© 2019. Published by The Company of Biologists Ltd | Journal of Cell Science (2019) 132, jcs237891. doi:10.1242/jcs.237891

CELL SCIENTISTS TO WATCH

# Cell scientists to watch – Kassandra Ori-McKenney and Richard McKenney

Kassandra Ori-McKenney received her Bachelor's degree in Neuroscience and Behavior from Vassar College, Poughkeepsie, New York, before joining the laboratory of Richard Vallee at Columbia University, New York, for her PhD. She moved to the University of California, San Francisco, for her postdoctoral training with Yuh-Nung Jan on the role of the microtubule cytoskeleton in neuronal development in *Drosophila* with the aid of a Jane Coffin Childs fellowship. In 2016, Kassandra became an Assistant Professor at the Department of Molecular and Cellular Biology at the University of California, Davis (UC Davis). Richard McKenney completed his PhD on regulatory proteins that influence the activity of the motor protein dynein in the laboratory of Richard Vallee after a Bachelor's degree at Xavier University, Cincinnati, Ohio. For his postdoctoral work, Richard moved to the laboratory of Ron Vale at the University of California, San Francisco, to continue his work on the regulation of dynein motor activity. Richard joined the Department of Molecular and Cellular Biology at UC Davis in 2016 as an Assistant Professor. Kassandra and Richard share their laboratory space, as well as equipment, ideas and meetings. Their research groups are interested in the microtubule cytoskeleton, microtubule-associated proteins (MAPs), activities of the motor proteins kinesin and dynein, and their roles and functions in neuronal transport and human diseases. Kassandra is funded by grants from the Pew Foundation, Simons Foundation, the March of Dimes and the National Institutes of Health (NIH). Richard is funded by grants from the March of Dimes and the National Institute of General Medical Sciences (NIGMS).

Richard McKenney and Kassandra Ori-McKenney

**What inspired you to become a scientist?**

Kassandra (Kassie) Ori-McKenney (KO): I never aimed to pursue anything in the life sciences because my entire family comprises musicians, artists, writers and teachers; with excellent grades in these subjects, I was expected to eventually pursue a master's of fine arts, for example. Then, one day, my best friend had a brain aneurysm. I found myself sorting through the personal grief, but also being somewhat fascinated by why something like that happened. What were the causes? I started thinking about the human brain in general – something I hadn't really given thought to before – and began to take a variety of science classes in college. That's where my interest and curiosity piqued because, suddenly, I wasn't really good at anything anymore. Biology classes were really challenging for me and I loved being challenged. I also loved the fact that there were a number of unknowns in science that I could continue to study and pursue.

Richard (Rick) McKenney (RM): As a kid, I loved dinosaurs, going to the museum and seeing all those skeletons and models, and I also loved seeing animals at the zoo. I've just always been more fascinated with the natural world than other subjects and never really took to the arts, the theatre and so on, although I do have appreciation for quality cinema. However, I like to tell people – which is the truth – that I stumbled into my life in academia: I was not a stellar student and I wouldn't say that I was trying very hard in my younger days; yet, somehow I found my way to research. If I'm being really honest, a large part of that was due to following an ex-girlfriend (laughs). She wanted to move to New York City after we graduated college and I wanted to stay with her, so I had to find a job. Fortunately for me, Richard Vallee had just moved to Columbia University and he was hiring a technician. I applied and got the job, and that's really how I got into the business of full-time research. As an undergraduate I joined a lab at a neighboring university where I was completely horrible at bench work and I don't think I accomplished anything in a couple of years – so it's still kind of surprising to me that I ended up in research (laughs). Also, the girlfriend that I mentioned broke up with me, thankfully. It coincided almost to the month with Kassie joining the Vallee lab at Columbia. It was serendipitous and, in the end, the best thing that ever happened to me (laughs).

**What questions are your labs trying to answer just now?**

KO: Both our research programs are centered on our singular love: the microtubule cytoskeleton. I have become incredibly and increasingly interested in microtubule-associated proteins (MAPs). In general, these are the proteins originally found to co-purify with polymerized mammalian brain tubulin and are traditionally classified as microtubule bundlers or as stabilizers. For example, the view regarding the MAP tau is that, when hyper-phosphorylated, it falls off of the microtubule and forms aggregates, which causes microtubules to just completely de-polymerize. A lot of people think that this is what MAPs do because this dogma is in textbooks. I became interested in trying to find out if this is true or not and to dissect what their real functions are. We also focus on tau, in particular, and its role in traumatic brain injury using *Drosophila melanogaster* as a model system. Currently, there is only one person in the lab working on it, but it's starting to pick up and we're really excited about finding out the effects and results of giving flies traumatic brain injury – from the molecular to the behavioral levels.

RM: Working in Richard Vallee's lab on cytoplasmic dynein was my very first introduction to what a motor protein actually is, and

Kassandra Ori-McKenney's and Richard McKenney's contact details: Department of Molecular and Cellular Biology, 3224/5 Life Sciences, 145 Briggs Hall, University of California, Davis, CA 95616, USA.
E-mail: kmorimckenney@ucdavis.edu; rjmckenney@ucdavis.edu

Journal of Cell Science (2019) 132, jcs237891. doi:10.1242/jcs.237891

**The only passion greater than science: family!** Richard and Kassandra with their two children Madeline (6) and Colin (4). The family loves spending time at the pool and on camping trips in many of the great spots around California.

I instantly fell in love with them. Against everyone's advice, I maintained my interest in dynein as a postdoc in Ron Vale's lab. But it turned out to be really fruitful; so, when I started the lab, of course, our main interest was still the mechanism and regulation of the dynein motor. We are also looking to differentiate ourselves, and have expanded into examining the regulation of some members of the large kinesin family, and how these regulatory mechanisms may be impacted upon in human diseases. It's not a new field but I think there are still a lot of open questions about how the cell controls the activity of particular classes of kinesin motors. More broadly, we are interested in understanding and reconstituting the dual activities of kinesins and dyneins. We think they are assembled onto single cargos using an endogenous cargo recruitment machinery, and we'd like to find out how the cell integrates their motor activities for efficient cargo transport, which became a joint project with Kassie's team.

**Could you tell us more about your joint projects?**

RM: It's been fun to work with Kassie on some aspects of tau biology. After using single-molecule microscopy and biochemistry to re-examine tau's behavior, we have a recent paper that centers on how tau self-assembles on microtubules and how this is potentially related to the self-assembly of tau in tauopathies, like Alzheimer's disease. We observe that self-assembly of tau on microtubules can compartmentalize those microtubules and act as what we call semi-permeable barriers – some molecules can get in and other molecules can't. That is a fascinating concept because, as Kassie mentioned, if you google 'tau function' you'll find all these models of tau acting as a 'stabilizer' of microtubules – but I would go as far as to say that this is probably totally wrong. So the question is, what is tau doing? Why do we have tau and what is it doing before it turns into these famous aggregates that are observed in Alzheimer's disease, etc.?

KO: Because you can also get rid of tau, and both mice and flies are mostly fine without it. If it's so important but you can completely get rid of it – what does it do and why do we have it? Again, its actual function and the redundancy with other MAPs are still unknown, and that's very interesting. Presumably, there are other MAPs that can pick up the slack for tau in its absence. So how does its neurodegenerative phenotype arise? We're guessing it's through the neuronal spread of aberrant tau that has self-associated into filaments, and that's an area we're incredibly interested in exploring further.

RM: We just started working with the Alzheimer's Disease Center, here at UC Davis, to provide us with patient samples that we're hoping we can use in some assays to determine how the presence of actual pathological tau aggregates affects the dynamics of the tau molecules we observe in our assays. We're quite excited to try to get those experiments going.

**Talking about common projects – how is the daily life in a joint lab?**

RM: We run the lab as a singular environment. One of the many reasons we came to UC Davis was that they offered us contiguous lab space that is not divided; we share everything – equipment, benches…

KO: Our offices are just across the hallway from each other, so we're often heard just shouting across (laughs).

RM: It's really an integrated space that drives interactions between everybody and I would say that, if you were to interview anyone in the lab, they would never say labs but would just say 'the lab'. We're one big lab in that respect.

KO: We find our joint lab meetings incredibly useful because now that we are diversifying a bit in terms of techniques and fields we're getting into, it's essential to have people thinking on different levels, to provide feedback and offer unique insights into each other's projects. During my postdoc in a lab that was also jointly run by Lily and Yuh-Nung Jan, one of my favorite aspects of lab meetings was that I was surrounded by twenty people, who all worked on completely different projects. Some of the questions that they asked made me think about my data in a very different way; I would never have gotten the same questions from a biochemist or someone completely immersed in the cytoskeleton field. So that's what we're hoping to create here: to bring on people who work at the organismal level, the cellular level and at the molecular level. And I believe that's a lot easier to do when you have two labs.

RM: By now, we can also pull from a pretty deep set of resources. Kassie's got freezers full of MAPs, proteins and constructs, and I've got freezers full of motors and dynein, and so on. We have reached a critical point where we can say, oh wait, we have this reagent and that reagent, let's try that experiment. It's a really exciting time that we can do this now with the many resources we have generated here together.

**"…it's essential to have people that think on different levels to provide feedback and offer unique insights into each other's projects."**

Journal of Cell Science (2019) 132, jcs237891. doi:10.1242/jcs.237891

**Do you share mentorship as well?**

RM: From that angle, Kassie has her people and I have mine; and on a day-to-day basis I would say that there's an invisible barrier. In lab meetings and joint meetings, it's more of a 'free-for-all', where we give our own opinions and they can digest that, and then we discuss it either individually or as a group later on. I am a bit sensitive and I think that we pay attention – we wouldn't want a new person feeling like they have two demanding bosses.

KO: As Rick said, we still have our separate meetings, and I feel that's very important to establish and maintain an individual bonding mentor–mentee relationship.

**What challenges did you face when starting your own lab?**

KO: Based on stories I've heard, it was easier for us to come in together.

RM: I have to admit that Kassie is the much more organized one of the pair here (laughs), so I definitely relied heavily on her skills, and it would have been much more challenging for me alone to have done all of that.

KO: Being able to put our heads together to figure out what we needed to be functional, right from the beginning, was very helpful because the minute we started our lab, the clock was ticking. We felt a lot of pressure almost instantly. Starting a lab is not easy and you have a grace period before you have to publish, but not a long one. It's like any other industry, if you are not producing results and maintaining your reputation then you become irrelevant. And, so, getting a project off the ground became paramount.

RM: So, it was key to determine what that project would be. Then, the most-challenging part was finding people who are a good fit for the lab, and who want to work with you and who you want to work with – you're not trained to evaluate people in this way during your postdoc.

> **"…learn how to pivot away from projects when they are not working; give yourself many opportunities to find success."**

**How do you make sure students develop their potential and prepare for the next steps in their careers?**

KO: We have active conversations in our lab about the opportunities during a PhD, and what students want to do and what they want to pursue – an academic career or a career in industry? Do they want to do something else? I think one of the most important aspects of that is just to encourage students to figure out what they are passionate about, what really drives them. No matter what field or profession you go into, doing an excellent PhD is important and sets you apart. From our side, it is crucial to manage expectations and to pick the right projects.

RM: One of our favorite words is 'pivot'.

KO: You get negative, reproducible results and sometimes that's interesting and you continue the project. But sometimes it just ends a project altogether and you need to be able to pivot that member of your lab away from a project to which they have already devoted a substantial number of months. You have to keep their spirits up and still inspire them, because this is how science works. It's predominantly rejection and negative results, but we will get there!

RM: I find it unfortunate that there are graduate students who are very successful and, yet, they're scared to pursue academic science as a profession. It's a very valid point that the academic job market is saturated but the reporting on it has done a very effective job of scaring away many great young scientists I have met. I totally agree with the school of thought that we should prepare graduate students for a broad range of outcomes from their PhD but we also are, maybe, doing a little too much fearmongering, which is preventing talented people from even considering staying in science. That's something that I'm still trying to work on here.

**What is the most important advice you would give to someone about to start their own lab?**

RM: Have some projects in your mind that you want to start right away and that are feasible, and learn how to pivot away from projects when they are not working; give yourself many opportunities to find success. Find a minimal publishable unit and put it out – make it very clear to the outside world that you have a functional lab and that you are producing something. As I said, we were able to hit the ground running in a lot of ways and, I think for me, it helped a lot. Also, it seems that a lot of new faculty are really preoccupied with bean-counting their money. Don't worry about the money upfront. Assume that you got a start-up package and worry more about productivity, which will then allow you to bring in more money.

KO: I felt pretty miserable my whole first year because every single project I started – even the ones that seemed like small seed projects – didn't work. Now, usually most of my hypotheses were wrong and that's fine, and I never had an issue with it because it was only me, and I'm an optimist. But now 90% of my hypotheses are wrong and I need to explain to other people that this is actually my track record (laughs). But, latching on to a project that's actually producing repeatable, robust results is essential, and to continue to pivot until you find a project that has legs, I think that's really important.

**Having established your lab now, are the challenges that you're facing different today?**

KO: I don't know if we're ever going to feel like we've hit our stride. We're really hard on ourselves and also very hard on each other, and I think that we continually try to push each other to be the best we can be, in the bluntest ways possible.

RM: I do feel more comfortable in the role now than I did in the first year, let's put it that way. One current challenge is that we're coming up on some lab turnover and, so, that is something new. This goes along with finding new people to take on these projects, which relates to my earlier comment that, in general, finding the right people is probably the hardest part of the job.

KO: You create really wonderful relationships with your lab members and you want all of them to be like that. Finding more excellent people, recruiting them, making them excited about science, I think that's going to be a constant challenge.

**How do you get the most out of the meetings you attend, particularly in the early stages of your career?**

KO: We were very lucky as graduate students because our mentor Richard Vallee allowed us to go to many conferences – specialized conferences, such as the dynein meeting in Japan, as well as the annual ASCB meeting. It can be intimidating and very daunting at the beginning of your career but it is really helpful. To avoid 'conference regret' – i.e. I should have talked to this person, etc. – I started formulating plans for every conference I subsequently went to: I would write down names of all the people I wanted to have a brief conversation with to see who I connected with, who I could form a collaboration with, etc. This helped to allay some of my fears and anxiety about going to conferences. You don't connect with everybody but there are certain people with whom you share

Journal of Cell Science (2019) 132, jcs237891. doi:10.1242/jcs.237891

scientific interests and get along with really well, and that's the gold standard right there for conference interactions.

RM: When we were graduate students, Kassie and I still remember a small, select group of senior group leaders, who actually paid attention to us and talked to us (shout out to Steven King, University of Central Florida, Orlando!). It's amazing how that made you feel when you were a graduate student. I try to remember that every time I go to a conference and try to give that same feeling to any young students I may meet.

**Could you tell us an interesting fact about yourself that people wouldn't know by looking at your CV?**

RM: I guess my secret would be that I always wanted to be astrophysicist but I was never smart enough to do that. I always found questions about the universe almost more fascinating than questions about biology, and I've read books on black holes and time warps, and Kip Thorne's books. I really enjoy this subject but I'm terrible at mathematics and I got Cs in physics, so I made the decision that this wasn't for me but secretly always found that astrophysics would be amazing (laughs).

KO: I do flower arranging, now that I have a beautiful garden. We love to camp and hike with our kids. In general, we love travelling. It's harder now with children but my major passion was going to far-off places on a tiny shoestring budget. I love planning unstructured travel.

RM: We always joked that she would become a travel planner if she were to fail in graduate school.

KO: I still have lots of travel-related lists: the ten best cemeteries in the world, the ten best water falls, the ten best rivers… I still have lists of every city I wanted to visit and their major highlights, just in case I go.

RM: You're also a bit of a cartographer, you love maps and planning.

KO: If I had lived in the 1400s, I definitely would have found a way to be a cartographer. Studying MAPs in the present day is the next best thing.

Kassandra Ori-McKenney and Richard McKenney were interviewed by Manuel Breuer, Features & Reviews Editor at Journal of Cell Science. This piece has been edited and condensed with approval from the interviewees.