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PERIODICALS

The Leakiest Pipeline: All Too Few Women Get to Run Their Own Neuroscience Labs

BY ORLY AVITZUR, MD, MBA, FAAN

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TEN OF 64 member neurologists of the National Academy of Medicine are women, and only three of 37 neuroscientists — less than 10 percent of those who hold tenured positions at the National Institutes of Health's National Institute of Neurologic Disorders and Stroke — are women.

We like to believe that we've made great strides when it comes to career opportunities for women, and, in some ways, that's true. Women earn over 70 percent of doctoral degrees in health sciences, according to a 2014 report by the Council of Graduate Schools. About half of neurology residents today are women, and almost one in three practicing neurologists are women.

But female academic neurologists earn the least of all specialties, and

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TARGETED IMMUNOTHERAPY TREATS PATIENT'S RECURRENT GLIOBLASTOMA

BY KURT SAMSON

For the first time researchers have safely eliminated recurrent glioblastoma, without significant toxicity, using a patient's own genetically-modified T-cells.

Glioblastoma, a rare but deadly cancer affecting fewer than 200,000 people each year in the United States, has a median survival just over 14 months. Fewer than 3 to 5 percent of patients survive for five years or longer.

In a proof-of-concept case study, published in the December 29 *New England Journal of Medicine*, investigators at the City of Hope Comprehensive Cancer Center in Duarte, CA, reported that a patient with recurrent multifocal glioblastoma of the brain and spine, who received autologous chimeric antigen receptor (CAR)-engineered T-cells targeting a brain tumor-associated antigen, had complete remission of tumors without serious toxicity.

The 50-year-old patient was enrolled in a phase I clinical trial and had failed to respond

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Early Return to Activity after Concussion May Reduce Post-concussive Symptoms in Youth

BY SARAH OWENS

Children and young adults who resumed physical activity within the first week of an acute concussion had a reduced risk of persistent post-concussive symptoms four weeks later compared to those who did not engage in any physical activity, according to a report published on December 20 in the *Journal of the American Medical Association*.

Current pediatric concussion guidelines, including the most recent version of the AAN's sports concussion guideline released in 2013, recommend a period of physical and cognitive rest following a concussion until post-concussive symptoms like

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IN AN UNADJUSTED ANALYSIS, the researchers found that persistent post-concussive syndrome occurred in 24 percent of participants in the early physical activity group compared to 43.5 percent of participants in the no-activity group.

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neurologists have the widest gender pay gap, as we revealed in an article in the November 17 issue of *Neurology Today*. Women comprise only 15 percent of full professors in neurology and only 11 of 101 neurology department chairs, according to an analysis that was presented during a poster session at the 2016 AAN Annual Meeting. A mere ten of 64 member neurologists of the prestigious National Academy of Medicine are women, and only three of 37 neuroscientists — less than 10 percent of those who hold tenured positions at the National Institutes of Health's National Institute of Neurologic Disorders and Stroke (NINDS) — are women.

ARTICLE IN BRIEF

Disparities in the number of tenured women neuroscientists who head up their own labs have not improved greatly over the years. Officials at the NINDS and various neuroscientists offer reasons why they think that is still the case and where there is room for improvement.

The reasons why vary, women and men neuroscientists shared in interviews with *Neurology Today* — from women being presented with fewer opportunities to present at academic symposia and become more visible for their work, to a perception that women are "innately" less accomplished at science and make family life and children a priority over their career paths. Indeed, *Neurology Today* reached out to many women neuroscientists for this article. A number declined requests for interviews, presumably out of concern about being thrust in the spotlight, while others did not respond.

DR. BEN BARRES: "I think everyone would like to think much more has changed than has actually changed."

DOES GENDER MATTER?

"I think everyone would like to think much more has changed than has actually changed," said Ben Barres, MD, PhD, professor of neurobiology, developmental biology, and neurology at Stanford University School of Medicine, who pioneered the development of novel methods for the purification and culture of neurons and glial cells and has authored 150 scientific articles. His 2006 article in *Nature*, "Does Gender Matter?," was triggered by the now infamous statement by Larry Summers, president of Harvard University at the time, suggesting that the under-representation of female scientists at elite universities may stem in part from "innate" differences between men and women.

Dr. Barres, who wrote from the perspective of a transgendered person, had the unique vantage of having experienced gender bias firsthand as a woman during his early career. Shortly after he transitioned, he said he heard a faculty member say, "Ben Barres gave a great seminar today, but then his work is much better than his sister's."

"You become aware of the differences in how people treat you," he told the *Stanford Daily* in 2013. "When I was at MIT, I couldn't get into a good lab, and they were all headed by men. I had the grades, I worked hard, I had everything I needed."

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"Nothing has changed," he continued. "Women also assume that things are okay, but they aren't. There's a lot of work left to do. There are real barriers, and they're pervasive." Although Dr. Barres is widely recognized for having gone well above and beyond in his defense of women in science, he suggested that women also need to be less complacent.

THE QUEST FOR TENURE

Bibiana Bielekova, MD, is one woman researcher who says she could not be complacent, and she decided to do something about it. After completing a three-year postdoctoral research fellowship at the National Institute of Neurological Disorders and Stroke (NINDS) Neuroimmunology Branch, she remained there for an additional five years as a staff physician, focusing on the development of novel therapies for multiple sclerosis (MS). In 2005, Dr. Bielekova became an associate professor of neurology with tenure and director of the Waddell Center for MS at University of Cincinnati, but moved back to the NINDS as an investigator in 2008. She was told that she would return to a tenure track because she had not demonstrated independence.

"At the time, I did not particularly care because above all, I was interested in developing new treatments for MS and thought I could do so more readily at the NIH," she explained. In 2015, Dr. Bielekova broke through the first hurdle towards tenure when the board of scientific counselors recommended her for tenure. The board concluded that she "is an excellent physician scientist. Her international reputation is well-deserved and strongly supports consideration for tenure."

But the second hurdle, director support, was tougher. "My director told me that he would not be starting the tenure procedure, that he was going to think about it for an additional two years," she said. Dr. Bielekova, whose laboratory is studying mechanisms of immunoregulation and immune-mediated central nervous system (CNS) tissue injury in MS and other neuroimmunological diseases, filed an Equal Employment Opportunity complaint against her institute's director and two others in January of 2016.

DR. AMY R. BROOKS-KAYAL said underrepresentation at academic symposia are one of the unique challenges facing women neuroscientists.

"I realized at that point that many women in my position had made the decision *not* to fight for a number of very good reasons; besides the legal fees, you expose yourself and make yourself more vulnerable, and the process is very isolating and unpleasant," she said. "I felt that it was my responsibility to the next generation of female neuroscientists to do something for them."

"Women are considered second-rate citizens," she told the *Washington Post* in an interview last August. "They are fully aware that this is happening, the leadership. It's happening with their blessing." Just 22 percent of the tenured research scientists at intramural NIH are women, up from 19 percent in 2011, according to the institution. About 38 percent of the scientists now on the track toward tenure are women, up from 36 percent in 2011. At the NINDS, three women and 34 men hold tenured positions.

"I'm concerned about the drop-off in numbers of women with tenure. It's bad for women and it's bad for the NIH," Walter J. Koroshetz, MD, FAAN, director of the NINDS told *Neurology Today* in a telephone interview. Currently, the tenure track at the intramural (internal research) program at NINDS includes six men and six women; two of these women have already started the tenure process and their research has been rated as outstanding.

THE IMPLICIT ASSOCIATION TEST

The Implicit Association Test (IAT) measures attitudes and beliefs that people may be unwilling or unable to report. The IAT may be especially interesting if it shows that you have an implicit attitude that you did not know about. For example, you may believe that women and men should be equally associated with science, but your automatic associations could show that you (like many others) associate men with science more than you associate women with science. Take the test and see: **https://implicit.harvard.edu/implicit/takeatest.html**

Dr. Koroshetz said he is unable to comment on the Bielekova case due to the pending legal action, but, he added: "Like in any other neurology department, the pieces in the NINDS clinical program need to fit together, and multiple factors come into play before deciding to bring someone on for life. Also unique to the NIH, where all support comes from tax dollars, sometimes, hard programmatic decisions need to be made by the director in order to make the most of the taxpayer's investment in neurology research."

Dr. Koroshetz had worked under Anne Young, MD, PhD, for 20 years at the Massachusetts General Hospital and under former NINDS Director Story Landis, PhD, FAAN, for ten years, and trained a number of women neurologists in Boston. He considers himself a strong proponent of women in neuroscience and neurology. He is working with Hannah A. Valantine, MD, chief officer for scientific workforce diversity at the NIH, on a committee dedicated to trying to resolve the gender balance as soon as possible.

He explained that NIH salary limits can be prohibitive to hiring women clinician-scientists at the tenured level, who, by definition, are very successful at their universities and hospitals. Intramural NIH can be much more successful at recruiting early-stage women clinician-scientists because NIH's 100 percent research mission and the stable resources are so attractive. The other constraint in hiring at NIH is the flat funding it received between 2004 and 2016, which made funds for recruitment dependent upon attrition by retirement. Since becoming NINDS director last year he has only hired one tenure track-investigator, a woman physician-scientist.

SEEKING R01 RESEARCH GRANTS

The competitive R01 research grants (the signature research project grant mechanism used at the NIH) have also been under scrutiny. In a December 2016 *Scientific American* viewpoint, "Science Has a Gender Problem," Dr. Valantine explained that after three to four years of a research grant, scientists must convince the NIH that they have gotten results to continue receiving money for more research.

"In a text-mining analysis of comments used by 'peer' scientists to review grants, researchers discovered that those reviewers used more laudatory words such as 'outstanding' and 'excellent' to describe women's applications yet scored them lower than submissions by men," she wrote, concluding this evidence suggests that reviewers use different standards to judge applications from women.

"I think the NIH has an enormous responsibility along these lines that they are not fulfilling," Dr. Barres told *Neurology Today*. "Given that it is illegal to use federal funds to train primarily men and not women, and given that R01 research grants provide much of the funding for the research that is done, I believe that one of the criteria when reviewing R01 grants should be the diversity of the trainees in that faculty member's lab."

At present, all that is judged is the quality of the proposed research, he explained, "but given that there are not sufficient funds to fund more than about 10 to 20 percent of R01 grant applications these days, it would be earth-shattering if NIH decided to use as a secondary review criterion the diversity of the principal investigators' past and present trainees."

He proposed that science would still be the primary criteria, but in this competitive environment, if faculty [were aware that] diversity of trainees could tip the balance, he believes that it would go a long way in consciously reminding them of their obligations to train diverse students and postdocs.

Dr. Koroshetz is indeed concerned that women are being lost between the end of their training and application for an R01 grant. He said that at the post-doc level there is gender equity, and women who apply for a first R01 are equal or slightly more successful in getting funded. However, men are twice as likely to submit a new RO1 application as women, he noted. A study he finds insightful from the University of California, Berkeley concluded that "family formation — most importantly marriage and childbirth — accounts for the largest leaks in the pipeline between PhD receipt and the acquisition of tenure for women in the sciences."

Dr. Koroshetz feels we need to level the playing field for women in science. In an effort to mitigate this "leaky pipeline," new NINDS post-doc grants can be funded for an additional six months for those who have children.

Dr. Koroshetz believes that the NIH has become hypercompetitive over the past two years due to budgetary constraints. "It takes someone who is almost obsessed with a career in science to stay on board; I think many talented women scientists with a passion for research ultimately decide to move to a job with more security for the sake of their family, and our collective challenge is to enable them to follow their passion."

UNDERREPRESENTATION IN ACADEMIC SYMPOSIA

Amy R. Brooks-Kayal, MD, FAAN, professor of pediatrics, neurology and pharmaceutical sciences at the University of Colorado and chief of child neurology and the Ponzio Family Chair in

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Pediatric Neurology at the Children's Hospital Colorado, said multiple career challenges are unique to female neuroscientists, including underrepresentation at academic symposia.

"We need to encourage organizers to provide (gender) balance because those forums provide unique opportunities to allow scientists to present their work," she said.

When there is preferential selection because male speakers are thought of first, they become better known for their research by the audience, they have improved chances for getting papers accepted by journals, and ultimately, can build better resumes leading to better career options, including tenure, she explained.

Dr. Brooks-Kayal is optimistic, however, that speaking up can help remedy these inequities. After a recent symposium in her field in which no women were chosen as speakers, a group of colleagues brought their concerns to the organizers and they committed to include women as speakers in the future and achieve better balance. "We may have to look a little harder to find women speakers, but it's important so that we don't transmit that implicit bias — that men are more qualified than women — to future generations," she said.

Dr. Bielekova believes that implicit (unconscious) bias is the main reason women are held back from tenure. "How we speak, dress, and attack problems is different from white males so they view us in a different light," she said.

Dr. Barres said he has observed that talented women enrolled in universities are still having trouble being admitted into the very best labs (crucial for their future success) and are not given the same hallway advice or treated in the same confidence-building way as men are. He agrees that much of this is just due to the same old unconscious bias.

"But the older I get, the more I think a lot of that bias is not so unconscious," he added. "I have long trained an equal number of male and female grad students and postdocs in my lab — and I understand that how they eventually do is in great part in my hands. It is my job to build the confidence of both the men and the women, to maintain their passion for research, and to make sure they have the skills to survive in a competitive world in their own labs."

"The women in my lab are every bit as creative and smart as the men," he continued, "and they will 'lean in' and have the same ambition and success as men, in an environment that supports and promotes this."

If others took this on as a responsibility, more women could be successful, he said.

Orly Avitzur, MD, MBA, an associate editor of Neurology Today *and chair of the AAN Medical Economics and Management Committee, is co-chairing a full-day workshop at the AAN Annual Meeting with Janice Massey, MD and Barbara Hoese on women in leadership on Saturday, April 22, 2017, for those interested in gaining better understanding of gender issues in neurology. The program will also feature Katie Donovan, an expert on equal pay in the workplace.* •

LINK UP FOR MORE INFORMATION:

- Graduate Enrollment and Degrees: 2004 to 2014. Council of Graduate Schools. **http://bit.ly/graduatedata**
- Avitzur O. In Practice: Gender salary inequality worst in neurology: What can be done to remedy the matter? *Neurology Today* 2016: 16(22):17-18. **http://bit.ly/salarydisparity**
- AAN Annual Meeting Abstract P2.390: Miller E, Elkind M. Days of the giantesses: Voices of women pioneers in neurology. **http://bit.ly/Abstract-womenresearchers**
- Teo N. Transgender professor advocates for women in science. *The Stanford Daily* 2013. Oct 4, 2013. **http://bit.ly/transgenderprofessor**
- Bernstein L. Health & Science: At NIH, one woman says gender bias has blocked promotions. *The Washington Post* 2016. Aug 28, 2016. **http://wapo.st/2jvLDl9**