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PROFILE

Evolving With Septins: Interview With Michelle Momany

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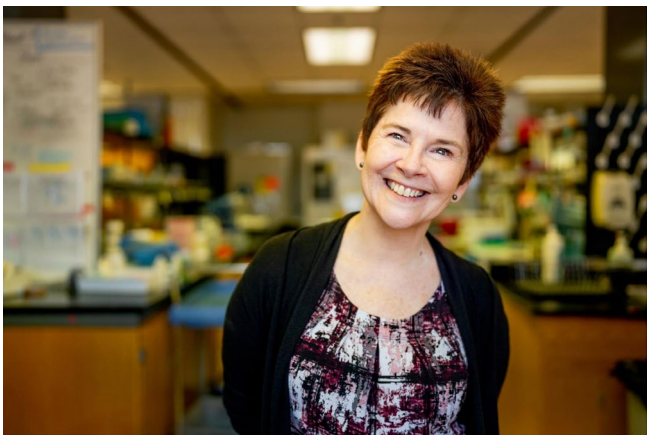

Michelle Momany is Professor of Fungal Biology in the Plant Biology Department at the University of Georgia and a long-standing contributor to the development of septin biology in fungal systems. Her work helped extend septin research beyond budding yeast, notably through the use of filamentous fungi, and was among the first to demonstrate evolutionary continuity between fungal and animal septins. Combining cell biology, genetics, and comparative analysis, her research has addressed how septins assemble, how they contribute to cell shape and division, and how septin diversity has evolved across eukaryotes. Alongside this work, she has studied fundamental aspects of fungal growth and the biology of *Aspergillus fumigatus*, including mechanisms relevant to antifungal resistance. She has also held senior academic leadership roles at the University of Georgia and is a National Academies Education Fellow in the Life Sciences, and a Fellow of the American Association for the Advancement of Science, the Mycological Society of America, and the American Academy of Microbiology. Michelle Momany. Photograph by Jason Thrasher (Athens, GA). Used with permission. Published with the interviewee's written informed consent.

1 | Ondřej Kučera: Septins Are Sometimes Described as a Fourth Component of the Cytoskeleton. Do You Find This Framework Useful?

Michelle Momany: Yes, I do. Thinking about septins as a cytoskeletal element helps explain their involvement in many cellular processes, much like actin or microtubules. It also provides a useful conceptual framework when communicating with colleagues because it places septins in a familiar context and helps guide how people think about their functions.

2 | Michaela Horger: With That in Mind, Could You Describe Your Current Research Program and Where Septins Fit Within It?

Michelle Momany: My lab currently explores two main research directions. One focuses on septins, primarily using *Aspergillus nidulans* as a model system. This work began with cell-biological questions but has increasingly expanded into comparative and evolutionary analyses of septins. One current project examines the cell-cycle consequences of septin deletion in *A. nidulans*.

What I'm really interested in, and where I'd like to go next, is what I think is one of the biggest questions in the field: how septins nucleate, if "nucleate" is even the right word for septins given the way they snap together in a modular fashion. I am particularly interested in membrane contributions, cell wall integrity, how septins pull things together, and how cells decide where septins will assemble.

The other part of my lab works on *Aspergillus fumigatus*, an opportunistic pathogen that primarily affects immunocompromised individuals. Our work in this area addresses two questions. One concerns the cell biology and genetics of spore dormancy and germination, which are poorly understood but central to pathogenicity. The other is more applied and focuses on azole resistance. Azoles target ergosterol in the fungal membrane and are the first-line antifungal treatment in the clinic.

3 | Michaela Horger: Can You Walk Us Through How Your Research Path Led You to Focus on Fungal Morphology and the Cellular Structures That Define It?

Michelle Momany: Initially, as an undergraduate, I thought I would pursue immunology or tumor biology, but after spending time in an immunology lab I realized that animal work was not for me. What I missed was microscopy and the ability to do rapid, reproducible experiments.

When I reflected on what drew me to immunology or tumor biology, the common thread was differentiation: how cells acquire different shapes and specialized functions based on different interpretations of the same genetic code. That led me to fungal systems, where differentiation can be studied with relatively simple cell types. During my PhD, I worked on chitin synthases and their role in shaping fungal morphology, which established my long-standing interest in the cell wall and morphogenesis.

For my postdoctoral work, I wanted a system where classical genetics could be applied. I recall reading the classic yeast cell cycle genetics papers from Pringle and Hartwell and was fascinated by how morphology could report cell cycle stages. That's really what hooked me on fungal biology. At that time, septins were just beginning to be cloned in *Saccharomyces cerevisiae*, and I cloned the first septins from a filamentous fungus, *Aspergillus nidulans*, using degenerate PCR primers and cosmid library screening, approaches that now seem quite archaic.

4 | Michaela Horger: When You Moved Into Septin Research During Your Postdoc, What Was the Field Like at That Time?

Michelle Momany: At that time, almost everything we knew about septins came from *S. cerevisiae*. There was little appreciation for fungal diversity, and a strong assumption that conserved genes must be used in conserved ways. That made it difficult to publish work from filamentous fungi, where septin behavior often differs substantially. Grant reviewers frequently questioned why we were studying septins outside budding yeast. Progress was slow, and some researchers left the field because they could not secure funding.

When I started my lab, we began knocking out, tagging, and localizing septins in *A. nidulans*. Eventually we started looking systematically at septins across fungi. Taking advantage of newly-available fungal genomes we identified orthologs of the core septins—the *CDC3*, *10*, *11*, and *12* equivalents—in multiple species. This work established that these core septins were broadly conserved. In the course of building that dataset, we noticed additional sequences that didn't fit into the core groups. That was the first hint that the framework of fungal septins was incomplete.

5 | Michaela Horger: What Prompted You to Assemble a Broader Dataset of Septins, and How Did That Work Lead to the Identification of Non-Core, or Group 5, Septins?

Michelle Momany: I was struck by claims in the literature suggesting that there were no orthologues between fungal and animal septins. From an evolutionary perspective, that simply did not make sense. Together with Russell Malmberg, a colleague in bioinformatics at UGA, we assembled a much larger dataset and showed that septins form conserved groups across fungi and animals.

What later became known as Group 5 septins initially appeared as a collection of sequences that did not fit the established core groups. At the time, we did not view this as a major discovery, but rather as evidence that the existing framework was incomplete. Subsequent work, including more recent phylogenomic analyses with collaborator Masa Onishi at Duke, has shown that septin diversity is far greater than originally appreciated, particularly in algae and ciliates.

6 | Michaela Horger: From Your Earlier Work on Core and Non-Core Septins to Your Later Structural and Evolutionary Work, Has Your Conceptual View on Septins Changed Over Time?

Michelle Momany: Very much so. Technological advances, especially in sequencing and protein structure prediction, have transformed how we think about septins. Although I am trained as a cell biologist and microbiologist, I have always been comfortable engaging with protein structure and evolutionary analysis. That perspective has become increasingly important.

One of the biggest changes came when more genome sequences became available. Before that, if you saw evolutionary changes in a population, it was hard to ask what protein-level features were involved. Having more data let us dig deeper into what these evolutionary signatures meant for the proteins themselves.

A pivotal moment was seeing the first septin crystal structures presented by Alfred Wittinghofer at the Second International Meeting on Septin Biology, in Ascona, Switzerland in 2007. It was the first time anyone could see how multiple subunits actually interacted. I went back and traced the interactions in the supplemental figures of the crystal structure paper and realized that some of the highly conserved residues we had spotted in our phylogenies were exactly at those interfaces. Later work in my lab with Ben Auxier (currently at Wageningen University) used emerging computational tools and crystal structures to show that these conserved residues were holding subunits together. Connecting evolutionary conservation with molecular mechanisms became, and remains, a central theme in how I think about septins.

7 | Michaela Horger: Reflecting on Your Journey in Septin Research, Is There Any Advice You Would Give to Your Younger Self?

Michelle Momany: I probably spent too much time chasing publication in high-impact journals, at the expense of publishing solid work more efficiently. That pressure is real, particularly early in a career, but it can come at a cost to trainees and scientific progress.

8 | Michaela Horger: What Advice Would You Give Students Entering Septin or Fungal Biology Research Today?

Michelle Momany: Curiosity is essential. You need to be genuinely interested in the questions you are pursuing. I would also encourage students to look beyond narrow disciplinary boundaries. Much of the progress in my work has come from integrating cell biology with structural and evolutionary approaches.

At the same time, practical realities matter. Funding, strategic planning, and choosing collaborators wisely all influence what is possible. And finally, the lab environment matters enormously. Liking the people you work with and feeling supported is critical for sustained, productive research.

9 | Michaela Horger: Looking Ahead, What Are The Most Exciting Questions in the Septin Field Over the Next Five to Ten Years?

Michelle Momany: I think the central question remains how septins nucleate and assemble at specific cellular locations. What signals tell them where to polymerize and depolymerize? That is such a fundamental process and we still do not fully understand it. Recent work, especially that from Amy Gladfelter's lab at Duke, has started to look at how alpha helices might insert into membranes and how lipid composition, packing, and saturation influence that process. I think that gives us our best clue so far, but there is likely more to uncover.

Our own recent work also points to sphingolipids as being critical for septins. It seems they both monitor and regulate the membrane, maybe floating along it until they encounter a specific cue, slowing down, colliding, and assembling. Understanding that interplay between septins and membrane properties is still a major open area.

From an applications perspective, there is an exciting potential in synthetic and comparative approaches. For example, we showed that replacing the *Saccharomyces cerevisiae* CDC12 septin with its ortholog from *Aspergillus nidulans* (AspC) can change yeast into pseudohyphal cells. This kind of mix-and-match experiment could help us understand how septin structures and membrane interactions determine function, and I expect this to shape the field in the coming years.

10 | Ondřej Kučera: You Strike Me as Someone Who Enjoys Hands-On Experimental Work. Is That Impression Accurate?

Michelle Momany: I would not say that I currently do a great deal of bench work. There have been extended periods in my career, particularly during administrative roles, when I was rarely in the lab. That said, I do enjoy being able to step in occasionally—whether helping with microscopy or participating in environmental sampling projects. I would describe it more as dabbling than running experiments day to day.