Tony Hyman

Eureka moments are rare, so when scientific lightning strikes, you grab the nearest witness. For Tony Hyman, the innocent party was Stanley Prusiner. It was 1990, and Prusiner, who would win a 1997 Nobel Prize for discovering the infectious prion, was minding his own business, heading for the elevator at the University of California, San Francisco (UCSF). Suddenly a bug-eyed postdoc with a British accent burst out of the Tim Mitchison lab and dragged Prusiner inside to become the second person on Earth to watch a video playback of a labeled microtubule attaching to a kinetochore.

"I don't think Stan knew me at all," Hyman recalls. "I'd come to Tim's lab to set up a real-time assay to look at microtubules on isolated kinetochores. We had to do everything from scratch—image processing, labeling the microtubules, marking the polarity. It took a couple of years to work through all the technical aspects, but this day I was doing the experiment and finally they [the microtubules] moved! I was so excited I ran outside and everyone in the lab was off at a seminar. But there was Stan Prusiner coming down the corridor, so I said, 'Stan, come in here and look at this.' I could see that he was thinking, 'Who is this?'" Still Prusiner made the right congratulatory noises as Hyman narrated his revolutionary video. "I'm sure he's forgotten all about it," says Hyman, who hasn't. "It was absolutely a Eureka moment. The adrenaline rush I remember to this day."

Hyman's ex-PI, Tim Mitchison, is at a loss to remember the first time he met or heard of Tony Hyman. Mitchison, now at Harvard Medical School, is older than Hyman, but both are products of scientific households, London childhoods, and British higher education. So where did they meet? As an undergraduate at University College London (UCL), Hyman had been a student of Tim's father, Av Mitchison, the renowned zoologist and immunologist. Or was it through John White at the Laboratory of Molecular Biology in Cambridge, where Hyman was a graduate student in the lab that perfected the first practical confocal microscope? Surely they met during Mitchison's "disastrous" year as a Medical Research Council staff scientist in Mill Hill after coming home from UCSF with his doctorate. They'd definitely become friends by the time Mitchison accepted an assistant professorship back at UCSF and signed Hyman up as his first postdoc. Indeed, says Mitchison, Hyman got to San Francisco first while he waited for his visa. "By the time I got there, Tony had the laboratory set up," Mitchison recalls. Hyman also knew all the key technical people in the building and all the scientific supply representatives. "Tony was unbelievable about getting good prices on equipment," according to Mitchison. The lab needed centrifuges, and Mitchison still remembers one rep coming to him nearly in tears, begging, "Please don't make me talk with Dr. Hyman again."

The imaging system Hyman created for the Mitchison lab revealed microtubule dynamics in never-before-seen detail. Later in his own lab at the European Molecular Biology Laboratory (EMBL), Hyman pursued what Mitchison describes as "classic cytoskeleton problems": spindle attachment, motor protein movement, centrosome assembly, and cell cycle control. Even today Hyman works on a classic problem in developmental (and stem cell) biology: asymmetrical cell division. But from the beginning, says Mitchison, his first postdoc also showed real organizational flair. "Tony is an institution builder," says Mitchison. "Always has been. I don't know where that comes from; perhaps it's some innate ability, but he loves getting things started and building institutions."

The Days of HeLa

Hyman's organizational knack spills over from the lab. This year Hyman is the Program Chair for ASCB's 2012 Annual Meeting in San Francisco. He is also organizing the scientific program for the 2013 European Molecular Biology Organization meeting in Amsterdam. On other fronts, Hyman is campaigning to move researchers away from immortalized cancer cell lines toward embryonic stem cells derived from mice or differentiated human cells converted into their precursors. "The days of HeLa cells are over," Hyman and co-campaigner Kai Simons declared last year in *Nature*. "So although HeLa cells and other immortalized cells derived from cancer patients are good for investigating what cells have in common, they are completely inadequate for addressing the next big topic in cell biology: cellular diversity

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in normal tissues."

Whatever the next big topic, Mitchison suggests that if you want to see Hyman giving full expression to his institution-building genes, go to Dresden. Until German reunification in 1990, Dresden, the once-glittering Baroque capital of Saxony, was known for its destruction in a controversial 1945 Allied bombing raid and for 40 grim years of Soviet-style reconstruction. In 1998, Dresden was chosen for a new Max Planck Institute for Molecular Cell Biology and Genetics (MPI-CBG).

At 35, Hyman was the youngest of the five founding MPI-CBG directors. At 29, he'd been a group leader at EMBL in Heidelberg when he returned from his UCSF postdoc (turning down attractive job offers from high-profile U.S. institutions, according to friends). EMBL was a bold move for a British scientist who'd been born in Haifa, Israel, and spoke not a word of German. But Hyman was attracted by the independence offered by Simons, the Finnish cell biologist who'd shaped EMBL from its earliest days. In 1998, Simons came to Hyman with a new offer: Build a new MPI from scratch in Dresden. The design reflected many of Hyman's ideas on everything from the institute's single entrance to a ban on individual coffee pots. Everyone would come in the same front door at MPI-CBG and congregate at a coffee bar staffed by a waitress, not a change-eating drink dispenser.

The planning is evident in more than the physical layout, says Mitchison. "If I remember correctly, they sent Tony ahead [to Dresden] to set up the day-care center. Isn't that so German? Can you imagine that here, building a new institution and even before breaking ground, you recruit the day-care director and find a building for her?"

More important, MPI-CBG gave Hyman the leverage to scale up breakthrough technologies. An early effort was a functional genome project using the new technology of RNA interference to identify every gene used in the *Caenorhabditis elegans* embryo during the first round of cell division. That project, says Mitchison, "gave Tony a taste of modern automated approaches that could be applied right across biology."

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The Great Migration

Arshad Desai, now at the University of California, San Diego, and his wife, Karen Oegema, also at UCSD, were present at the creation (or at least the unveiling) of MPI-CBG. Recruited out of the Mitchison lab by Hyman, they joined him at EMBL Heidelberg just in time for the great migration to Dresden. Desai, who came to work with Hyman on imaging kinetochore assembly, says the move was flawless; every contingency was covered—from the refrigerated trucks to move *C. elegans* stocks, to the backup refrigerator trucks in case of breakdown. What is more important, says Desai, is what Hyman was able to do from his new base at MPI-CBG. "Tony is very good at what I would call process engineering. He really knows how to attack problems with technology and do it on a scale that most of us just couldn't dream of doing." Hyman can gather the resources, create the pipeline, and attract the right people for large projects. Says Desai, "He's extremely good at noticing what technology might be able to do, like using the new molecular biology tools to generate large banks of cell lines. It's just natural for him."

UCSF's Jonathan Weissman, a longtime fan of Hyman's work and a recent collaborator, sees Hyman in another light. "Tony is fundamentally a cell biologist, and of course the cytoskeleton is one of the most fundamental aspects of cell biology." But the label doesn't really convey how his friend thinks, says Weissman. "I think of him as someone who thinks about shapes and structures in the cell. The cytoskeleton stuff comes as a natural aspect of that, but it's only one facet. The other side of Tony is that he's someone who is methodically innovative." Behind Hyman's big methods projects, Weissman believes, "There's an overarching theme to what he's doing, and it's thinking about structure and organization in the cell at a physical level."

To get directly at the physics of the cell, Hyman has cultivated interdisciplinary collaborations with Frank Jülicher at a second Max Planck Institute in Dresden, the Institute for the Physics of Complex Systems (MPI-PKS). That induced Cliff Brangwynne to accept a postdoc in the Hyman MPI-CBG lab

after finishing his physics doctorate in David Weitz's soft condensed matter group at Harvard. Brangwynne was eager to learn "real" biology with Hyman but enjoyed keeping an office at MPI-PKS for serious equation hammering. "Tony really appreciates this kind of hybrid science," says Brangwynne, now at Princeton. "This cross fertilization of ideas is really important to him."

The cross-town approach paid off in a 2009 *Science* paper with Brangwynne, Jülicher, and Hyman looking at germline P granules in *C. elegans* through the physics of soft condensed matter and describing them for the first time as liquid droplets. P granules appear in the germline cells of all animals and are thought to be involved in asymmetrical cell division. Describing the condensation of P granules as a product of classic phase transition, the paper suggested that an entirely new physical–chemical mechanism might be structuring the cytoplasm.

The People's Car

It was an unusual paper in many ways, says Brangwynne, but then Hyman is not your usual boss. A prime example, he says, is the Hyman lab's staff car, the "Trabi." It is a vintage but drivable Trabant, the ex–East German "people's car" with a two-stroke engine that whines like a moped. The lab has a fine cream-colored specimen of indeterminate model year. "There was this 30-year period when the factory didn't change a thing, so it's really difficult to figure out," says Brangwynne, who conspired with fellow postdoc Alex Bird to convince Hyman that the lab needed a Trabant customized with mitotic spindles painted on the doors. It premiered at a Friday afternoon "beer hour" after MPI-CBG's weekly seminar talk. The Trabi putt-putted to the front door with its jacked-up sound system blaring music hotwired from Bird's iPod and the backseat loaded with beer. It was an immense hit, Brangwynne reports. The MPI-CBG Trabi has become a photographic attraction around Dresden. Do tourists recognize the mitotic spindle? "People seem to think that it's an outer-space thing," Brangwynne sighs.

A mitotic spindle on a Cold War memento could be a fitting emblem for Dresden, where Hyman and his wife, American cell biologist Suzanne Eaton, have now lived for 12 years. They met at UCSF, discovering a mutual passion for serious cycling and serious music. Eaton and her Steinway grand piano followed Hyman to Heidelberg, where she'd been offered a fellowship in the Kai Simons lab. In 1997, she became an EMBL staff scientist. In 2000, Eaton moved to MPI-CBG as a group leader while the Steinway and the family moved to a breathtaking prewar apartment overlooking the River Elbe. Now as their two sons, Max, 14, and Luke, 13, move through the German education system, Hyman finds himself reflecting on his own troubled school years. "I think a lot about education now because of my boys. I like the quote from Albert Einstein: 'It is a miracle that curiosity survives formal education.' I was almost universally bad in school, but somehow my curiosity did survive."

"Looking back, I really respect my parents' attitude to my education. I always tried hard. I wasn't lazy. There was some feeling that my brain just didn't function in a way that would pass exams, and they were happy with that."

He credits his parents. His father, Anthony, a physicist turned historian of science, and his mother, Laura, a trained artist and painter, encouraged educational achievement for Tony and his siblings but recognized that he was not a

Hyman and lab members with the "Trabi."

conventional student. "Looking back, I really respect my parents' attitude to my education. I always tried hard. I wasn't lazy. There was some feeling that my brain just didn't function in a way that would pass exams, and they were happy with that."

His grammar school in London gave him a solid grounding in science, but his A-level results were not good enough for a university place. His attention was often elsewhere, he recalls, especially on bicycle building and on hair-raising rides with his mates through central London traffic. He "drifted" into a technician's job at the UCL zoology department, cranking out tissue culture medium. Arriving at work early one morning, Hyman found a researcher, Terry Preston, still at his bench after an all-nighter. Hyman had to know what kept him up all night, so Preston sketched out his experiment to get at the effect of ionic strength on movement in amoebae. Hyman soon had his own piece of the problem and a spot at the bench. Eventually the admissions committee found an undergraduate place for UCL's newest researcher.

Today Hyman pursues two of his great outside interests from school days: bicycles and flutes. In Dresden, he rides regularly with what he laughingly calls the "Max Planck *squadra*," a pack of amateurs who will click off 100 kilometers on a good day's ride. The flute dates from his days as "a typical middle-class English schoolboy who was supposed to take music lessons." Yet the flute lessons took, although Hyman's tastes evolved from classical to jazz. In San Francisco, he added the saxophone to his chops and now plays both in jazz groups. More recently, he splurged on a superior flute, which rekindled his interest in classical. "I thought, 'Why not? I'm a director now.'"

Becoming a Max Planck director was not the most probable outcome for an English schoolboy who was not good at exams. "Either my brain matured late or I finally discovered how to focus on one thing," says Hyman. "It's certainly true that I can get easily distracted, but the way my brain works is that I see things pictorially. I see my experiments visually. In my mind, I can see how they could work." As a scientist, an innovator, and a parent, Hyman thinks that schools screen for one kind of intelligence, at a great cost in human imagination. "You don't just want minds that are good at exams in high positions. You want a variety."

In the Hyman way of science, variety is what you get. ■

—John Fleischman

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—Thea Clarke