People & Ideas

Carol Dieckmann: An eye on organellar biology

Carol Dieckmann studies the *Chlamydomonas* eyespot and mitochondrial gene expression.

Carol Dieckmann says she always wanted to be a scientist. As a kid, her friends called her "Nature Lady," and she loved exploring tide pools with neighborhood friends in San Diego. But the world of science really opened up to her once she discovered the microscopic world and molecular biology. From then on, nothing could hold her back.

Dieckmann published her first paper as an undergraduate at UC Irvine in California. This taste of success in the lab was tantalizing and propelled her into graduate school at UC San Diego and a postdoc at Columbia University. In New York, she encountered the two problems that would preoccupy her throughout the rest of her career: regulation of mitochondrial gene expression (1–3) and the assembly of the eyespot (4–6)—the light-sensing organelle of the alga *Chlamydomonas*. We called her at her lab at the University of Arizona to discuss what drew her out of California and into the study of these two subjects.

REGULATORY SWITCHES

One of the two subjects your lab works on is mitochondrial biology…

I first started working on this as a postdoc in Alexander Tzagoloff's lab. When I joined Alex's lab, I wanted to study how nuclear gene products regulate mitochondrial genes. We knew it was pretty much a one-way street and that there would be proteins encoded in the nucleus that would be translated in the cytoplasm and then imported into mitochondria to regulate mitochondrial gene expression.

> "Most of the regulation of gene expression [in mitochondria] goes on post-transcriptionally."

Alex had already started making this huge collection of nuclear mutants that affected respiration, and we decided that I would survey this collection for mutants that affected cytochrome *b*, which is the only mitochondrially encoded subunit of the CoQ–cytochrome *c* reductase complex. My naïve thought was that we would find transcriptional regulators.

At the time, most of the regulation we knew about in the nuclear genome was at the transcriptional level. But over the last 30 years the general picture that has emerged is that there is very little transcriptional regulation in mitochondria. Most of the regulation of gene expression occurs post-transcriptionally, at the level of RNA stability, processing, and translation, and so what I ended up working on were proteins that regulate mitochondrial messenger RNAs.

What part of this problem are you working on now?

The interesting thing is that there are only seven messenger RNAs that are made from the yeast mitochondrial genome. Each one of them is affected by a different set of proteins that regulates its stability and translation.

These mRNAs have to be processed out of longer transcripts, some of which also encode tRNAs, two ribosomal RNAs, and a small RNA that is part of an enzyme called RNase P. The activity of this enzyme is to cleave the 5′ presequences off of tRNA precursors. Several years ago we made the observation that mutations in the genes that code for enzymes in the mitochondrial fatty acid biosynthetic pathway (and an extension of that pathway that makes lipoic acid) are defective in processing tRNAs. Our hypothesis is that the protein subunit of mitochondrial RNase P is modified by a fatty acid that's made from this pathway inside the mitochondria. We have identified which residue we think is modified, and we're looking into why this fatty acid modification is necessary.

From a regulatory point of view, it's interesting that fatty acid synthesis and tRNA processing should be linked. In all organisms, lipoic acid is attached to pyruvate dehydrogenase, the enzyme that converts pyruvate to acetyl CoA. Acetyl CoA in turn is a precursor for fatty acids and lipoic acid, so it's a positive feedback cycle. Positive feedback tends to make changes in metabolism more switch-like instead of oscillatory, so the idea is that, in yeast, if you're fermenting and then you want to switch to respiration, this may allow you to quickly ramp up respiration. At the same time, you'd also be making a fatty acid that affects tRNA processing, which would affect gene expression and possibly assist in the switch.

PHOTO COURTESY OF DR. TELSA MITTELMEIER

Carol Dieckmann

EYEING NEW PROSPECTS

How did you start working on the* Chlamydomonas *eyespot?

When I first went to New York as a postdoc, I regularly went to the New York area yeast group meeting. One of the people that I met there was Susan Dutcher, who was studying flagellar function in *Chlamydomonas*. She came to the yeast group meeting because she'd done her graduate work in yeast and wanted to stay up to date. She heard me give a talk one night and came up afterwards and told me she thought I'd be really interested in this organelle in *Chlamydomonas* called the eyespot. I said, "Oh? Why is that?"

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and she told me that components in the cell membrane and the chloroplast collaborate to make the eye. I thought that was very cool, but at the time it wasn't possible to transform *Chlamydomonas*. I promised I'd come back and work on it if they ever figured out how to do that. As it turned out, that didn't happen until after I got my faculty position here at Arizona. But then I was able to take a sabbatical and visit Susan's lab to get started on it.

We've come a long way in our analysis of the eyespot. One of the really interesting problems is that in general this single-celled organism has bilateral symmetry, except that it only has one eye and it's placed asymmetrically relative to all the other symmetric elements in the cell. I became fascinated with the whole problem of how the eyespot gets placed. The other problem we've been pursuing concerns how the eyespot is assembled.

Our best hypothesis right now is that the eyespot's location is specified by a microtubule-based system. Just below the flagellar basal bodies are four microtubule rootlets, and the eyespot is always associated with one specific rootlet. We think that the photoreceptor rhodopsin, which is found in the cell membrane in the eyespot, traffics from the Golgi to the eyespot along this rootlet and is anchored there by a protein in the chloroplast membrane called EYE2. After that, pigment granules—they're what make the eyespot orange—get recruited beneath the chloroplast membrane.

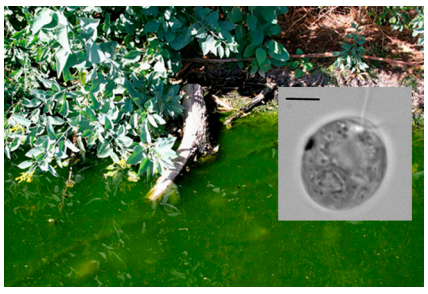

IMAGE COURTESY OF DR. TELSA MITTELMEIER

Green algae growing in a Tucson pond. *Chlamydomonas* (inset) is found in freshwater environments worldwide.

A DIFFERENT VISTA

What did you work on before your postdoc?

I did my graduate work in Stuart Brody's lab at the University of California, San Diego. I worked on something completely different: circadian rhythmicity in a fungus called *Neurospora*. I was particularly interested in a set of mutants that were defective in the mitochondrial enzyme ATP synthase. They are defective in keeping time; their "clock" runs faster than that in wild-type strains.

So you switched organisms but not organelles for your postdoctoral work?

I was really interested in trying to use molecular biology to study protein import into mitochondria, but back then nobody was transforming anything but bacteria, and they'd only been doing that for a few years. I knew I couldn't do it in *Neurospora* yet because the tools hadn't been developed.

Jerry Fink was in San Diego for a day or two to give a seminar. I requested to meet with him and asked him for suggestions about where I could go to learn how to do transformations. He said, "Well, in a couple years, everybody's going to be transforming yeast. You should really go work with somebody who knows about yeast mitochondria." I hadn't thought about that, so I asked him for suggestions on good labs and he suggested Alex Tzagoloff in New York. I just laughed because, when all my friends had asked me where I wanted to go for my postdoc, I'd said, "I'll go anywhere except New York City."

> "We've come a long way in our analysis of the eyespot."

Why didn't you want to go to New York?

Well, I had grown up primarily in San Diego. I was a Southern California beach girl—I lived right by the ocean, and we spent a lot of time at the beach and in the water, sailing and body surfing. I just thought that I wouldn't survive in New York without all that. But I did, and actually I had a wonderful time in New York. Also, after about a year I discovered that the cultural advantages far outweighed the negatives. I really enjoy dance, and it's a wonderful place to be for that. And food—the restaurants there are great, better than in Tucson!

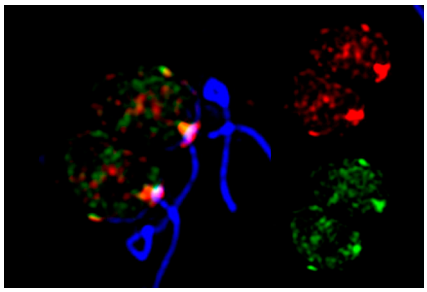

IMAGE COURTESY OF DR. TELSA MITTELMEIER

***Chlamydomonas* labeled with antibodies to rhodopsin (red), EYE2 (green), and acetylated microtubules (blue).**

There aren't any beaches in Arizona, either…

Fortunately I love the desert, too. I grew up not too far from the Southern California desert, out in Borrego, and this area is lush in comparison because we get a lot of summer rain. We have a lot of huge cacti, and the plant life and animal life are pretty amazing out in the wild areas. Anybody who is interested in nature should really visit Tucson. And I still get to swim—I just have to do it in a pool.

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