Intersect, Vol 12, No 2 (2019)

Connecting Disciplines with ChEM-H: An interview with Dr. Elizabeth Ponder

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Dr. Elizabeth Ponder currently serves as the Director of Planning and Operations under the Stanford ChEM-H program. Dr. Ponder joined Stanford ChEM-H in 2014, leading and planning initiatives with the faculty executive committee. Dr. Ponder's distinguished background includes having completed her Ph.D. in microbiology and Immunology at Stanford University and a subsequent postdoctoral Fellowship in pathology, also at Stanford. She previously served as executive director of the Henry Wheeler Center for Emerging and Neglected Diseases of the University of California-Berkeley.

JS: Stanford's ChEM-H program has become very well known around the research campus for its interdisciplinary recruitment that ties some of campus' most distinguished physicists, chemists, and bioengineers towards a common goal of improving medicine for human health. Can you tell us a little more about the history of the program, and where you came in?

EP: Sure! ChEM-H was formed as the idea of Professor Chaitan Khosla, who is a professor of chemistry and chemical engineering here at Stanford. He had this vision that if we could help colleagues in these very diverse fields of chemistry, engineering, and medicine, learn to speak more fluidly with each other, and understand each other's work in a more fundamental way, that we would be able to direct that research towards questions with the most potential for human health impact and advance those projects quickly. The common element between these fields of biology, chemistry, and medicine is at the level of the molecule. So, we like to think about that as the least common denominator between these very diverse fields and the thing that connects us. If we can help individual researchers, trainees, and our colleagues, then the problem solvers like engineers would be aware of clinical needs and unmet needs, like our clinician colleagues, and tie that all back to fundamental molecular questions. I think we can unlock new fields of science and drive innovations in health space.

JS: What is the history of ChEM-H?

EP: ChEM-H was formed in 2014, although I think the idea was percolating before that. Our goal is to identify and cultivate people who already spanned these divides in the field. So, people who have an area of depth in maybe clinical sciences and also in some areas of physical or biological science. In the formation of the institute, we recognized that we needed a physical space where we could bring people together. So, you may have noticed the big construction site here near the Shiram building that will be our new research complex that will be shared with the Wu Tsai Neurosciences Institute—and that's scheduled to be completed in late 2019.

We also realized that we wanted to invest in new talents, so ChEM-H is in the process of hiring numerous new faculty. Since we were founded in 2013, ChEM-H has helped recruit 8 faculty to Stanford, and we plan to recruit 12 more faculty—we have several ongoing searches. Those faculty searches include: Peter Kim, who is the former head of research at Merck Pharmaceuticals, and previously was a professor at MIT; Carolyn Bertozzi, who was at Berkeley for many years and is probably one of the preeminent chemical biologists in the world; and then a series of junior faculty, so people like Stanley Qi, Polly Fordyce, Lingyin Li, Jonathan Long, Laura Dassama. These are all people who naturally, in their research programs, could fit in a long list of departments here at Stanford,

and we can partner with various departments to recruit these very interdisciplinary young talented faculty to the campus, in order to increase the diversity of interdisciplinary players who have this molecular focus to their research on the campus.

JS: What do you find then, to be the most exciting, troubling, and also motivating aspects of your oversight of the ChEM-H program?

EP: I think what is so exciting is that ChEM-H has tapped into a demand among our faculty and our students that was clearly already existing here at Stanford for an outlet and a platform around which to connect and drive forward new interdisciplinary work. I would say that we have gotten a lot of enthusiasm and support from the faculty candidates that we have brought in, even though those candidates could end up in any number of departments. We have found strong partners in those departments that we have hired in so far.

We have also found great demand in the graduate student population for some of the programs that we have run, including this Chemistry-Biology interface training program, where we have a Ph.D. program that is an add-on to your home Ph.D. program, and you get to do research rotations outside of your own home department. There are some additional meetings and activities for those students to help them get greater access to our clinician science network in the School of Medicine, and that has been a hugely popular and has grown rapidly in the past few years. We have a post-doctoral society that was driven by the postdocs themselves to self-organize, and we have engaged undergraduates through the research program that I mentioned to you before and this entrepreneurship program in formulating biotech ideas. I feel that there is a lot of interest in our community, and ChEM-H is trying to tap into that existing pool of interest and create programs that meet the unique needs of our community.

I would say that one of the most exciting things that we've been working on is the establishment of a series of knowledge centers, and these are centers that bring together professional expertise, high-tech equipment, and unique research skills to allow researchers to add a new element or a new area to their research programs. For example, the first of these was a medicinal chemistry center. We recognized that a lot of faculty around our campus had identified a particular drug target for a disease or something of that nature, but they didn't know how to go from this genetically validated target to something that could be a drug-like molecule developed into a therapy. We recognized that hiring one more chemistry faculty member was not going to solve the problem, as these faculty are not looking for new types of chemical reactions as you would find in sort of an academic chemistry lab but more tried and true medicinal methods that are used in the biopharmaceutical industry all the time. ChEM-H was able to recruit Mark Smith, who is the head of this knowledge center using medicinal chemistry from industry and who is an

expert in this area of, "how do you assess this biological target and optimize small molecules." He has made a huge impact on helping a broad range of faculty convert their interesting research discoveries into drug development programs. He has about 6 active drug discovery projects going on now, is in multiple patents and publications, and I think even 3 biotech start-ups spun out using technology from his group in the past year.

I feel like this is an area where ChEM-H can help create the platform for students and postdocs to come and learn new skills that are not as typical in academia or are not so easy for a one-off lab to bring in house. Through this knowledge center platform, they can learn about these new areas, bring them back to their research groups, and form their own career trajectories on these interactions.

JS: So it creates one huge collaboration network!

EP: Yeah! It is certainly many small collaborations, but it creates a platform on which to setup those collaborations. After Medicinal Chemistry, we then also launched a knowledge center, the Macromolecular Structure Knowledge Center, which helps faculty access technologies, like SLAC up the hill, to study the 3D structure of various molecules. Again, there is a huge demand for expertise and mentorship in that area, and it can require some hand-holding and mentorship to understand how they can best take advantage of the technologies that are offered at SLAC.

Our third knowledge center is now around metabolic chemistry, so it's about understanding metabolism and metabolites and unknown small molecules that are used in our own guts and by our bodies and how we can do new chemical discoveries to answer a variety of biological questions. So, we have founded different types of technologies or knowledge bases that are not that common on our campus here and that require professional scientific staff and education to add-in a new bend to all kinds of research programs that are on campus.

JS: What interests drove you from biochemistry towards immunology and presently the goal of supervising this vivid research between academia and even corporate biotechnological interests? Also, could you elaborate, over your experience and changing trends that have been observed in recent times, what would you emphasize as increasingly vitally important for researchers to note in the future of immunological research—both again, from the biotechnological realm and from academia?

EP: I would say I was drawn to ChEM-H because of my interdisciplinary background. As an undergraduate, I studied chemistry and biochemistry in a chemistry department, but I was always interested in how the chemistry of our bodies affects health and disease. So, when I applied to graduate

school, I made the jump from a chemistry background to microbiology here at Stanford because I was interested in these disease areas, while I knew my core training in chemistry would allow me to understand biological processes at a deeper level. I felt like that was a reasonable leap; through that process, I felt particularly interested in infectious diseases like malaria, which led me into an interesting path with a non-profit organization and engaging in biotech from a global health-nonprofit perspective. Through these experiences, I began to appreciate the level of innovation that is driven in academia, and while the for-profit and non-profit drug developments and biopharmaceutical industry are valuable for creating real products out of these innovations, the innovations still lie in academia. So, it was still attractive to me to come back after a few years away getting new experiences. Coming back to Stanford—well first to Berkeley, then to Stanford—to kind of say, now that I have taken a step away from academia, I think I can bring some new perspectives and new approaches to management and organization to inform programs that will help prepare students for academia and to make an impact in the world in whatever they do next.

I think what's been exciting has been tapping into my own interdisciplinary background, with my own experiences jumping in between fields, to help inform new programs here at ChEM-H and help ask students questions about our faculty about what they hope to do with their student and how they want to help prepare them for a variety of future careers. I would say that, if I was giving advice to a young student today on what's hot in these fields or what they should work on, I would say it's less important what specific scientific problem or specific research project you're pursuing, and it's more important that you find a strong mentor who you feel has your best interests in mind, asks you hard questions, helps you think about what's important to you, and has an open mind about what directions your career might want to go. I think finding a strong mentor who can provide honest advice and be open-minded about all the possibilities that lay before you is a powerful thing.

I would say—particularly as an undergraduate—try to get as varied an experience as you can. I think it's also important to keep in mind that your faculty member is a professor, so they went probably from undergrad to grad school to postdoc to their professor-ship. They may have never had another job, particularly in some fields that have a very traditional path that lead to a professorship. So, they might not be the best person to advise you on all the career opportunities that lie out there with your training. You should be sure to cast a wide net, particularly early in your education, so you can see what the options are out there and shape your experience to allow you to try many things, not just following along one person's path because it's the only path they know.

JS: A lot of people in the general community have always held a long-standing perception that fields such as physics or mathematics have little

bearing or impact on the scope of medicinal research that materializes itself through the forms of pharmaceutical drugs or new medical devices. So, ChEM-H along with other leading institutions' interdisciplinary initiatives has been seeking to change that perception. What would you emphasize as to be the key takeaway from the program, for other universities trying to follow an example, as well as what do you believe could be certain key research initiatives such as the rise of antimicrobial resistant bacteria in fields or subdisciplines like immunology? Do you think there should be a common, overarching research goal that ties together many of these interdisciplinary research initiatives across these universities?

EP: I would say that ChEM-H has not made a specific list of health challenges that we hope to tackle. I think we have focused more on this idea of helping to create a platform on which we can address hard challenges, but not necessarily to pre-define what those challenges are. For example, we are interested in the microbiome and the relationship between the microbiome and your health. So, for instance, your gut is filled of bacteria, your bacteria are different from my bacteria, and there has been a lot of work in the field just to profile what's there. There are even some popular companies that are trying to tell you to eat different foods to change your gut microbiome. It's not clear how much of that is real yet, but I think it's a interesting field.

At ChEM-H, we are trying to say, "okay, we all have different bugs in our guts, they're all slightly different, there are clearly some connections between this profile and health, but we don't know precisely what that is yet. Could we take this down to the next level?" It's not so much the bacteria themselves, but in part all of the chemicals—all of the molecules, the nutrients, things that come out of your food, pass through your bacteria, can be converted into various types of small molecules, chemicals, etc., and are absorbed by your body. We have this flow of chemistry between all of these sorts of elements. Something we were interested in was, what are the chemical reactions happening there, and what are the chemicals causing these visible health differences that we see that correlate with these bacterial differences? If one strain of bacteria is missing, and those people have a higher risk for this disease or are less affected by this drug, what is causing that? Ultimately, at that level, we may be able to ask more practical questions about how we might be able to change the microbiome, or even bypass the microbiome altogether, and substitute a small molecule for what's missing when that bacteria is missing.

JS: What would you claim to be the driving force that unifies these medicinal researchers and brings them forward to these projects that typically may lie out of their previous field/scope of work? And, I know you've already touched on this a little bit, but as ChEM-H continues to grow in number of participating faculty and prominence of its research,

what is your personal vision for the program's future in the next 5 or 10 years?

EP: I think one of the big drivers of all this in ChEM-H is the H in ChEM-H, which stands for human health. It is so easy when you're working in these fundamental, basic science fields to dive so deep into the details of a scientific problem that you lose sight of its connection to some health problem down the road. Most faculty would like to see whatever it is they discover have an impact on society, or on health, or on something of that nature. I think helping our faculty steer their research in the direction of a human health problem is not so hard to do, and a lot of it is just helping faculty be aware of where there are big questions that they could "point" towards.

I think people joke about this sometimes, maybe in engineering, that you build a hammer and then you're just looking for a nail to hit with that hammer, as opposed to saying, "Is it a nail I should be hitting, or is it something else?" What we want to do is to tell you what's out there—"Is it a nail, a screw, or something else?" —so you can build the right tool to address that problem. A lot of our work to connect our clinicians with our basic scientists starts driving towards that.

I would say one of the programs that is only in our pilot stage now but is super exciting and representative of this is a program to test molecular hypotheses in human subjects. The idea is that there are so many molecular questions in science that you could ask directly in human clinical samples; you don't need to necessarily to work through a mouse model for everything anymore. If you ask a thoughtful question and have some assistance in understanding what patient population you would need those samples from, you might be able to get more quickly to this hypothesis you have that could connect your basic science topic of interest to a future drug. ChEM-H has been piloting a program where we incentivize a basic scientist and a clinical scientist to propose a pilot-scale clinical study. This is not a study where you give someone a new drug, but more one that you would collect blood samples, urine or stool samples, or other things and ask a very thoughtful question comparing these two different subsets of clinical samples.

We have helped facilitate that by providing access to a clinical research coordinator or professional person who helps organize and investigate clinical research studies. We have just started to make our second round of awards in this area, and we think it is exciting and drawing some interesting new ideas out of our faculty community, building that molecular hypothesis-driven research bridge with people who have access to clinical samples where you could ask those questions directly in samples. So, if you are wrong, you don't waste the next 10 years studying an interesting phenomenon in mice that has no relevance to human disease—and if you are right, it might help guide your research in a more direct way towards something that might impact human health. I

would say that's one of our most exciting areas and is representing all of these fundamental fields to the clinic, and we think that, ultimately, that might allow us to develop and deploy new therapeutics and other health interventions more quickly.

JS: Is it more through incentivizing programs such as these that you see the future of ChEM-H in the next 5 or 10 years to grow, or how else would you envision success?

EP: I would say supporting innovative, interdisciplinary research is definitely core to our mission. We have a long investment in training programs—our Ph.D, program is helping train students from another discipline; we have an undergraduate program, a postdoc society—so investing in trainees and helping to cultivate the future in interdisciplinary leaders is also very core to our mission. Also, we have these platforms for collaboration, these knowledge centers that are fundamental, and we view the knowledge centers as something that is dynamic. Today, the demand is medicinal chemistry, structural biology support, and innovation around metabolite analysis, but who knows what the next one will be. We are always keeping an ear out to our community as to what is the next emerging field where we could make an impact by launching another sort of knowledge center area.

We are most excited for our research complex to open. All of this has been happening in a very distributed way across the campus—we have temporary space here and there—and we are excited to come together in a research complex next year and create an exciting environment to not just draw in the immediate ChEM-H community but also to have a hub to attract students and faculty from across the campus to get involved in what We are doing.

JS: I'll be looking forward to seeing ChEM-H's facility next year. Thank you so much for all your time, Dr. Ponder, and for sharing your perspectives with us.

EP: Thank you, thank you very much.