

5 Questions With James C. Tsai, MD, MBA

Dr. Tsai reflects on his research interests in neuroprotection, visual function, and glaucoma surgery as well as the benefits of a liberal arts education to exploring these topics.



What led to your glaucoma fellowship at Moorfields Eye Hospital in London?

During my residency at Doheny Eye Institute and my fellowship at Bascom Palmer Eye Institute, I came to recognize the value of learning from

outstanding clinicians, especially with regard to taking care of patients with a chronic disease that is difficult to manage like glaucoma. I decided what would most benefit my future patients would be for me to obtain the best possible training from exceptional academic physicians worldwide. To my knowledge, Moorfields is the oldest eye hospital in the world, and some of their approaches to managing glaucoma were quite different from what I had learned at Doheny and Bascom Palmer. I became a better clinician from my exposure to that diversity of opinion. I had many great mentors at Moorfields, but Professors Roger Hitchings and Peng Khaw particularly stand out. I formed a lot of friendships during my time at Moorfields; it was a wonderful opportunity to gain a European perspective and to enhance my global passion for ophthalmic education and training.

The search for neuroprotection in glaucoma has been fraught with disappointment. What is needed before neuroprotection can become a part of clinical practice?

This pursuit is going to be a difficult road, but our patients are asking us to travel it. Now that we know that elevated IOP is not the only cause of glaucoma, we need to investigate what kinds of therapy would be effective for our patients in whom IOP is not the major causative risk factor. That is why the scientific field is interested in neuroprotection, neuroenhancement, and neuroregeneration.

In 2001, Stephen Strittmatter, MD, PhD, a neurologist at Yale School of Medicine, identified a receptor-mediated Nogo inhibition of axonal regeneration in the central nervous system.¹ Since my arrival at Yale in 2006, Dr. Strittmatter and I have been collaborating on

FAST FACTS

- Robert R. Young professor of ophthalmology and visual science, chair of the Department of Ophthalmology and Visual Science at the Yale University School of Medicine, and director of the Yale Eye Center in New Haven, Connecticut, 2006 to present
- Chief of ophthalmology at Yale-New Haven Hospital, 2006 to present
- Chair of the Advocacy and Governmental Relations Subcommittee, Patient Care Committee for the American Glaucoma Society, 2011 to present
- President of the New York Glaucoma Society, 2011 to present; elected member of the American Ophthalmological Society, New York Ophthalmological Society, and American Eye Study Club
- Secretary for English Language Region for the Pan American Association of Ophthalmology, 2011 to present
- Chair of the Glaucoma Subcommittee for the National Eye Health Education Program of the National Institutes of Health, 2010 to present
- Chair of the Global Ophthalmic News & Education Network Advisory Board of the American Academy of Ophthalmology, 2008 to present
- Past president (2011-present) and president (2008-2010) of the Chinese American Ophthalmological Society
- Chairman of the Medical Advisory Board of The Glaucoma Foundation, 2006 to present
- Former member of the Medicare Evidence Development Coverage Advisory Committee (MEDCAC) of the Centers for Medicare & Medicaid Services, 2008 to 2010
- Past Consultant to Ophthalmic Devices Panel of the Food and Drug Administration, 2001 to 2008
- Associate examiner of the American Board of Ophthalmology, 1999 to present
- Recipient of the American Academy of Ophthalmology's Senior Achievement Award (2009) and Visionary Award from Fight for Sight, Inc. (2007)

research projects to investigate the effects of inhibition of the Nogo receptor in promoting neuroenhancement in glaucoma. Previously, my laboratory confirmed the neuroprotective effects of cytokines such as erythropoietin. Given the apparent success of erythropoietin in animal models of glaucoma, we are undertaking new experiments to study the neuroprotective and neuroregenerative properties of novel anti-Nogo receptor-blocking compounds.

The amount of noise and variation with standard automated perimetry has required clinical trials of neuroprotective drugs to be planned for 3 to 5 years to reach an observable outcome. For neuroprotection to become a part of clinical practice, researchers must find a means by which to shorten the duration of these clinical trials, thereby making it more attractive for industry to pursue the clinical development of neuroprotective agents. A key to this effort will be for the academic glaucoma community to develop new visual function technologies (other than standard automated visual field testing) to characterize and confirm disease progression. That is why my collaborators and I have explored the efficacy of the isolated check visual evoked potential (VEP) for this purpose.

How does the testing of VEP fit into the development of neuroprotective drugs?

Currently, the majority of our clinical studies have not looked at whether we are preserving visual function in glaucoma. All they have assessed is whether there has been a reduction in IOP in patients with glaucoma. These are very different measures. In the latter, lowering IOP only decreases a validated risk factor for the development and progression of glaucoma. Because a significant number of neuroprotective agents are unlikely to lower IOP, we cannot rely on this outcome to demonstrate their potential efficacy. It is my hope that isolated check VEP technology will provide information on visual function in addition to data obtained with more conventional visual field testing. Although I do not anticipate that testing with VEPs will become a standard component of glaucoma management in the near future, I do believe that it will become a valuable research tool in the study of neuroprotective agents.

How did you become involved in current research on glaucoma drainage devices, and what impact will these studies have on surgeons' use of this treatment modality?

I have been honored to serve as the thesis advisor to Panos Christakis, a Yale medical student who was the

first author of the recent publications from the Ahmed Versus Baerveldt (AVB) Study. (Ike Ahmed, MD, at the University of Toronto is the lead principal investigator.) At Yale, every medical student must complete a thesis to graduate, and Panos approached me about serving as his thesis advisor. I have enjoyed my role as a consultant to this international surgical trial as well as as a mentor for this talented and exceptional medical student who was recently matched at the University of Toronto for his residency in ophthalmology.

The Tube Versus Trabeculectomy (TVT) Study, the Ahmed Versus Baerveldt Comparison (ABC) Study, and the AVB Study are familiarizing surgeons worldwide with the indications for, effectiveness of, and unique complications of glaucoma drainage devices. This research has provided glaucoma surgeons with greater insight into how to individualize their glaucoma surgical procedures to achieve the best outcomes for their patients. As a result of these studies, I believe that surgeons will have a greater interest in using these aqueous drainage devices.

You recently became a member of the Board of Trustees at Amherst College. What do you hope to achieve?

Amherst has been one of the major influences in my life, and it provided me with a strong liberal arts background in science. While there, I majored in neuroscience, which entailed my taking courses in the social sciences, mathematics, and the humanities in addition to the traditional sciences.

As a member of Amherst's Board of Trustees, I have supported the college's efforts to build a new, state-of-the-art science center. I hope to help the college in promoting global academic excellence and the utility of an undergraduate liberal arts education for scientists, engineers, and physicians. In my opinion, for medical care to be successful, we must treat the whole person and not just his or her disease. The liberal arts can teach us a lot about humanity and suffering. Its broad education will allow us as physicians to connect better with our patients and individualize their therapy.

Given the challenges inherent in practicing medicine today, I have to remind myself daily what an incredible privilege it is to be a physician. Patients respect and value our clinical judgments, and we clinicians are in a unique position to make a difference in their lives. There are few professions where, everyday, one can see the direct impact of one's knowledge, hard work, skill, integrity, and compassion. ■

1. Fournier AE, GrandPre T, Strittmatter SM. Identification of a receptor mediating Nogo-66 inhibition of axonal regeneration. *Nature*. 2001;409(6818):341-346.