FACES OF MASS SPECTROMETRY

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Where Curiosity Leads, Innovation Follows

Richard Huang was introduced to mass spectrometry as an undergraduate in Taiwan. After his initial focus on proteome profiling, he soon became interested in studying protein mechanisms through structural characterization. This discovery prompted Richard to pursue a PhD at Washington University, where his research involved the use of structural mass spectrometry to analyze the higher-order structure of proteins. After earning his PhD, Richard accepted a post-doctoral position with the National Institute of Standards and Technology (NIST). During this time, Richard worked on hydrogen/deuterium exchange mass spectrometry, which he found intriguing because of its robust range of emerging applications. This opportunity encouraged Richard to pursue a career in the pharmaceutical industry to carry out innovative research through the use of mass spectrometry.

Richard kicked off his career in industry by working as a research scientist at Bristol-Myers Squibb. While there, he used mass spectrometry to characterize biologics and assist with the selection of promising therapeutic candidates. Richard then made a transition to Johnson & Johnson Innovative Medicine, where he currently works as Director of Mass Spectrometry in Biologics Discovery. Richard enjoys this position because it allows him to engage with challenging questions and develop innovative techniques to accelerate the discovery of novel therapeutics that can benefit patients. In addition, Richard emphasizes that he continues to be inspired by the drive and creativity exhibited by his group members.

Over the course of his career, Richard has published more than fifty peer-reviewed articles and book chapters. He believes such contributions are valuable not only because they help one to grow as a scientist but also because they serve to promote a productive culture of collaboration, which can lead to collective growth among peers. Richard has been a member of ASMS for seventeen years. He characterizes this involvement as an important component of his career journey, highlighting that he appreciates the many ways that researchers in this community have worked together to push boundaries while also generating significant impacts.

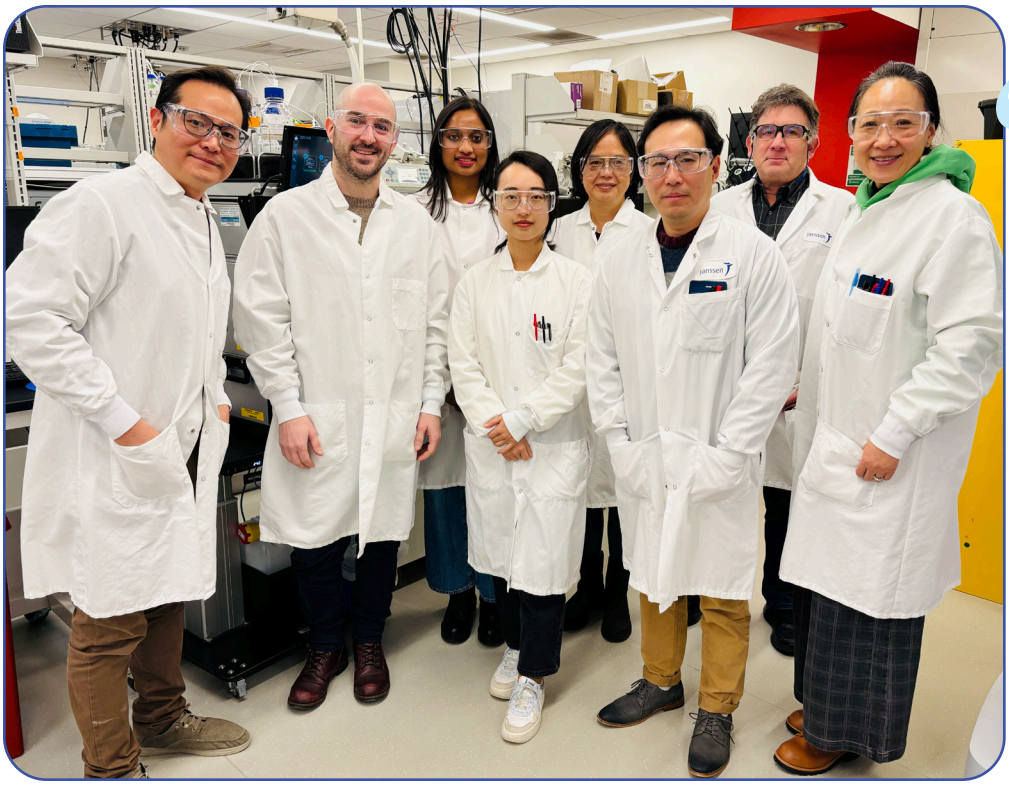
Looking ahead, Richard is excited about the many ways in which developments in areas such as instrumentation sensitivity, data analysis software, and high-throughput workflows are poised to accelerate research and therapeutic design. Moreover, within the context of the pharmaceutical industry specifically, Richard believes that advances in sensitivity and resolution have established the integral role of mass spectrometry in the process of high-throughput molecular characterization, which he describes as a promising future direction for the field.

Did your interest in mass spec begin during your education in Taiwan, or during your Ph.D. from Washington University under the mentorship of Professor Michael Gross?

I began my research in the mass spectrometry field as an undergraduate in Taiwan, focusing on proteome profiling of cancer cell lines. After graduation, I continued this line of research as a research assistant in a joint project at Academia Sinica in Taiwan. While I found proteome profiling to be fascinating, my growing interest in understanding protein mechanisms of action through structural characterization motivated me to pursue a PhD with Prof. Michael Gross at Washington University. There, I used structural mass spectrometry to investigate the higher-order structure of proteins and their interactions with ligands.

When did you decide you wanted to pursue mass spec specifically in the pharmaceutical industry?

Upon completing my PhD, I joined the National Institute of Standards and Technology (NIST) as an NRC postdoctoral



> *I am consistently inspired by the energy, scientific momentum, and diverse ideas that my group members bring to the table, which often lead to novel approaches and strategies for tackling complex issues.*

Richard and his J&J mass spec team members in the lab welcoming fantastic 2025. From left to right: Richard, John Patrick, Pooja Madhav Raju, Mengqi Chai, Tun Liu, Kyoung-soo Choi, Steven Pomerantz, and Helen Zou. Missing in the photo: Yoshitomo Hamuro. (Photo courtesy of Richard Huang.)

fellow, where I worked with Dr. Jeffrey Hudgens on hydrogen/deuterium exchange mass spectrometry (HDX-MS) for assessing conformational similarities of protein molecules. During my tenure, I witnessed significant advancements in the automation and data analysis of HDX-MS, which began to emerge as a robust technique for conformational characterization in the pharmaceutical industry. This evolution in mass spectrometry, particularly in the characterization of complex molecules, motivated me to shift my career path and engage in cutting-edge research within the pharmaceutical industry, utilizing mass spectrometry.

How did you come to your current position at Johnson & Johnson Innovative Medicine?

I began my industrial career at Bristol-Myers Squibb as a research scientist, where I focused on the characterization of biologics using mass spectrometry. My research centered on understanding the stability profiles of biologics and the mechanisms of target engagement during the early discovery phase, aiding in the selection of the most promising therapeutic candidates. Subsequently, I made the decision to transition to Johnson & Johnson Innovative Medicine to broaden my career path and to drive innovation in mass spectrometry applications within biologics discovery.

How did you decide to focus on protein higher-order characterization by mass spectrometry?

Mass spectrometry is an emerging field characterized by its sensitivity, resolution, and the ability to couple with various chromatography separation techniques. These features enable the investigation of native protein complexes, offering wide-ranging applications, especially at the molecular level. I find this particularly fascinating as the technique, especially from a higher-order structural perspective, provides a powerful avenue for addressing challenging questions related to the complexity of protein therapeutics.

What is something you enjoy most about leading the mass spectrometry group at Johnson & Johnson Innovative Medicine?

Johnson & Johnson Innovative Medicine is a diverse and inclusive company, reflecting the values of my team as well. We actively seek new talents whenever opportunities arise to foster innovation and push the boundaries of applying mass spectrometry to address challenging and critical questions. Our goal is to develop best-in-class or first-in-class therapeutic molecules to benefit patients. I am consistently inspired by the energy, scientific momentum, and diverse ideas that my group members bring to the table, which often lead to novel approaches and strategies for tackling complex issues (Figure 3). I particularly enjoy the daily learning and brainstorming processes that occur while collaborating with my team.

We understand that you have authored more than fifty peer-reviewed articles and book chapters. How has publishing works helped you to grow as a scientist?

Publishing high-quality research is one of the best ways to remain at the forefront of scientific inquiry. It motivates you to push your boundaries in identifying novel and more efficient approaches to tackling challenging questions. Furthermore, publications serve as a platform to share groundbreaking observations and ideas with the scientific community, fostering a collaborative environment that drives innovation and facilitates collective growth among

It is inspiring to see researchers collaborate, pushing boundaries and creating a significant impact within the analytical community.

PhD defense party at Wash U in 2012. From left to right: Don Rempel, Richard, and Michael Gross. (Photo courtesy of Richard Huang.)

scientists. I learn a great deal from reviewing other publications, and I am grateful to be a part of the evolving field of mass spectrometry

Can you tell us about an emerging topic or research question in your field that you are excited to explore?

Mass spectrometry has long been regarded as the gold standard for understanding the intrinsic properties of protein therapeutics, ranging from linear sequences to higher-order structures. With advancements in sensitivity, resolution, and duty cycle of the instrumentation, this technique has been widely adopted to study protein therapeutics in complex matrices. Additionally, recent developments in chemistry and biological assays have positioned mass spectrometry to play a pivotal role in elucidating the interaction mechanisms of protein therapeutics within cellular environments. Such insights can significantly enhance our understanding of therapeutic behavior in vivo. While this area presents challenges, I believe we are approaching a point where the enhanced instrumentation sensitivity, the improved data analysis software, and the development of high-throughput workflows will enable us to acquire this vital information in a quicker way, ultimately accelerating research and therapeutic design to benefit patients.

As a member of ASMS since 2008, what lessons have you learned from your membership there?

ASMS has been an integral part of my career journey. I joined as a graduate student and benefited immensely from the innovative work in instrumentation development shared by groups worldwide. Over the past seventeen years of membership, I have not only seen my own career flourish, but I have witnessed the evolution of techniques and the expansion of research across academia, federal agencies, and industry. It is inspiring to see researchers collaborate, pushing boundaries and creating a significant impact within the analytical community.

Can you tell us about a moment of discovery or surprise that you have experienced as a researcher?

There was a time when researchers faced challenges in understanding the poor target engagement of certain therapeutics. By implementing HDX-MS and native mass spectrometry, we uncovered unexpected binding stoichiometry, which was subsequently validated through co-crystal structure analysis. This serves as a compelling example of how we can harness the power of mass spectrometry to gain molecular insights into the binding mechanisms of therapeutics and inform molecule design.

Dinner with PhD mentor, Michael Gross, in Alexandria, Virginia in 2019. (Photo courtesy of Richard Huang.)

Richard with his wife (Xinliu Gao) and daughter (Olivia Huang) at the Golden Gate Bridge, San Francisco in winter 2022. (Photo courtesy of Richard Huang.)

Since entering the field, has the role of mass spectrometry in the pharmaceutical industry changed in a way that has impacted your work?

The research landscape in the pharmaceutical industry is undergoing significant evolution, especially concerning throughput and precision. Advances in mass spectrometry's sensitivity and resolution, along with enhanced separation capabilities in chromatography, have positioned mass spectrometry as a key player in high-throughput molecular characterization. To fully harness the speed and accuracy of measurements, substantial innovation in workflow design is necessary to ensure the quality of the information gathered. This represents an exciting and promising future direction for mass spectrometry within the pharmaceutical sector.

When you are not working, are you ever able to travel back to Taiwan?

Despite the interruptions caused by the COVID-19 pandemic, I have made a continued effort to return to Taiwan biannually, if not annually, to reconnect with friends and reunite with family. Recently, these trips have become even more enjoyable, particularly since I've been able to bring my eight-year-old daughter along with me. It has been a delight to witness her excitement as she explores new experiences and delicious food in Taiwan. My family members have also thoroughly enjoyed spending time with her