

INTERVIEW WITH PROFESSOR CAROLINE KANE:

From RNA Polymerase Transcription Factors to BSJ Advisor

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The history of Berkeley Scientific Journal at Cal starts at 1996, with several undergraduates involved in research who wanted to create a new avenue to publish their research. The first faculty sponsor was Professor Caroline Kane, whose passionate support of undergraduate education through the Biology Fellows Program earned her the College of Letters and Science Award for Distinguished Research Mentoring of Undergraduates in 2002. She earned her PhD from UC Berkeley and has studied the mechanisms of genetic expression and regulation. Although she is retired, she is an active emerita who facilitated BSJ's transition to a DeCal course in the MCB department by signing on as the faculty sponsor.

BSJ: Could you tell us a little about your past research?

Kane: My research focused on what happens in the nucleus of a cell. I got into this type of research partly because I've been interested in the molecular level of cells for a very long time. As an undergraduate, I was interested in looking at things from a mechanistic and biochemical level. This, along with my interest in genetics, led me into the nucleus to study the genetic readout through the process of transcription. I didn't focus on finding a gene; rather I focused on the actual process of synthesizing RNA from DNA.

Specifically, I looked at transcript elongation. I focused on RNA polymerase II, which, in eukaryotes, is responsible for transcribing protein-encoding genes. My lab focused on the purified RNA polymerase from mammalian cells, as well as yeast. We looked at purified protein factors that regulated the process, and we also used yeast as a genetic organism to be able to make mutations in various

components in the transcriptional machinery and see what the phenotype was. Then, we saw whether we could correct some of the phenotypes by over-expressing some of the regulatory genes.

I finished my career by working biochemically with proteins from Hepatitis C virus. The virus has an RNA-dependent RNA polymerase and an RNA genome, but we asked similar questions like: "what's the mechanism and how is it regulated?" This enzyme also turned out to be regulated at the level of elongation.

BSJ: A couple of your past papers study transcription factors; aren't those typically involved in the initiation step?

Kane: Partly – transcription factors are involved with initiation, but they also influence the elongation phase, termination, transport out of the nucleus, and a whole bunch of other things. A couple of these transcription factors are TFIIF, which is also involved

with initiation, and TFIIT, which associates with other factors in vivo during the initiation process, but its influence is during elongation. We also discovered and worked on a phosphatase, which is an elongation factor that acts on RNA polymerase itself by dephosphorylating a region of RNA polymerase that regulates its elongation properties.

BSJ: Are there any direct applications of this research or is it more pure science?

Kane: Both – some of the factors that we've studied have been used by others looking at the regulation of HIV. Some of the spinoff has been identifying proteins that are influential in regulating the transcription of retroviruses when they insert themselves into the host's genome. With the Hepatitis C virus, we identified the activity of one of its proteins that acts on its RNA polymerase. It's also a protein whose sequence has only been found in other Hepatitis C viruses so far. It's completely new as a target for possible drug development. We wouldn't do that, but by publishing it, we would hope that somebody would pick it up and apply it. Although with HIV, that's the only work that really was easy for people in my seminars to see the direct application.

BSJ: Is this specific to particular retroviruses or retroviruses as a whole?

Kane: It's not clear. At the level of DNA, HIV is regulated at the elongation phase, but because its structure is so similar to that of other retroviruses, the expectation would be that other retroviruses, upon insertion into the DNA, would also be regulated at the level of elongation. I'll back up to say that the year before I retired, there were several papers that came out from other research groups doing global transcription analysis suggesting that 90% of the genes in a eukaryotic cell primarily regulates during DNA elongation because of where they found the RNA polymerases in vivo. This was opposed to what previously had been thought by most eukaryotic transcribers, except our lab, I guess; this was that everything important happened during the initiation reaction. Lots of important stuff happens there, but a lot of important stuff also happens in rearranging the chromatin to enable elongation as well as in starting

and stopping the polymerase. All kinds of decisions are made by the cell during elongation because it can regulate there, and the cell will regulate every place that it possibly can. This changes what the rate-limiting step is, depending upon what is packed in the cell and what signals it is receiving.

BSJ: So what are you doing now as a professor emeritus?

Kane: Now that I am retired, I am still advising undergraduate students who are a part of the Biology Scholars Program. I have office hours once a week, and I make appointments other times for both undergraduates as well as graduate students. I work with and advise some

postdoctoral fellows, and I have talked to some of the assistant professors about issues with being a professor. I'm not teaching in the classroom except as an occasional guest lecturer, but I've been working on other projects. I've been working with the American Society for Cell Biology (ASCB) on an image and video library, which will be a publically available database with the ultimate goal of being as useful as the protein and nucleic acid database. It will be useful to both educators and the general public. We got funding for two and half years, and now we are transitioning it away from ASCB to a group down at UC San Diego called the National Center for Microscopy and Imaging Research. They will use their supercomputers and also set up an international network – a federated network is what it is called – just to keep plugging images into this library to make it more available. The image library has some unique difficulties compared to nucleic acid and protein sequences because of the memory that is required. These are big files. When you get to movies, the files are even bigger, so it is a different scale of infrastructure. It has been great fun because I am not a card-carrying cell biologist. I even took a microscopy course at a marine biology lab to make myself even more conversant with the newest technologies.

I also do some volunteering work. I volunteer with an education and work-force development nonprofit called Biotech Partners that works with high school students and first year community college students from groups that are underrepresented in

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the sciences as well as low-income first-generation students. These aren't the high rollers; rather these are students that teachers see as having a spark of potential in them. When they join our program for education, we get them a job, and teach them soft skills about how to navigate the entire world of a system, and that is a great deal of fun. I am also an official California Wildlife Rehabilitator, so I volunteer at a wildlife hospital.

BSJ: That is incredible. You are definitely feeling retired?

Kane: (laughs) Yes! Well, I think when my grandparents retired, there wasn't that much to do and you had to worry about your health a little more. I'm lucky enough to be healthy and I have lots of interests, and I do spend more time with my husband even though it sounds like I'm just as busy as I was when I was on the faculty. (laughs) I get to pick and choose what I say yes to.

BSJ: We wanted to zoom in on where you said you mentor undergraduates, because you are BSJ's faculty advisor for our new DeCal. When we were writing the syllabus and preparing the DeCal, it came to our attention that you were there right when we started. We wanted to know whether you could give us your version of the history of BSJ – from how

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it started to how you've seen it grow.

Kane: I give complete credit to the founding students Shervin Kordary Pishavar (Editor-in-Chief), Philip Chan, Tony Ko, Amin Matin, and Khae Seaphanh (senior editors). I can just see their faces now. The founding students were members of the Biology Fellows Program, which is an undergraduate research program funded by the Howard Hughes Medical Institute. They came up with the idea of being able

to publish their work with them as the publishers so that they could provide an opportunity for undergraduates to publish their work outside of the journals that I would publish my work in. They also wanted an opportunity for undergraduates to learn about the process – what goes into writing a paper, reviewing a paper, and actually getting it published. They learned the amount of effort it takes: funding, timing, good writing, getting faculty at the time to review the papers, and getting them back in a timely fashion, revisions of the papers, and then reaching your publication deadline.

I can say that Leah Carroll has been an angel in all of this too. I was the director of the Biology Fellows Program, which was why the students came to me to begin with and I already knew Terry Strathman and Leah Carroll in the Office of Undergraduate Research. It was just a good match. They were able to provide the initial founders with an office and the founders really did their homework. They looked into other scientific journals published at other campus, of which there were very few, but the Columbia School of Journalism was paying attention to them. This is back in 1995 and 1996. They looked at the 2 or 3 other journals on the Berkeley campus that were published and what went into them and they decided that they wanted to be more rigorous in terms of the review of the papers and what was accepted. It wasn't just,

"submit a paper and we'll publish it;" it really was paying attention to the science as well as the writing that went into it. The goal was to make it a real showcase by including interviews with interesting and controversial people or issues that would beef up the journal. BSJ was to be something in the mold of Nature Publishing Group – which publishes editorials, interviews, news, as well as scientific information – and to be of a quality so that people would put it on their bookshelves. Until I retired, I

had all of them from 1996 onwards on my bookshelf and I'm sure Leah has probably got them in her office too. I could pull them down and show them to visiting faculty members who are giving seminars and things.

I watched the trials and tribulations of the founders, as they tried to be sure it would continue by recruiting others into the fold. Because most of them arose from the biological sciences, the most difficult part initially was incorporating more chemists, physicists, mathematicians, and engineers. They got some of those types of papers and a smattering of those types of students, as well as those in non-science disciplines who participated in the editorial activities. Occasionally they would have people who didn't step up to the plate, so to meet deadlines, there was a lot of scrambling and there were a lot of all-nighters. I tried to say, "just delay the publication two weeks or so," but these guys said: "no – it's gotta go out! we've got a deadline, it's got to go out." The students still did well in their classes too. I'm not sure how because I know they were all sleep-deprived and undernourished. (laughs)

It was fun for me to follow it through several generations of editors and editorial boards and I could see when they brought in junior people to be on the editorial board. You could almost pick who was going to be rising to the occasion to be one of the more senior editors two, three or four years down the road. It's also been fun also to watch students that graduate go on to do a whole variety of things. Your founder was an entrepreneur and I know he founded at least two companies and sold them. I'm sure you can Google him. One of the editors got his PhD in pharmacological chemistry and is running a research lab now. Another editor got an MD/PhD from Harvard and is now practicing medicine. You all are illustrious folks here and in whatever you go on to do.

BSJ: How long were you advising BSJ until Leah and Terry took over?

Kane: The Fall of 2001.

BSJ: The journal is award-winning.

Kane: Yes, the Columbia School of Journalism Award.

BSJ: Can you talk about the kind of awards we've won and when we started getting recognized as a journal?

Kane: While the original editor was still here on campus, he submitted the journal as a nominee to the Columbia School of Journalism. Not everyone who is nominated gets a prize; it's very competitive. We were all blown away because the journal was still very young – only a couple of years old – when it was given the awards for an undergraduate research journal in the United States. Berkeley has a wonderful school of journalism, but the Columbia School of Journalism is kind of a pinnacle so their imprimatur is an important one. That's the main award I'm familiar with. There may be other awards you have gotten since then. And that wouldn't surprise me a bit because the quality of the journal has remained so high.

BSJ: Was BSJ one of the first journals that published undergraduate research on campus?

Kane: No, it was not the first. In fact, one of the other journals that is listed on the center for undergraduate research site preceded it, but it was a journal that wasn't purely scientific. It covered the waterfront. The McNair's Scholars journal also had just started publishing, but it is reviewed such that faculty members approve what's been written and then the staffers review it for type of writing. I used to have all those on my shelf too, and it was a terrific journal because all the students are published, but it's just not reviewed in the same way. It doesn't have interviews and news features that you put in about the sciences and issues around that, so it's smaller and it covers the waterfront in terms of disciplines.

BSJ: From the sound of it, a lot of the editors had their own research that they were trying to publish. So initially that research section was quite heavy. When did the features and interview sections start coming into play?

Kane: They were in the play from the very beginning because the editors decided that a journal that had just the research papers would be of less interest to the student community and maybe even to the faculty than a journal that interviewed a controversial member of the faculty or administration or a journal that talked about a scientific issue that might be controversial. Initially it included poetry and some artwork by multitalented students who were also doing research. They included that to show that: "yes, you can be a geek, yes, you can be a nerd – I am very happy to be a nerd, but I do a lot of other stuff besides my science."