



Dear Friends,

This issue is jam-packed with information about MS research, and ways for you to get involved. A good way to start, is to increase your knowledge and understanding of the disease. A superstar in that department is our friend, Laura Kolaczowski, who serves as Co-Principal Investigator of iConquerMS™. In February, Laura attended ACTRIMS, the annual gathering of MS scientists from North America, and this month's issue begins with her account. That's followed by an article about iConquerMS, a community of people created and supported by ACP and led by Laura, whose 3500+ members are actively involved in MS research in ways that go beyond attending conferences (valuable though that may be). They are influencing research agendas and study designs, participating in research studies and disseminating research results, all in order to live well today and in the future. Read about studies that are benefitting from their input and how you can register to become involved.

Last but not least, we welcome Case Western Reserve University epidemiologist and MS researcher, Farren Briggs, whose column, "*MS Researchers Identify New Biological Mechanisms Regulating IL7R Expression*," is the first of what will be a monthly column entitled "New Developments in MS Research." ACP met Professor Briggs in 2015, when he began using patient samples and clinical data from our Repository to pursue his principal research interests: identifying factors that influence people's susceptibility for MS, and identifying the factors that influence the progression of the disease. For more about Farren's work, see the November, 2016 issue of this newsletter [here](#). We are thrilled to bring you Farren's first article and look forward to publishing others in the series.

ACTRIMS 2017

By Laura Kolaczowski

Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) held its annual meeting last month, and over 800 participants gathered to share their latest work in MS research. I joined Robert McBurney and Hollie Schmidt, respectively CEO and VP for Science of ACP, in attending and presenting a poster, [Initial Characterization of Participants in the iConquerMS™ Network](#). Ours was one of hundreds of posters presented at the conference.



For the uninitiated, a poster presentation is a vehicle employed by scientists or research teams, to present information about their work to other scientists gathered at professional or academic conferences. Typically, the posters are displayed in a separate room or area of a trade show floor. During scheduled “poster sessions,” researchers position themselves next to 2’ x 4’ posters, on which their work is described, while other conference attendees wander around the room, stopping to learn more from presenters about topics that interest them. Those who are presenting walk listeners through their hypotheses, research methods and outcomes and answer questions.

Aside from the poster sessions, there were keynote and other featured speakers, who covered about a range of topics related to current research on MS. As I sat and listened to them, I had to marvel at the inquisitive nature of science and how far we have come in MS research. For example, one group of presentations focused on the human microbiome, our gut and skin, that hosts billions and billions of microbes (or microbiota) that build our defenses against germs and disease. When we are talking about MS, a disease of the central nervous system, what makes a researcher think they should examine poop for clues? It turns out the human gut and how we are processing the food we eat may be complicit in some way with MS, and the severity of the disease course, according to the talks I heard at ACTRIMS.



Multiple Sclerosis in the Age of B Cell Therapy, was shared by Dr. Stephen Hauser, from UC San Francisco, as the opening talk. For some time, Dr. Hauser and a group of his peers, have thought that perhaps treatment of MS should focus on the role of B cells instead of T cells as our current MS therapies do. Remembering the differences between T and B cells is an ongoing challenge for me (hint: the two types of cells play different roles in helping our bodies eliminate invaders, such as bacteria. T cells directly attack infected cells, whereas B cells primarily produce proteins called antibodies that hijack invaders as they travel in the blood. The function of antibodies is to act as a flag on the infected cell so T cells recognize which cells to destroy). Nonetheless, I did come away from his talk understanding more about the development of a new MS drug, Ocrevus (ocrelizumab), which is currently awaiting FDA approval. This drug will be the first that targets B cells. It has captured additional interest because, if approved, it will also be the first disease modifying therapy for people with Primary Progressive MS (PPMS).

I wrote about the Gut, B Cell Therapy and more, from the presentations at ACTRIMS 2017, and you can find those in my column [Engaging Thoughts](#), published in *Multiple Sclerosis News*

Today on February 23. Attending conferences such as ACTRIMS give us the opportunity to share our work with people who otherwise might not be aware of iConquerMS and ACP, and to learn about their research efforts, and network with possible collaborators.

To see our poster on iConquerMS™, click [here](#). Interested in being part of the community contributing to the type of research presented in this poster? Join iConquerMS by clicking [here](#).

Power MS Research With Your Participation

We've recently published articles related to the Accelerated Cure Project (ACP) Repository and the research being done with its biosamples and data. In this issue, we focus on another of ACP's initiatives, [iConquerMS™](#), the people-powered research network that ACP launched in 2015.

Developed in collaboration with a major university and a communications firm, iConquerMS takes the original Repository concept of a centralized and open-access resource for researchers, and shape-shifts it in a variety of directions. Instead of being conducted in the MS clinic, anyone with access to a computer can join iConquerMS and participate from their home, office, or other location. And instead of having a limited "research subject" role, the members of iConquerMS are included in driving and shaping both the resource and the research being conducted with it, in unique and powerful ways.

Many other initiatives exist to collect health information from people with MS. They range from classic clinical research studies (which may have stringent rules about who is eligible to participate), to online and paper surveys, to social networks that compile the information shared by their members and then repurpose that information for research.

iConquerMS is different from them in many ways. First, participation is open to all affected by and with an interest in MS. And while members do contribute health information via surveys, there are many other ways for them to engage with and impact MS research.

So what do we mean by "engage with MS research"? It can start with completing surveys about yourself (age, gender, race, geographic location), your experience of the disease (age at diagnosis, type of MS, symptoms and how they affect you), your treatment history, and other aspects of your quality of life. ACP removes any identifying characteristics from your data,



combines it with data contributed by others and makes it available to researchers for the purpose of developing a better understanding of MS and its impact.

Through iConquerMS, to date more than 2,000 people have chosen to participate in this way. Their data may help uncover the causes of MS, inform us about who will respond best to various treatments, and help us understand better what complementary activities people could be doing to manage or improve their symptoms and well-being. As we say in iConquerMS, “Your information has power!” The act of sharing it is another way to fight MS.

Engaging in research through iConquerMS can include suggesting research topics of importance to you, and providing your feedback on topics and research studies being proposed by others. Members of iConquerMS receive updates on the initiative’s activities, such as what researchers are learning, and they can also learn about opportunities to participate in focus groups or clinical studies.

Perhaps most notably, iConquerMS is governed by a majority of people with MS. Through a Governing Board and two committees -- Engagement and Research -- some iConquerMS members contribute their professional and life experiences in order to design, grow, and manage the initiative. These individuals work closely with ACP and its founding partners to ensure that iConquerMS accelerates MS research in the ways and avenues that matter most to people with MS. We hope that you will consider becoming an iConquerMS Champion and work to engage and educate others on the initiative. Or alternatively, join the Board or one of the committees and become a leader in this global movement of people-powered research.

Your level of engagement with iConquerMS is up to you.

Today, over 3,600 people with MS have enrolled to be part of the iConquerMS network. All 3,600 have formally consented to participate in research. A majority of them also contribute baseline and 6 month data about their demographics and MS characteristics, including medications, symptoms and quality of life, by answering questions posed in online surveys. Many of the surveys take less than 5 minutes to complete and while a small number of them take longer, the answers that participants have contributed make up a trove of data that is enormously valuable to researchers.

The value of building a network committed to working with researchers is underscored by iConquerMS’s activity over the past year. At present, there are 6 scientific studies that have been funded and are underway, and another 10 that are awaiting grant funding from various sources to proceed. They include:

- A study being conducted by researchers at the famed Cleveland Clinic, to understand issues related to access to insurance for people living with MS. The scientists want to know what kind of insurance people with MS have (health, life, disability, long term care, none?) and want to understand how having different types of insurance impacts people’s lives. For example, if you have insurance through your own or a spouse’s employer, do you fear losing it

in the event the employment ends and, if so, how does that impact your mental and physical health?

- A study being conducted by scientists at Harvard Medical School and the Massachusetts General Hospital, whose collaboration is named [The Mood Network](#). The study is testing an online approach to treating stress in people with medical conditions and their caregivers. They are experimenting with an online mindfulness treatment model, seeking to understand its effectiveness in reducing stress and its acceptability across a varied population.
- A large scale study proposed by ACP that will follow people on all the available Disease Modifying Therapies for a period of 4 years, in an effort to understand what factors influence how each individual does on a particular treatment. Knowledge gleaned through the study could translate into guidance for patients and health care providers considering treatment choices.
- A study proposed by researchers at Brigham and Women's Hospital in Boston to understand the extent to which people with MS use complementary and alternative medicine (things like yoga, meditation, acupuncture) and to what extent they combine it with more mainstream medical interventions.

People enrolled in iConquerMS have already contributed meaningfully to some of these studies, by participating in ad hoc surveys that the researchers developed in collaboration with the Research Committee of iConquerMS and the staff of ACP. For example, in preparation for seeking funding of ACP's study related to treatments, ACP asked people enrolled in iConquerMS to identify the functions and capabilities, e.g., mobility, mood, or energy level, that matter most to them when selecting a disease modifying therapy. More than 800 iConquerMS members responded, and their input profoundly influenced the design of the study.

Thirty years ago, the most common images associated with medical research were a slide under a microscope or a line of test tubes in a rack. But today, the image might just as likely be letters and numbers flitting across a computer screen. We have come a long way, baby, and the present and future of medical research depends on grouping, comparing, sorting and analyzing large amounts of data about people affected by disease. Your information, combined with the data of thousands of others, helps researchers uncover critical patterns and insights.

Joining iConquerMS is straightforward. Just click [here](#) on your computer or mobile device. After you click the "Join Now" button, you'll need to provide your email address and complete your personal profile. Once you've provided informed consent, you'll be ready to contribute data, ideas, and insights, and to shape and drive research as never before. For those of you who haven't yet enrolled, we look forward to welcoming you at www.iconquerMS.org very soon.

New Developments in MS Research, a monthly column

by Farren Briggs

MS Researchers Identify New Biological Mechanisms Regulating IL7R Expression

Our immune system is comprised of many different cells that are the great guardians of our bodies – protecting us from invading pathogens, and removing infected and malignant cells, while overlooking healthy cells. This defense system is coordinated through precise but dynamic signaling of various proteins and receptors. In multiple sclerosis (MS) and other autoimmune disorders, there is a disruption to the cellular symphony, leading some immune cells (e.g. T cells) to mutiny and attack healthy tissues. A prominent source of this disruption results from an above average burden of common genetic alterations (variants occurring in at least 5% of a population) in genes involved in the immune system.



Our genes are the units of heredity that make up our unique biology. In the same way that they determine the color of our eyes or the shape of our nose, genes can determine our vulnerability to disease. One of the earliest genes associated with the onset of MS is *IL7R*, which encodes the interleukin-7 receptor (IL7R) essential for survival, proliferation, and maintenance of T cells. IL7R can be found on the surface of immune cells or freely floating throughout the body, however a genetic variant that shifts the balance from the surface-bound subtype to the free floating subtype has been confirmed to increase one's risk for MS. This month, two studies were published investigating additional mechanisms that contribute to this shift in IL7R subtypes.

The first study by Galarza-Muñoz and team was published in *Cell*¹. I was fortunate to be a part of this multidisciplinary approach to identifying other genes that contribute to the shift in IL7R subtypes. We conducted two experiments simultaneously. The first experiment was carried out in two cell models, where the influence of 89 different proteins on IL7R synthesis was investigated. The absence of an enzyme, *DDX39B*, involved in assembling proteins from genes, was shown to dramatically favor the shift of IL7R subtypes to the free floating variety. The second experiment, which I conducted, was a statistical analysis of genetic data from over 4,088 individuals with MS and 7,444 unaffected individuals. Due to the large number of individuals who were willing to share their genetic data, I was able to detect a significant statistical interaction between the *IL7R* variant and a variant in *DDX39B*. Individuals with the interacting *IL7R* and *DDX39B* variants, were almost three times more likely to have MS than those without these two alterations. Thus, both experiments independently implicated *DDX39B* as shifting the balance of IL7R subtypes and increasing risk for MS. They also highlight the value to scientists of ordinary people's willingness to share biological samples and data about themselves. This is true for people with MS, as well as for others who can serve as "healthy controls."

The second study by Bina and team was published in *Neuroscience Letters*². The majority of our DNA does not encode a protein, and for many years scientists thought the non-protein coding regions were “junk DNA.” However, within the past decade various patterns have been detected in our “junk DNA.” Some of these patterns include genes encoding non-protein molecules (examples of these are called long non-coding [lnc] RNAs) that facilitate or disrupt actual protein synthesis. In 2014, a gene encoding a lnc RNA was detected near the *IL7R* gene, and was shown to influence the expression of IL7R protein – and thus named *lnc-IL-7R*. Bina and team conducted an exploratory analysis to compare the level of lnc-IL-7R and IL7R subtypes in blood from 36 individuals with MS and 30 unaffected individuals. Higher levels of lnc-IL-7R was statistically associated with lower levels of both IL7R subtypes, but more so for the surface-bound subtype. There was also preliminary evidence demonstrating that IL7R subtype patterns were associated with age and gender, and the length of time an individual had MS – suggesting a role for IL7R disruption in the progression of MS.

Collectively, these studies suggest multiple independent mechanisms regulating IL7R expression, and that IL7R may contribute to MS progression. By understanding how the immune system goes awry and by shedding light on biological mechanisms predisposing individuals to contract MS, we researchers hope to help improve the time to and accuracy of a MS diagnosis, and to positively contribute to the greater knowledge needed to develop novel therapies.

1. [http://www.cell.com/cell/abstract/S0092-8674\(17\)30286-6](http://www.cell.com/cell/abstract/S0092-8674(17)30286-6)
2. <http://www.sciencedirect.com/science/article/pii/S0304394017300940>

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