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Simon Atkinson admits that when he first took up an appointment in nephrology at the Indiana University (IU) School of Medicine 15 years ago, he had little special knowledge of kidney cell biology. "No real background at all beyond learning about them [kidneys] in physiology classes," Atkinson recalls, "and, of course, eating them in pies." That was back home in his native England, where steak and kidney pie is a pillar of the national cuisine.

Atkinson's graduate training had been in basic cytoskeleton work, first at the Medical Research Council (MRC) in Cambridge, UK, with Murray Stewart and then as a postdoc at Johns Hopkins University in Baltimore with Tom Pollard. Studying the formation of myosin "thick" filaments with Stewart, Atkinson had picked up a range of electron microscopy and biochemistry skills. In Baltimore, Atkinson had been in on the ground floor of the "Arp2/3 revolution." He was one of the co-authors with Laura Machesky and Pollard of the historic 1994 paper that first described the novel branching proteins that are a critical mechanism for cell motility. With Joe Kelleher and Pollard, Atkinson was also an author of a key follow-up paper that identified the Arp2/3 gene sequences in *Acanthamoeba.*

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Crawling amoebae are not ailing human kidney cells, but Atkinson took the word of Bruce Molitoris, the chief of nephrology at IU's medical school in Indianapolis, that he needed basic cell researchers to restructure his clinical department. Molitoris was an M.D. who had been bitten by the basic research bug during a fellowship at the University of Colorado with cell biologist Dick McIntosh. Molitoris believed that cell biologists like Atkinson would bring basic research insights to bear on kidney cell biology.

It was a great niche for a basic scientist, says Atkinson. With a joint appointment in biochemistry and molecular biology, Atkinson took on the kidney's exotic cast of specialized cells. "It turns out to be an area where there's a lot to do and not many cytoskeleton people working," Atkinson explains. "A lot of basic questions still haven't been answered, and many of those involve basic biology in the cytoskeleton."

Atkinson's research centers on the cellular impact of ischemic kidney failure and particularly on the proximal tubule cells (PTCs) where solutes are recovered. PTCs are energy hogs, bristling with extra mitochondria to crank out the ATP that drives active transport of sodium out of the cells. Even a brief cutoff in their blood supply, whether from trauma or toxins or as a surgical complication, can start PTCs down the pathway to renal failure. Injured PTCs can repair themselves, enter apoptosis or necrosis, or possibly recruit neighbors to de-differentiate and replenish their numbers, according to Atkinson. "In the actual injury process during the ischemic event and the repair process, the cytoskeleton is critical. If you do things that interfere with actin function or go upstream and interfere with Rho GTPase function, then you can either prevent aspects of the injury or [affect] the repair process."

Blocking Apop

Atkinson is excited about using the techniques of cell biology in a direct way to develop new treatments for kidney patients. After physician Pierre Dagher identified p53 as a potential target in ischemic kidney failure, Atkinson collaborated with Dagher, Molitoris, and others in the division to investigate the use of RNA interference as a way to prevent apoptosis. Using a rat model of ischemic injury, they injected naked siRNA and used intravital microscopy to document endocytic uptake of the siRNA by PTCs and the ensuing sharp drop in p53-driven apoptosis.

Other measures supported the finding that interfering in the p53 pathway significantly lessened renal injury. The results, published last summer, were so promising that Molitoris and other M.D.s who coauthored the paper are moving toward a limited clinical trial with surgical patients at high risk for kidney failure. Atkinson intends to stay firmly on the scientific side of the resulting trial. "I'd run a mile if I ever saw a patient coming down my hall," he laughs.

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"Simon's a wonderful model," says Pollard, Atkinson's former PI, now at Yale. Pollard believes that the line between cell researchers and clinicians needs erasing. "There's exciting, important work for basic scientists to do in a department of clinical medicine. Simon is a great example of that. He's been a great member of this team working on kidney diseases because of his strong background in biochemistry, molecular biology, microscopy, and cell biology. Yet he's also benefited greatly from being exposed to all these clinical problems."

Like most careers, Atkinson's has been driven by a combination of the scientific and the personal. The personal starts in Southampton on England's south coast, where his father was sent by the Royal Navy during World War II to teach radar engineering. His father went on to a civilian career teaching electronics at the local polytechnic college. His mother taught English literature at the "A" level, the university entrance standard. "So the old 'Two Cultures' line ran right through our house," says Atkinson.

His older brother may have tipped him across the line. As a university student, his brother took up fruit fly genetics and brought home his collection of "wild types," gathered in a public market. "The fruit flies would get all over the house and really annoy my mother," recalls Atkinson, who was still a schoolboy. His brother went on to a career in epidemiology. Atkinson went off to study biophysics at King's College London (KCL), with vague career plans.

The teacher who captured Atkinson's imagination was the English evolutionary biologist Tom Cavalier-Smith. Atkinson vividly remembers Cavalier-Smith's "Fundamentals of Biology" at KCL. "He knew more about biology than any person I've ever met," Atkinson declares. "He lectured and held 'discussion' sections. The discussion sections were really a chance for him to stand in front of the class and think out loud about some aspect of biology that was marginally relevant to whatever he'd been lecturing about recently. We (the students) really didn't have much to do except listen, and listening to him was what really got me hooked on biology."

Borrowing Laureates

Atkinson followed those interests in 1987 to Cambridge. In those days, the MRC was still famed for its seedy buildings, first-rate equipment, cramped bench space, and everyone-eats-together staff canteen. At lunch or teatime, you couldn't avoid sitting down with biology legends like Sydney Brenner or Cesar Milstein, Atkinson recalls. "You'd be working in the lab at night and Max Perutz would come wandering in, looking for a pipette tip or something."

At the MRC, Atkinson also met American postdocs who urged him to cross the Atlantic for a fellowship. Through Murray Stewart, he met Tom Pollard. According to Pollard, Atkinson fit right into his Hopkins lab crew and not just for his contributions to Arp2/3. "The Atkinson-Machesky era in our lab was the era of the practical joke," Pollard remembers. "It wasn't just the summer, there was always *something*. Laura usually got blamed but I strongly suspect that Simon was her evil partner. I think he just covered his tracks better."

Machesky, now at the Beatson Institute in Glasgow, Scotland, won't give away old secrets but concedes that Atkinson had hidden talents. For example, he answered Pollard's demand for shorter faxes by reducing a 40-page lab report to an image the size of a postage stamp. This was in the pre-PDF era. It took work.

Machesky says she was not surprised that Atkinson has forged a successful basic research career in a clinical division. The Pollard lab always had a semi-clinical perspective, she recalls, starting with Pollard, who is an M.D., and on through a string of physician-scientists who flocked to the lab. "But Tom always insisted that the basic biochemistry had to be figured out first—molecule A goes into molecule B to give you molecule AB. And that's the way Simon thinks."

Atkinson left Baltimore with two other significant discoveries. One was the ASCB Public Information Committee (PIC). The

suggestion that he might be interested in joining came over afternoon tea in the Hopkins laboratory of Kathy Wilson. She became PIC Chair in 2000 and pulled Atkinson on board in 2001.

String Family

Atkinson's second (and arguably greater) discovery in Baltimore was Joan Duwve. She was a Hopkins medical student who'd left a career in international public health, having decided that family practice was her true calling. They were married in 1992. Her family's roots in northern Ohio were another factor for Atkinson to choose Indiana. After a decade of practicing family medicine in Indianapolis, Duwve went back into public health to become the state's Medical Director for Public Health and Preparedness. They have two children, David, 16, a high school junior facing the career choice between physics and international politics, and Anna, 13, facing the choice between oboe and violin.

Duwve is also an accomplished violinist, and David, a promising cellist. So the opening was there, says Atkinson, for a family string quartet, if a cell biologist in his forties could pick up the viola from scratch. About his viola lessons, Atkinson remains game but not hopeful. His son now has a viola-joke-of-the-day "widget" on his Mac and pelts his father with the latest.

Atkinson's viola jokes are a cover, says his division chief Molitoris, for his real musical talents as a church chorister. "Simon's choir singing is really very impressive," Molitoris reports, "It's at a very high level." Molitoris also adds that Atkinson is renowned as a dedicated father, cheerfully involved in Scout camping trips, music lessons, and teen transportation.

Atkinson also exemplifies a new approach to teaching biomedicine, says Molitoris. The National Institutes of Health has long been pushing Ph.D.s to get more clinical exposure and M.D.s to study more of the cellular and molecular foundations of disease.

"Simon is clearly out in front on this approach," says Molitoris. "It's hard for some basic [research] people to get outside the cell. If there's a fault in our system it's that while cell biology is important, we've let go of physiology. To advance things, there has to be this middle area with people who understand the physiology of how cells work together to create organ function. Simon bridges that gap. He can explain that to students, and he can take it to his research side as well." ■

—John Fleischman

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Don't Miss These Sessions at the Annual Meeting!

Emerging Science: Synthetic Biology

Sunday, Dec. 6, 2:30 pm–4:00 pm

Synthetic biology aims to engineer biology in a facile and predictable way. Our deep understanding of cell biology provides a central foundation for these efforts. Moderated by Pam Silver, Harvard Medical School, the panel (Chris Voigt, University of California, San Francisco; Christina Smolke, Stanford University; and Ron Weiss, Princeton University) will introduce the area of synthetic biology and discuss efforts to engineer genetic circuits, organelles, metabolic processes, and cellular interactions logically.

Translational Research Session: Ciliopathies—Human Genetics Partners with Basic Cell Biology

Tuesday, Dec. 8, 2:00 pm–3:30 pm

This session will describe how basic cell biological studies of the assembly of cilia and flagella, often carried out with organisms such as the green alga *Chlamydomonas*, have led to new insights into a host of human diseases. These diseases include polycystic kidney disease, Bardet-Biedel Syndrome, Kartagener's Syndrome (left-right symmetry defects), and many diseases that involve dysfunction of cilia. Cilia are found on almost every nondividing cell in our body. The study of such disorders has, in turn, informed the diverse roles of cilia in vertebrate and invertebrate processes that range from mating, to sensing the extraorganismal environment, to responding to paracrine cues. The session will be moderated by Nicholas Katsanis, Johns Hopkins University School of Medicine, and panelists will include Joel Rosenbaum, Yale University, and Elise Heon, The Hospital for Sick Children, Toronto. ■