

LPI on Health - 2009 Diet and Optimum Health Conference

Dr. Alex Michels, Post-doctoral research associate, LPI

LPI Young Investigator Award Recipient 2009

<http://lpi.oregonstate.edu>

Introduction/Conclusion: Naomi Hirsch, Environmental Health Sciences Center, OSU

Host: Sandra Uesugi, Environmental Health Sciences Center, OSU

Guest: Dr. Alex Michels, Linus Pauling Institute, OSU

[THEME MUSIC]

HIRSCH: Welcome to LPI on Health, a podcast series to inform you about the recent micronutrient research and events coming out of the Linus Pauling Institute at Oregon State University. For more information, visit our website at <http://lpi.oregonstate.edu>.

[THEME MUSIC]

UESUGI: This is Sandra, and I'm here talking with Alex Michels who is one of the recipients of the Young Investigator Awards at the recent 2009 Linus Pauling Institute Diet and Optimum Health Conference. Alex, can you tell us about the research that you presented?

MICHELS: Yeah, so the research I presented at the conference had to deal with the regulation of one of the vitamin C transporters in the body. There are two vitamin C transporters that exist in all tissue. They're called SVCT-1 and SVCT-2, and that just stands for Sodium-dependent Vitamin C Transporter.

And specifically, I was looking at SVCT-1. The current research is leading toward SVCT-1 involved in maintaining plasma vitamin C homeostasis, so either uptake from diet or absorption in the liver or excretion from the kidneys, so it prevents excretion from the kidneys. And we were looking at the regulation of that transport protein, and I specifically was looking at transcription factors that regulate the gene and came upon a novel transcription factor, HNF1, that was the regulator of this gene.

UESUGI: How are these transcription factors and transporters of vitamin C important to our everyday tissue function?

MICHELS: SVCT-1 has been...has only been discovered for about the last....or been known for the last 10 years, so there's not much known about it. But it really is thought to regulate how you obtain vitamin C and keep it in the body.

SVCT-2, which is the other vitamin C transporter, is more involved in how vitamin C is taken up into your tissues.

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So it's a two-part system. You have to regulate the amount of vitamin C in your blood, that's one system. And then you have to regulate how the vitamin C in your blood gets into every cell, two different transporters for two different systems.

So SVCT1 is pretty critical in maintaining your plasma level. Without it, you would be constantly excreting vitamin C and never maintaining it at a high level. The rest of your tissues would still be taking it up because they have SVCT2, but you'd probably be close to scurvy if you didn't have it because you'd be constantly urinating it out. If you don't have a certain level in your blood, then your tissues will never reach the point where they're full of vitamin C.

Now if you don't have SVCT2, that's more serious because then your tissues can't take up vitamin C, and it has to rely on certain other processes to get vitamin C into the cell. Mice who have had the SVCT2-knockout die shortly after birth because the brain development is strange so it suggests that vitamin C is very important for brain development.

UESUGI: Did you get involved in this vitamin C research in your graduate study here at Oregon State?

MICHELS: Actually, it's somewhat of an interesting story. When I came in Tory Hagen's lab in 2000... He works on aging, so he showed me all this stuff, you know, like "This changes with age, and this changes with age, this changes with age. And this is kind of something I'd like you to work on." And he showed me this graph that had animals, young animals, considered young animals. I think they were between 3 and 6 months of age and old animals that were between 24 and 36 months of age and showed that the vitamin C level dropped in heart, brain, liver. Why?

It's funny for rats because rats make vitamin C, unlike people. But he showed that the synthesis, the production of vitamin C, by those rats didn't change with age. So why did they have lower vitamin C in all their tissues? So he kind of handed that over to me and said, "Find out why."

So, finally, I got lead down the vitamin C transporter pathway. My first paper, which came in 2003, basically found out that SVCT-1, the transporter that I presented at the conference, declines with age in those rats. That kind of lead me down the hole "Why does it decline with age?" continuing the story.

UESUGI: So even if we take in more vitamin C it may not be getting into our tissues as well?

MICHELS: Actually, there was this big meta-analysis, which is basically taking all these studies what were done on vitamin C supplementation, and they looked at young people versus old people, and they did a large range of vitamin C doses. And

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you could see that under the same doses, young people were maintaining higher levels of vitamin C than the old people.

Now, the good thing about that is that regardless of age group, if you increase the amount of vitamin C, your plasma levels of Vitamin C, your blood levels, will go up even in the older group. If you took more, it would go up, it would just go up slower. The good news is that even for older people, you can take more and overcome that aging effect. And I think that is why the Linus Pauling Institute recommends more vitamin C for older people.

UESUGI: What did you study as an undergrad that lead you into biochemistry?

MICHELS: Well, I was a biochemistry major at the University of Illinois. My last year I did a thesis project on a neurotransmitter protein that bound to lipid vesicles, and we were just trying to figure out the interaction between these lipids, basically lipid bubbles, and this protein. And we had no idea what was going on, so they just gave it to an undergrad and said, "Work on this a little bit." So I learned a lot of interesting stuff, but then I realized that I didn't like that anymore and decided I was going to do something completely different than that in the future.

UESUGI: But you got to experience the process of research?

MICHELS: Oh yeah. Being in the lab was definitely informative because I got to figure out how to do an experiment, just going from start to finish. You go to a lab class, and you learn how to do an experiment the way they tell you how to do but when someone gives you a procedure and says, "Figure it out!" you have to sit down and realize first that no one's watching you, and no one's going to catch you if you make a mistake. It's a little bit of a learning process there, and there's still a learning curve that occurs from undergraduate to beyond, because when you get to a graduate level, it's even more on your own.

After I was done at the University of Illinois, I actually worked at the University of Chicago Hospitals for a year, Research Hospital. But I learned a lot of good techniques there, and actually, the time I spent there worked out very well when I finally got to a genetic component in my SVCT-1 research. I started doing some genetic work with these DNA plasmids that we would transfect into cells. In fact, I had some favorite techniques and favorite kits that I just brought right in. Nobody in the lab at the time had any clue on how to do this molecular biology work, and so when I said, "Well I've got to do this DNA work." They said, "Well, we don't know how to do that." I do! So I grabbed some stuff from some other labs, and we ordered a few things, and I was off. It still took a long time but it probably would have taken me two or three times as long if I didn't have that previous experience.

UESUGI: Had you been interested in doing research in college or was it the thesis experience that piqued your interest?

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MICHELS: Hmm. In high school, I had AP Chemistry and AP Biology. And so, you know, you do the small labs in there, and you learn a few things. And chemistry was always more interesting to me than biology. Chemistry class taught me how to do experiments, and kind of gave you a small idea of what being in a research lab would be.

And then you go to the college level and you start doing more advanced stuff and then you realize there's some really cool things that people can do with research. Especially cool, and this is probably when I started to get an appreciation for biology, is when we did a lab class with *in situ* hybridization in *Drosophila* embryos. And we got to hybridize a little piece of tagged RNA, and we got to see the color in these kind of transparent embryos, and I thought, "Wow!" But we could look at them, and you could see the color, I think it was along the backbone if I remember right. It was one of those things where it's like, "Oh, biology is not that bad! We can do some interesting stuff here!"

I kind of got turned onto biochemistry or genetic engineering by *Jurassic Park* of all things. The movie came out I think when I was in my senior year in high school, and I had read the book. And the movie just kind of sparked it all back up again. I was thinking, "Genetic engineering would be cool! Let's try that!" And actually, I guess technically, I did go into genetic engineering later, it's just not that I wasn't creating any dinosaurs or anything like that.

UESUGI: What do you like about being in the Linus Pauling Institute as a researcher?

MICHELS: Well, the biggest thing is that there's so many people from so many different disciplines. When I came out here, I was still working at the University of Chicago Hospital, I was applying for graduate schools. Well, I came to the biochemistry department here first, and then part of that included the Linus Pauling Institute. I started meeting with Balz and Rod Dashwood and Tory Hagen, and I realized that they're doing some cool things here, and these aren't just, I mean, they're in the Biochemistry Department. Balz Frei and Tory Hagen are both in the Biochemistry Department, but they're not like any other biochemists that I've ever seen. They're biochemists, molecular biologists, cell biologists with a little bit of nutrition thrown in and then Rod Dashwood's in toxicology. And I started to realize that this is a place where you can get a whole blend of all these different disciplines, and they come together, especially in meetings like the Diet and Optimum Health conference and at our LPI retreats, you start to get this feedback from all these different areas and start getting the bigger picture instead of this focused view on one molecule or one enzyme doing this one thing, and you can inhibit it. That's classical biochemistry. This is more like: How does it fit in life? And how can we do things like modulate it with diet in a more natural way? Or how does this impact overall human health?

When I got back from my trip, I just said, "I gotta go to that school."

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UESUGI: You know it was the one!

MICHELS: Yes, if it wasn't for the Linus Pauling Institute, I probably wouldn't be here, mainly because of the distance. I came from Illinois and my parents are still in Illinois. I think it was a good fit overall. I really enjoy being here. I guess I've enjoyed being here so much that I've been here for ten years!

UESUGI: It's not a bad place to be!

MICHELS: No, it's not.

UESUGI: While you're not in the lab, what do you like to do for fun?

MICHELS: What I prefer to do is spend time in the garden. But, you can't do that all year round. And right now, thankfully, now that it's warming up, I can spend most of the time in the garden. So occasionally, I come into work with grass stains on my knees, not realizing I didn't get them out the last time I washed them and dirt under my fingernails.

I love travelling. When I got to Oregon, I spent a long time just seeing everything there was in Oregon. I just thought it was an amazing place to go, and then up to Northern California and I think I've been from... I haven't been to Canada yet but I've been from Seattle all the way down to Tijuana.

UESUGI: One last question: Has working at LPI and observing and being a part of all this nutrition research changed the way you cook?

MICHELS: Definitely, being part of the LPI as well as being in Corvallis. I'd say it's kind of a combination. It's influenced my lifestyle in quite a few ways, the biggest being just how you observe food. You look at food a lot differently after working here for a few years. You try to not look at it in terms of its molecules, but sometimes it's hard not to. You look at a piece of food and you're wondering, "On a molecular level, should I be eating that?" Yeah, sometimes it's good not to pay too close attention but other times it is.

UESUGI: Well, thanks, Alex!

MICHELS: Thank you!

[THEME MUSIC]

HIRSCH: Thanks for tuning in. This podcast was produced in collaboration with the Environmental Health Sciences Center with funding from the National Institute of Environmental Health Sciences.

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On behalf of everyone at the Linus Pauling Institute, we wish you optimum health.
Have an awesome day!

[THEME MUSIC]