FACES OF MASS SPECTROMETRY / Iain Campuzano

Anne Brenner and J.D. Brookbank are science writers at Technica Editorial Services.

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Where Determination Can Lead

Iain Campuzano was introduced to mass spectrometry (MS) while pursuing his PhD at Southampton University, where he studied protein biochemistry and chemistry. From 2000 to 2011 (with a short 10-month period at Cellzome) he worked at Micromass and the Waters Corporation in their demo and proteomics applications lab. While there, he enjoyed working with cutting-edge MS instrumentation and traveling extensively, visiting customers in countries such as Israel, China, and Japan.

In 2011, Iain relocated with his family to Thousand Oaks, CA to join Amgen, a global biopharmaceutical company, where he currently works as a Senior Principal Scientist leading a group of research scientists over three research sites and across two countries. At Amgen, Iain performs small and large molecule MS analysis supporting many departments across Amgen, such as medicinal chemistry, protein engineering, and the structural biology groups. He is excited and inspired by being able to contribute to long-term therapeutic projects, seeing them progress from inception to clinical trials and eventually to patients. As a career highlight, Iain notes Amgen's development of LUMAKRAS, a highly successful cancer therapeutic for which MS played a major role.

Iain has published over 60 peer-reviewed articles and book chapters and holds 7 MS-related patents. He has conducted research in multiple areas of MS, including small molecule, peptide, nucleic acid and protein analytics, ion mobility and FT-ICR research, and proteomics applications. He has also presented at numerous ASMS sessions and will be presenting at this year's 2023 meeting. At these and other conferences, he aims to champion the innovative MS research that takes place in both the MS vendor and biopharmaceutical research settings. Additionally, Iain has served as a mentor for professionals in the early stages of their careers—supervising one Amgen intern and two Amgen post-doctoral scientists.

The trajectory of Iain's career and the scope of his research demonstrate the value of versatility and adaptability. This characteristic also translates to his interests outside the lab. During his spare time, Iain enjoys family time, reading, cycling, and competing in triathlons. He notes a strong level of self-belief and determination that has likely served him well both as a scientist and as an endurance athlete completing many difficult races.

How did you get your start in MS? Was it before, during, or after your PhD work at Southampton University?

During my PhD, which started in September 1994 in protein biochemistry and chemistry, my supervisor at the time, Prof. Peter Shoolingin-Jordan, purchased an MS, a Micromass Quattro II triple quadruple. The Quattro II was set up essentially as an open-access system where PhD students would just run their samples by loop injection. I saw the benefit and started using it for my protein, peptide, and small-molecule samples and research. The system was very easy to use, and the data quality was far higher than that from the Applied Biosystems Voyager MALDI-MS, which was an older departmental MS. This was also the first electrospray-based MS in our department. I'd also run/analyze my lab mates' samples on the Quattro II MS. Then, around 1997, another MS system was acquired: the Micromass LCT, which was operated by Paul Skipp. It was with this MS system that I first successfully acquired a spectrum with partially resolved charge states for a 190 kDa protein, 6-MSA synthase (a polyketide synthase). And with MaxEnt deconvolution, I was able to observe a single neutral Mw of 190 kDa. This obviously went in my thesis!

How did you start in your current position as a Senior Principal Scientist at Amgen biopharma company? Also, tell us about your time working with Micromass and the Waters Corporation?

> *If someone says it can't be done by MS, show them the data that proves it can.*

Iain in his lab at Amgen, next to a Waters Synapt G1, which has been modified to an RF-confining drift-cell, using parts supplied by Kevin Giles and Mike Morris (Waters Corporation). (Photo courtesy of Iain Campuzano.)

I started working at Amgen in March 2011 and was recruited by Paul Schnier. I flew out to SoCal Amgen in Sept 2010 for the interview and loved the company and area. I was offered the role in Nov 2010, and part of the relocation package was to come out for a week to get to know the area, which we did in Dec 2010—my wife, our 4-month-old daughter, and me. I was hired and officially started in March 2011, once my work visa was approved, as a Senior Scientist, performing both small- and large-molecule MS analytics to support medicinal chemistry and the X-ray crystallography group and associated therapeutic projects (Figure 1). Prior to this, I started my MS career at Servier R&D in Fulmer, north London, performing small molecule and metabolite MS and tandem-MS structure elucidation using a Quattro II and a QToF2.

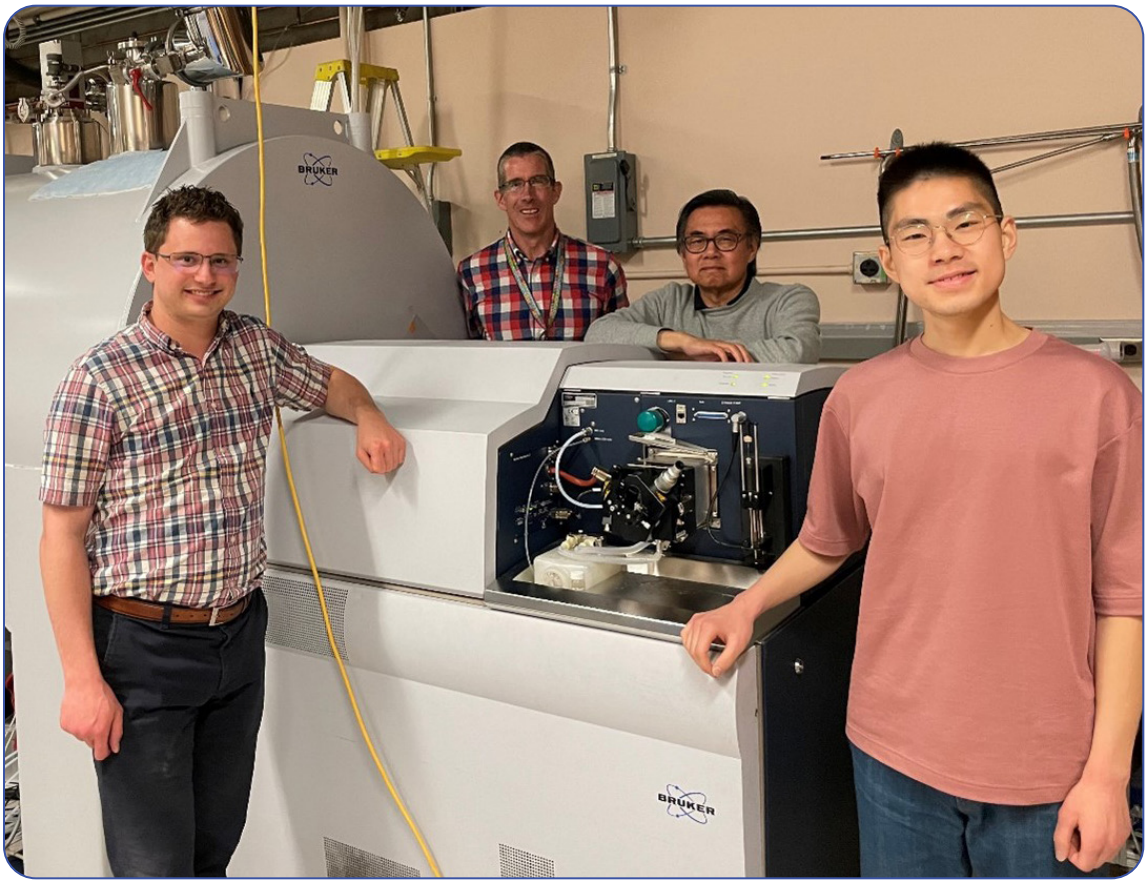
In August 2000 I joined the Micromass demo lab. This gave me great exposure to many different customers and their proteins. I was able to work with researchers like Prof. Dame Carol Robinson—whose work I have always admired—when she, Frank Sobott, Justin Benesch, and Helena Hernandez came into the Atlas Park demo labs to assess the new (at the time, 2001) QToF Ultima for native-MS analyses of protein complexes. In mid-2002 I briefly left Micromass and worked in north London for a small startup proteomics company called Cellzome with Walter Blackstock (and Bernhard Kuster, Cellzome Heildelberg). Then, I came back to Waters in March 2003 and worked in the proteomics applications lab until I left in March 2011. In those eight years, I traveled around the globe visiting customers and presenting at conferences and meetings. Japan was always my favorite place to visit because of the culture, history, people, technology, and food. Israel was also very impressive, in terms of its historical and religious significance. An interesting story about Atlas Park was that in the same scientific industrial estate a few years prior is where Alexander Makarov first developed the Orbitrap and published his seminal 2000 Analytical Chemistry paper on the Orbitrap theory and detector—it really is a small world!

What are some similarities and differences in working for a vendor versus for a biopharma company?

The differences are massive and really can't be fairly compared. My experiences at Waters and Amgen are just so different. The similarities are that you are part of a large global multi-billion-dollar company and a big team, all working toward a common goal, whether it be the next new MS to release at ASMS or a new therapeutic treatment for gravely ill patients. I learned many different things about the business and products at both Waters and Amgen. For example, at Waters, working with the Research and Development scientists on the latest and greatest MS instruments was always fun. And at Amgen, it is extremely satisfying to work on therapeutic projects from their inception with a team—seeing a therapeutic progress into the clinic and, ultimately, to patients—and to witness MS being involved in many critical stages.

What kinds of diseases has your work helped in terms of finding cures and treatments?

Cancer is a big therapeutic area of focus for many biopharmaceutical companies. There's a huge amount of MS analytical support for every oncology project, whether that be small molecule–based therapeutics or large-molecule biotherapeutics. I was lucky enough to be part of the highly



Iain with friends and collaborators at UCLA, next to the 15 Tesla FT-ICR MS instrument, where most of their collaborative research and data acquisitions were performed (left to right: Carter Lantz, Iain, Joe Loo, and Benqian Wei). (Photo courtesy of Joe Loo.)

successful LUMAKRAS story, and MS played a big role in its development. That was a huge project for Amgen because it was the first ever FDA-approved small-molecule therapeutic targeting solid tumors containing the mutated oncogene KRAS G12C. In 2016 we published a manuscript describing how we utilized a high throughput solid phase extraction MS method to screen an acrylamide library against recombinant KRASG12C, which formed the basis for further chemical series optimization and ultimately LUMAKRAS.

Is there an MS-based technology advancement or application on which you possess a unique perspective after having worked for both an instrument vendor and a biopharma company?

Like most mass spectrometrists in biopharma, I think I possess a view of the importance of how MS can progress a therapeutic project. One can argue that MS is this amazing molecule agnostic analytical technique—however, it is not the only analytical technique available. Having worked for Micromass and then Waters, it's easy to think that MS should be able to solve most, if not all, analytical problems. However, when working at Amgen, I was exposed to many more analytical techniques that are used in pharma and biopharma research (NMR, SPR, calorimetry, rheometry, negative stain-EM, and cryo-EM, for example). That's where I found that MS and many other analytical techniques are complementary, at various stages in the research pipeline. Still, it's always nice when MS provides the answer that other techniques can't!

What is your advice for students trying to decide between working for a vendor versus a biopharma company?

I'd suggest both! Work in an MS vendor first and get your grounding in MS applications and instrumentation. Then, work for a biopharma company, and apply that knowledge for the progression of therapeutic projects. Working for an MS vendor, one can work on all of the latest MS instruments and meet many customers from across the globe. If you like to travel and are interested in world culture, it's great fun working for an MS vendor. In biopharma, one can work on a project for over a decade, achieve a massive level of input, and then eventually see the therapeutic get to the clinic and patients. I would also encourage people to branch out into multiple different aspects and areas in the field of MS. I have conducted research and published on multiple MS areas, such as small-molecule medicinal chemistry support, accurate mass analysis and structural elucidation, ion mobility, proteomics, native-MS on multiple MS instruments (quadrupole, FT-ICR, ToF, and Orbitrap), and fundamental ion structure determination using MD and DFT calculations. I'd also encourage students to understand and appreciate fundamental MS theory, such as the nitrogen rule, double-bond equivalents, isotope theory, halogen isotope patterns, fluorine mass deficiency, and even versus odd electron ions. My advice would be: Don't be pigeon-holed into one area of MS research; I've always tried to be "area-agnostic". Be flexible and be able to adapt quickly.

Tell us how your experiences presenting sessions with ASMS helped you grow as a scientist?

Without a doubt, it has—I love ASMS. My goal at ASMS is always to champion the amazing MS research that takes place in both the MS vendor and biopharmaceutical research setting (Figure 2). I've given five oral scientific presentations at ASMS, and I also have an oral slot at this year's 2023 meeting. I always try to improve upon the last presentation in terms of how I deliver it; I don't think I'm ever fully happy with how I've delivered a presentation. The most rewarding and fun session was one I chaired and helped organize in 2016. It was titled "Fundamental Session: MD and QM in MS and Ion Mobility." Then, last year, I presented one of the opening Sunday Tutorial Lectures. This took a huge amount of planning and preparation, which I was doing up until the last day or so, trying to get the message right. This was the toughest talk I've ever prepared, but it was also the most fun and rewarding to deliver. I love presenting my own data—the more technical, the better.

Has the structure or pathway of MS-based technology advancements changed since you've entered the field?

During my PhD I remember the first nESI source on the Quatro II. One could not even see the nESI needle at the end of the probe once it was inserted into the instrument source. It would easily break and was somewhat trial and error. Then, over the next decade, the nESI source evolved over a number of iterations into a very easy-to-use and intuitive source. Working for an MS vendor for over a decade, I have experienced many instrument and technology advancements. I was lucky enough to work on the first QToF MS, and I saw it evolve over many iterations. I was also lucky to work on the first commercially available ion mobility platform that was T-WAVE. I have also seen the dramatic uptake of Orbitrap technology over the last 18 years, which has been incredible—obviously, there have been massive improvements in resolution. I should also note that MS in drug discovery, especially biotherapeutics, is significantly changing and evolving. It's no longer just a mass spectrometrist running a single sample on an MS. There are many other people involved who don't necessarily have formal MS training, such as protein chemists who are now able to generate their own MS data by running samples on a walk-up open-access MS. At specific stages in the biotherapeutic's progress through research, sample numbers can be very high. Therefore, high throughput is key, and efficient and effective data processing and management software are also extremely important—it really is a collaborative effort. There is also now strong emphasis on artificial intelligence and machine learning, and how it can aid in drug discovery. The landscape has changed significantly over the past five years, which is exciting and brings with it many new opportunities..

Iain with his wife (Kelly) and daughter (Isabella) on the Greek island Santorini. (Photo courtesy of Iain Campuzano.)

What kind of mentorship work have you done?

I had the opportunity one summer to supervise an intern at Amgen named Neelam Khanal at Amgen. She went on to complete her PhD with Prof. David Clemmer and now works back at Amgen in our Process Development department. There was also a postdoc, Jennifer Lippens, who was with us for two and a half years. She worked on membrane protein MS, and through her position at Amgen, we published six manuscripts as a result of her research. She is now working for Janssen Pharmaceuticals in Belgium. There was also Chen-Chun Chen who was an Amgen postdoc and served as a fellow in 2019 and 2020 as part of the LEAP Scholar program. She's now with Eli Lilly and Company in Indianapolis. We will publish a couple of manuscripts out of her research. I also manage and mentor my group here at Amgen through the many projects we support throughout the Amgen research pipeline.

What excites you about your current work? What would you say is an important aspect?

I find it very exciting to be able to use MS for almost all aspects of my work. MS can provide high resolution and very accurate solutions and answers to many analytical problems. The fact that we can and are hyphenating MS to many chromatographic separation methods (RPLC-MS, CEX-MS, HIC-MS, and SEC-MS, to name a few) makes MS so enabling. On more occasions than I can remember, MS has given the precise answer when many other low-resolution analytical techniques just provided a high-level "yes the samples are different" type of answer. However, it must be noted that all analytical techniques are important within biopharma, and all are required for a therapeutic treatment to progress from research into later stages of development and commercialization.

Can you share a turning point or defining moment in your work as a researcher/scientist?

I have always known I wanted a career in industry, as opposed to a career in academia. I have many very strong memories of when I acquired MS data that I felt were defining moments for a particular area. For example, in 2006, Kevin Giles and I (at Waters) were working together on the R&D test floor on one of the early Synapt G1 beta units. We were the first to acquire a T-WAVE ion mobility MS and tandem-MS spectra of GroEL, the 801 kDa chaperone protein complex, under native-MS conditions, which we later published in 2011. Additionally, the really high-quality

native-MS nESI spectra of GroEL, an ADC, and a membrane protein complex, in collaboration with Joe Loo (UCLA) (Figure 3), using his 15T FT-ICR MS, are very strong memories and defining moments for me. Also, as I mentioned before, there was last year's ASMS opening Sunday Tutorial Lecture, where I gave a presentation on MS in Industry: From Small Molecules to Multispecific Antibodies and Beyond. I'd been lobbying the ASMS committee for a number of years to give industry more visibility, and I was very happy for this opportunity to showcase and celebrate industrial MS and its associated applications. Although I still have multiple pieces of research that haven't been put on paper yet, my goal is to write them up. Even though I haven't worked in academia, I have still been able to publish over 60 papers, 7 MS-related patents, book chapters, critical reviews, and other scientific research across multiple areas.

What are some of your interests outside of the lab? We understand you enjoy triathlon and ironman competitions; could you tell us a little about those interests?

I enjoy reading when I have the time, especially political and global political–related books. I've traveled a lot around the world with my family (Figure 4), so I consider myself global in my outlook. I used to be big into rowing, but when I moved to Southern California, the rowing near Thousand Oaks was not good. So, I took up triathlons. In 2012, Amgen was sponsoring the Malibu Triathlon. When I attended an internal Amgen meeting about this event, I thought it would be fun to compete. I loved it, so I then entered more races in the 2013 season (Figure 5). In 2014, I entered my first half ironman competition in Aarhus, Denmark. Then in 2016, I competed in my first full ironman (2.4 mile swim, 112 mile bike, and 26.2 mile run) competition in Copenhagen, Denmark. My finishing time was about 11 hours and 40 minutes. I returned the following year with the goal of improving my time and was able to finish in 11 hours and 23 minutes. I also enjoy cycling every weekend in the Santa Monica Mountains.

Can you describe a relationship or major piece of advice that has impacted your career?

I have always had a strong level of self-belief, especially for what I think MS can do, along with where and how it can and should be applied. If I had the time, I'd try to publish every piece of research I've ever worked on—maybe it's this level of self-belief and determination that has gotten me through full ironman races! As for relationships, I'd have to mention the collaborative relationship I've had with Prof. Joe Loo for the past decade. This has resulted in more than 10 coauthored manuscripts, a joint supervised Amgen-UCLA post-doc, new application areas for FT-ICR MS, such as membrane proteins, and a great friendship with Joe, his wife Rachel, and his students. In terms of advice, a number of my publications that I'm most proud of are a result of the following mindset: If someone says it can't be done by MS, show them the data that proves it can.

Iain with his daughter (Isabella) at the LA Triathlon athlete finishers village. (Photo courtesy of Iain Campuzano.)