's bring awareness to important health issues and inspire interest in greater scientific research. That scientific research, in turn, bolsters the case for public policymakers who hope to bring information and therapies to the wider world. The effects that ripple out are both powerful and necessary.

For Healy, the conference represents not just a powerful gathering of specialists sharing critical information, but an embodiment of the liberal arts at St. Edwards. "We want students to see how they can expand their scientific questions to include questions of public policy and social activism," he says. "The [event] is a natural expression of the ethos of education here."

Global Health and Infectious Disease Symposium

The public is invited to attend the following free events scheduled for Friday, October 19. Attendees can register at **www.stedwards.edu/lucian**.

9 a.m.–12:15 p.m.: Pathogenic Proteins

- Eamonn Healy, St. Edward's University: Small Heat Shock Proteins: Pathogen or Protector
- Lary C. Walker, Emory University: Kochs Postulates and Infectious Proteins
- Neil Cashman, University of British Columbia: Transmission of SOD1 Misfolding and Familial ALS
- Simonetta Sipione, University of Alberta: GM1: An Experimental Approach for Huntington's Disease

1:30–2 p.m.: Health in the Americas

- Luiz Augusto Cassanha Galvão, Pan American Health Organization

2–3 p.m.: Health as a Human Right Across the World

- Speaker from the United Nation on the Right to Health to be announced

3–4 p.m. Panel Discussion on Health as a Human Right

All events will be held in the Jones Auditorium in the Robert and Pearle Ragsdale Center on campus.

The symposium is sponsored by the Brother Lucian Blersch Endowment and the Kozmetsky Center for Excellence in Global Finance.

webextra

ASK THE EXPERT

Huntington's disease affects thousands of lives every year. Professor of Chemistry **Eamonn Healy** is trying to do something about it by researching new avenues of treatment. *St. Edward's University Magazine* sat down with Healy to find out more about this disease, his research and what promising new treatments might be on the horizon. See the conversation at **www.stedwarsd.edu/webextras**.