In Memoriam: Ben Barres

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Ben Barres, professor of neurobiology at Stanford University and member of the *JCB* editorial board for over 15 years, passed away on December 27, 2017, after a lengthy battle with pancreatic cancer. Ben left an indelible mark on the scientific community as a scientist, an advocate for equality, and an unbelievably supportive mentor. As a scientist his creative approaches led him to remarkable discoveries about the importance of glial cells in the brain, and his passion elevated these cells from the "other cells in the brain" to a significant place in the consciousness of neurobiology. As an advocate, he fought for equal treatment irrespective of gender identity, sexual orientation, race, or ethnicity, and was an inspiring supporter of junior scientists. As a mentor, he provided a creative and vibrant atmosphere for his trainees to pursue research and the never-ending support for them to flourish as independent scientists. As his former trainees, we would like to give our thoughts on Ben, and the deep impressions that he left on everyone he interacted with.

Who was Ben Barres?

For Ben, science was all about identifying big questions. He taught us that the critical aspect of every project was the identification of a question that was important, interesting, and tractable. He instructed all his trainees to have the title of their talks always be a question, and for every slide in every talk to start with a question. He often joked that if a talk starts without a question, he walks out right away. To honor Ben, we will start each section with a question.

Who was Ben Barres the scientist?

Ben grew up in New Jersey, and he had a passion for science and math from a young age. This led to an undergraduate degree at Massachusetts Institute of Technology, where Ben majored in neurobiology, a major that he had to invent! Ben next attended medical school at Dartmouth College and did his neurology residency at Cornell. It was during this time that his interest in glia was first piqued, by looking at pathology specimens from patients with neurological disorders. Here, the glia profoundly changed their structure, leading Ben to wonder what this would mean for the function of neurons, both in health and disease (Barres, 2008). His medical training also informed much of his future research to ensure it had relevance to human disease and treatment.

Ben joined Harvard University for his PhD studies, where he was a phenomenally productive graduate student in the laboratory of David Corey, characterizing ion channels present in different glial cell types using electrophysiology. Ben would often say he loved his time in David's laboratory so much that he would still be there if David hadn't nudged him out, for the good of Ben's own career. Ben moved to London to carry out postdoctoral research with Martin Raff at University College London. In Martin's laboratory, Ben developed methods to purify different glial cell types from the developing brain (techniques that would later become the foundation of his own laboratory), and used these pure cultures of cells to identify many things, including that oligodendrocytes need signals from other cell types to stay alive. Ben maintained such reverence for Martin that throughout his career he would invite Martin to visit his laboratory for Raff pizza sessions, in which Martin would sit down with Ben's trainees to learn about their projects and give ideas about what they could explore.

Ben chose to start his own laboratory in the neurobiology department at Stanford University, noting that he chose the department not just because of the science but also because of the emphasis it placed on high quality teaching and mentoring (Barres, 2018). Ben's approach to science was to ask big questions. So rather than focusing on one type of glial cell to work out its function in the brain, Ben worked on all the different types of glia throughout his career, and made groundbreaking discoveries in each area. This approach earned him multitudes of honors including the Searle Scholar Award, the McKnight Investigator Award, the Klingenstein Fellowship, the Ralph W. Gerard Prize in Neuroscience, and many others.

Ben was a trailblazer, performing experiments that at the time ran counter to the prevailing dogma of how the brain works, but are now considered as textbook facts. His work was defined by asking big, simple questions that generated the most essential findings. A favorite comment about his work came after one of his seminars, where a colleague indicated that they loved his talks because he made such critically fundamental advances, you were left thinking that you couldn't believe no one else had thought of that before. Yet no one had, as Ben was always on the forefront of opening up new areas of research.

One such finding came from work where Ben purified and cultured neurons from the retina and found that, remarkably, even though he could get these neurons to survive without other cell types present, they failed to make any synapses.

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By adding back each cell type in turn, he found that astrocytes were releasing signals that instructed neurons to make synapses and controlled synaptic strength. This led to many more discoveries, including identifying the molecules astrocytes use to signal to neurons. More recently, the laboratory demonstrated that, in addition to inducing synapses to form, astrocytes also eliminate synapses by direct phagocytosis and by signaling to neurons to up-regulate complement proteins leading to phagocytosis by microglia.

Other projects in the laboratory looked at the ability of axons to regenerate after injury and discovered that the age of the axon determines its ability to regenerate, showing that intrinsic properties of the neuron and not just the environment are important for recovery. Ben made important discoveries in the field of oligodendrocyte development and myelination, including identifying a transcriptional switch that allows myelination to occur. In the area of the blood–brain barrier, work in his laboratory identified the cellular and molecular mechanisms that induce the barrier to form, identifying a role for brain pericytes that was previously unknown. Fitting with his training as a neurologist, Ben led projects that investigated how glial cells respond to injury, testing the hypothesis that changes to glia are causative in many types of brain pathology.

A major contribution to the glial field was the generation of transcriptome datasets of all different brain cell types, both from rodent and human. These were made freely available to the scientific community, fitting with Ben's open and generous approach to science, and have been invaluable resources to many researchers. We have been at many meetings where a speaker introduces a new gene in their talk, and you can see dozens of scientists in the audience (including Ben) open the Barres Brain RNA-Seq website on their phone to see which cell expresses the gene.

Ben's passion for science in general and glial cells specifically was infectious. After talking to him for a short time, it was difficult to understand why every scientist wasn't working on glia! Ben was a huge advocate for glia, cells that were often ignored by neuroscientists when he started his career, and could be heard in meetings during other people's talks screaming out "what about the glia?" from the crowd. He initiated international meetings on glia, wrote reviews, edited textbooks, and advocated for more funding for glial cell projects, all of which elevated the scientific community's understanding of the importance of these cells. Ben was also incredibly persistent. He worked on the role of astrocytes in synapse formation for many years before anyone would consider funding this field. His laboratory worked on methods to purify mature astrocytes for over a decade, before he finally had success, but he persisted as he knew the scientific question was important enough to warrant the effort.

Who was Ben Barres the advocate?

Ben was a powerful advocate for equality in science. Perhaps most notably, after Larry Summers, then president of Harvard, suggested that there were fewer female than male professors in science and engineering because women had intrinsically less aptitude, Ben wrote a landmark commentary in *Nature* explaining that bias, and not intrinsic differences, led to this discrepancy (Barres, 2006). As a transgender male, Ben felt that his experiences living both as a woman and as a man allowed him to understand how the two genders were treated differently. He pulled from his own experiences and combined them with well-vetted studies to explain the power of bias. His arguments have resonated with many people who had felt or observed bias throughout their lives. Ben's advocacy did not stop with gender discrimination. He also fought for equality for LGBT individuals and minorities, and in recent years he turned his attention to sexual harassment, identifying this as a problem especially for junior female scientists.

Ben Barres. **Photo courtesy of Stanford University School of Medicine.**

When Ben gave a science talk, he would stop midway through and give a 5–10 min interlude educating people about gender equality. Not at the beginning, not at the end, but midway through. Although shocking to some, this gave him a captive audience and allowed him to get his message across. Several years ago, Ben gave the plenary lecture to the University of California, San Diego, neuroscience graduate students at their annual retreat. Midway through his talk he stopped to discuss sexual harassment and to suggest guidelines he thought could reduce sexual harassment of junior scientists. This was the first time either of us had ever seen a standing ovation in the middle of a talk.

Although many of Ben's advocacy efforts received widespread media attention, there were far greater efforts behind the scenes. When he found that a funding agency or search committee had panels consisting primarily of white males, he would advocate for more women and minorities on the panels. He would look through upcoming meeting schedules and contact the organizers if their panels weren't sufficiently diverse. He would contact all major meeting organizations to ensure that there were appropriate sexual harassment guidelines for the attendees. We remember being at a Cold Spring Harbor Laboratory (CSHL) meeting with Ben where he was standing in a hallway in front of a series of artists' renditions of different famous scientists, all of which were male. We watched as he chided the administration for not having any portraits of female scientists, despite there being so many worthy women. On our next visit to CSHL, lo and behold, we were not surprised to find pictures of female scientists on the wall. However small one

may think some of these issues were, Ben felt that all change needed to occur to limit bias and garner equality.

Ben approached his advocacy very much like he approached science, with thoughtfulness and rigor, examining empirical data. Ben's advocacy also relied on another strength found in his research: persistence. When people weren't listening to cogent arguments, Ben would not relent; he would continue to advocate until there was visible change. He would talk about his constant pestering of the Howard Hughes Medical Institute to change the composition of their committees to include more women and minorities and to change their funding processes from nominations to open applications, changes that he thought were critical to ensure equity in whom they funded.

Who was Ben Barres the mentor?

Another indelible mark that Ben has left on the scientific community was his passion for mentorship, both for trainees in his laboratory and for junior scientists in general (Barres, 2013, 2017). He viewed the academic laboratory as a place where the mentor was there to provide resources, ideas, and support for trainees to pursue the science they were interested in. Ben gave his trainees space to think, to imagine, to explore, and, perhaps most importantly, to fail. He realized that a scientist needed to understand for themselves not only what worked but what didn't work in their path to independence. This allowed his trainees to feel an ownership of their projects and find what they were most excited about, and what directions they would like to take their career.

Training in the Barres laboratory was not solely about finishing a project; Ben's goal was to prepare his trainees in every aspect of science to be independent investigators. Ben would engage all of his trainees, whether senior postdocs or first year graduate students, to write fellowships and grants with him, to review manuscripts for top journals, to write reviews related to their work, and to present their work on campus and in external meetings. This was particularly true for international meetings as Ben hated to fly overseas (he said he would only travel overseas to visit his postdoc mentor Martin Raff or go to Hawaii). While some faculty might view these activities as diversions that hinder the trainees' ability to complete projects, Ben saw them as vital to prepare each person in the laboratory to become independent scientists and to have them recognized in the international community as experts in their field. Ben's support for his trainees did not end when they left the laboratory, as he supported his former laboratory members in every aspect of their careers.

Some of our greatest memories were attending his epic laboratory meetings. Monday mornings at 10 am, these meetings were scheduled for 2 h but rarely finished before 1:30 pm. Ben set an atmosphere where everyone felt comfortable sharing ideas, asking questions, and helping each other. No idea was too outlandish and no ideas were better just because they came from a more senior person. It felt like everyone was there to help push science forward, and it was an incredibly exciting and special place to be. The thought of Ben, walking up to the screen to stare at people's data from inches away, always brings back great memories.

In addition to his own trainees, Ben was dedicated to mentorship and advancement of all junior scientists. It is astonishing how many people have told us that Ben was their surrogate mentor. This ranges from graduate students and postdocs from other laboratories at Stanford, to people who met Ben at meetings, and those that corresponded with Ben after reading one of his papers. Ben's passion for science, his eagerness to discuss new ideas, and his dedication to helping young scientists drove him to engage everyone, especially if they wanted to talk about glia. He would often talk to people for hours after meeting them for the first time at a conference or develop epic email threads with people he had never met in person in an effort to help them.

Ben's dedication to support his scientific family was never more evident than in the past year and a half as he battled pancreatic cancer. When he was given this terminal diagnosis in March of 2016, his first action was to make a plan for each of his current trainees that would provide them with mentorship and funding so they could pursue their scientific goals. In November of 2017, Ben became limited to hospice care in his home. At this point, his singular focus was to update his reference letters for all of his trainees, past and present, and to put them in a secure location so that following his death they could be sent out whenever needed. It was remarkable, but not surprising to us, that his priority was to provide continued support for his people.

Who was Ben Barres the person?

Ben was one of the most energetic, engaging, and passionate people one could ever meet. He always had the time to find out how you were and to tell you what he was most passionate about at the moment. One of the classic Barres laboratory experiences was "Getting Benned." "Getting Benned" occurred when someone was getting ready to go home in the evening and Ben would stop by to chat. Ben would engage in conversations about any number of topics that were always incredibly engrossing, so that when you looked at the time you hadn't realized that hours had gone by. He had the amazing ability to get along with anyone, whether they were Stanford professors, aspiring students, or his neighbors' children.

Much of the framework of how Ben viewed himself was from the fact that he was a transgender male. Ben grew up as Barbara Barres in New Jersey, and transitioned to male in 1997. He would often talk about feeling uncomfortable with himself growing up, but not fully realizing where the discomfort derived from. It wasn't until his adulthood when he read more about what it meant to be transgender that he realized what he hadn't understood about himself. He was extremely reflective and philosophical about what it felt like to live as a woman versus a man, and how he was treated differently. He was very open about this aspect of his life and often would talk about how his life changed after starting testosterone treatment, whether it was his memory, his emotions, or his body.

After spending a lot of time with Ben, what one remembers most are his uniquely quirky personality traits. Entering his office with an agenda of what to talk about was completely useless. No matter what you wanted to accomplish, you would inevitably discuss whatever he was obsessed with at the moment. This often meant listening to how the newest fad diet was going to change his life, learning about the different coffee beans he was roasting, finding out what genes were expressed at cosmically high levels in the laboratories newest transcriptomics experiments, or guessing what was going to happen in the next Harry Potter book. Any conversation would also involve the inevitable shouting through the wall to hear the thoughts of his office neighbor, Tom Clandinin, who was always happy to oblige with a shouted response. These conversations were always educational, thought provoking, and exhilarating, and you often left with a bag of coffee and five more projects to conquer.

Ben had a particular affinity for the Harry Potter books and movies. He explained how he identified with the protagonist; a young kid who didn't fit in. He would take his laboratory to the openings of new Harry Potter movies so he could share the story with his trainees. When the students attending a CSHL Developmental Neurobiology course gave him a gift of a Harry Potter disc with a picture of his face pasted over Harry's, he made it his Stanford profile picture. For people who knew Ben, they recognized other aspects of Harry's personality in him. Harry was brave and caring, and would do anything for the people he cared about. Ben was brave. He fought for equality for everyone in science arguing for equal treatment for everyone—regardless of gender identity, sexual orientation, race, or ethnicity—at every opportunity and through every means at his disposal. Ben was caring. He would always put others before himself, working tirelessly to support and promote all his trainees in their work and lives. Beyond anything, Ben left a legacy of someone who cared deeply about everyone around him and would do anything to help them succeed.

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