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Academia Ophthalmologica Internationalis

January 15, 2025

Dear 2026 Helen Keller Prize for Vision Research Selection Committee,

I am pleased to nominate Professor Tien Y. Wong for the 2026 Helen Keller Prize for Vision Research. I have known Tien for many years and have always been impressed by his dedication and commitment to improving the quality of eye care for patients and populations around the world.

Tien is first of all an outstanding ophthalmologist and a physician-scientist who is also a remarkable academic leader in ophthalmology. Over 3 decades, he has made substantial scientific and professional contributions to ophthalmology, towards a better understanding of the global epidemiology, burden, and risk factors of visual impairment and major eye diseases. In particular, he has focused his work on leading causes of blindness in Asia such as myopia. Tien's seminal research from the early 2000s, documenting the prevalence, trends, and risk factors for eye diseases in Asia has resulted in significant advances in our understanding of these problems in Asia, which of course covers more than half of the world's population and is increasingly important since >50% of patients with visual impairment, by the year 2040, will be in Asia.

Education, Training and Career

Tien attended medical school at the National University of Singapore and completed his ophthalmology residency at the Singapore National Eye Center (SNEC) in the 1990s. He then completed medical retinal fellowships at SNEC and Westmead Hospital, University of Sydney, Australia. From 1996 to 2002, he continued his training in the US and obtained an MPH & PhD in epidemiology from Johns Hopkins University Bloomberg School of Public Health as well as a research fellowship at the University of Wisconsin, Madison, USA.

Tien joined the University of Melbourne as a young faculty member and was promoted to Professor in 2006 and subsequently became Head of Ophthalmology. When he returned to Singapore, he has held senior leadership positions including being the Executive Director of the Singapore Eye Research Institute and Chair of Ophthalmology at the National University of Singapore. From 2014 to 2021, Tien was Arthur Lim Professor of Ophthalmology and Medical Director at SNEC, which today remains one of the largest tertiary eye hospitals globally. SNEC is a major training and research center in Asia, and has trained numerous ophthalmologists and vision scientists around the world.

In 2022, Tien was appointed Chair Professor and the Founding Head of Tsinghua Medicine, a new academic healthcare system based at Tsinghua University, Beijing, China. His role in China is to set up a new academic health system that brings together multiple University Schools and related hospitals and healthcare related entities, including Schools of Basic Medicine, Clinical Medicine, Pharmaceutical Sciences, Biomedical Engineering, and related teaching hospitals.

I understand the aim of Tsinghua Medicine is to transform medical education, and promote translational and inter-disciplinary research across Beijing and China. He was the Vice Provost of Tsinghua University in 2023 and Senior Vice Chancellor of Tsinghua Medicine in 2024.

Research Focus, Outcomes and Impact

Tien has had a remarkable scientific track record. He has a prolific academic research output, and has published >1500 peer-reviewed papers, including papers in all the major journals such as the *New England Journal of Medicine*, the *Lancet, JAMA*, and *Nature Medicine*. His papers have been cited nearly 250,000 times and he has a H-index of >200. He has been a Highly Cited Researcher for five years in succession (2020- 2024).

Tien's research contribution is broad and covers diabetic retinopathy, agerelated macular degeneration and myopia, three of the major causes of blindness worldwide. This has spanned classic epidemiology and population studies, clinical and translational research projects and studies in Singapore, Australia, US and elsewhere. Two areas of his research are of particular significance from my viewpoint

Diabetic Retinopathy: A key focus of Tien's work has been on diabetic retinopathy, which he has made two-decade long research discoveries and contributions covering epidemiology, clinical research and clinical trials. For example, in Singapore, Tien initiated a large population-based study involving 10,000+ Chinese, Indians and Malay subjects in Singapore, called Singapore Epidemiology of Eye Disease (SEED) Program, in which he has examined the prevalence and risk factors of diabetic retinopathy in Asia (Wong et al. Arch Ophthalmol 2008; Wong et al, Ophthalmology 2008, see **References 1,2**).

He has led global collaborative teams to document the size and burden of diabetic retinopathy globally (Yau et al. Diabetes Care 2011, **3**) and show that "classic retinopathy signs" are common even in persons without diabetes, which challenge the current diagnostic criteria for diabetes itself (Wong et al., Lancet 2008, **4**). Based on this paper, *WHO* and the *American Diabetes Association* have reviewed the diabetes diagnostic criteria.

Closely aligned to his epidemiological work is in the field of retinal vascular imaging. He led research that have led to the generation of unique, novel techniques showing "retinal vascular changes" could be useful to understand pathways and key mechanisms in the development of diabetic retinopathy and its related systemic complications, such as stroke and kidney disease. He has shown that identifying and measuring subtle changes in the retinal blood vessels using advanced computer imaging techniques (such as quantifying in micrometers the widening of the retinal venules) may provide signals of early, subclinical stages of DR disease and thus a patient's future risk of DR. His pioneering work on using retinal imaging to predict stroke (Wong et al, Lancet 2001, 5), coronary artery disease (Wong et al, JAMA 2002, 6), hypertension, congestive heart failure (Wong et al. JAMA 2005, 7) and subclinical small vessel disease stroke (Lindley et al. Lancet Neurology 2008, 8), amongst others, have been widely cited and used as the basis for many different research programs.

This retinal vessel analysis program has also been applied in studies across the US, Australia, Asia and Europe, which have resulted in extensive and seminal papers on retinal vascular imaging published.

Artificial Intelligence: The second area that I would like to highlight is in the more recent but exciting field of AI in ophthalmology that Tien and his team have made in the past decade. AI is, of course, now a key focus research area in the US and globally.

Tien's principal innovation is in the early development, use and application of AI and deep learning to detect diabetic retinopathy from retinal images (Ting et al. JAMA 2017, **9**). From 2012 to 2017, his team led the initial development, evaluation and clinical validation of his AI-deep learning algorithm (SELENA+) that could accurately detect diabetic retinopathy (>95%) and related diseases such as macular degeneration and glaucoma. This was then tested and validated using 500,000 images across 10 populations of diverse ethnic groups and countries, including more challenging settings such as Zambia, Africa.

Tien demonstrated that such Al-deep learning methods applied to the same digital retinal images can also accurately detect and predict a range of systemic chronic diseases, such as chronic kidney disease (Sabayanagam et al. Lancet Digital Health 2020, **10**), optic disc papilledema (Milea et al. NEJM 2021, **11**), heart disease (Cheung et al. Nat Biomed Eng 2021, Rim et al. Lancet Digital Health 2022, **12**, **13**), Alzheimer's disease and dementia (Cheung et al. Lancet Digital Health 2022, **14**). These approaches provide opportunities to screen community-based populations for kidney, heart disease and dementia without the need for inaccessible and expensive tests such as cardiac CT scans or brain MRI. Tien Wong's work laid the foundation for a new inter-disciplinary field, now termed "oculomics", where imaging of the eye is a "window" to study and predict systemic cardio-metabolic diseases.

To integrate and implement SELENA+ and other AI-deep learning algorithms into the healthcare system, Tien conceptualized and started Singapore's first national "telemedicine" screening program for diabetic retinopathy, referred to as the Singapore Integrated Diabetic Retinopathy Programme (SiDRP). Then, to demonstrate the value of integrating AI-deep learning to SiDRP, he led economic modelling studies (Xie et al. Lancet Digital Health 2020, **15**). The SELENA+ algorithm was eventually integrated and implemented in Singapore's public healthcare system and represents one of the world's first country-level adoption of an AI algorithm as a software-asa-medical-device (SaMD) solution (Gunasekeran et al. NEJM AI 2024, **16**).

Tien has continued to work on novel AI-deep learning methods to predict future risk of diabetic retinopathy (Li et al. Nature Medicine 2024; **18**) and the world's first integrated vision-large language model (vision-LLM) to assists primary care providers with individualized diabetes management guidance (Li et al. Nature Medicine 2024; **19**). Tien has now outlined a roadmap for the evolution of future medical AI models, moving from current disease-centric models towards models focused on "maintaining health", a concept referred to as Universal Health AI (UHAI). (Ma et al. NEJM AI 2024; **20**).

Professional Contributions, Honors and Awards

Tien has contributed to many international and national committees including Boards of the International Council of Ophthalmology (ICO), the Asia Pacific Academy of Ophthalmology (APAO), Opthalmology Foundation, and ARVO. He has been recognized with numerous prestigious awards, such as the Alcon Research Institute Award, the Arnall Patz Medal from the Macula Society, the Eisenhower Fellowship and the Singapore Presidents Award for Science and Technology. Of note, he is an elected member of the Academia Ophthalmologica Internationalis (AOI) and the American Ophthalmological Society (AOS), one of few Asians in these two prestigious learned societies. More impressively, Tien is one of few ophthalmologists worldwide (and the only one outside of US, I believe) to be elected as a foreign member of the U.S National Academy of Medicine.

For his work in medical education and healthcare services in China, Tien was awarded the Beijing Great Wall Friendship Award in 2024, the highest honor (given once every 3 years) to foreigners who have made significant contribution towards the development of Beijing and China.

In conclusion, Prof Tien Wong has led a stellar career as an outstanding academic ophthalmologist-leader who has made substantial and impactful scientific, professional, and academic contributions to our understanding of the epidemiology, burden and management of visual impairment and major eye diseases.

For these reasons, I strongly recommend Professor Tien Wong for the 2026 Helen Keller Vision Prize.

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Richard L. Abbott, M.D. President Academia Ophthalmologica Internationalis

Top 20 Representative Publications (from >1,500 paper) *Corresponding author

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Nomination for Professor Tien Y Wong for 2025 Helen Keller Prize for Vision Research

It is my deepest honor to nominate Professor Tien Y Wong for the 2025 Helen Keller Prize for Vision Research

I have known Tien for several decades now as a professional colleague, physician-scientist and international collaborator.

Our primary area of interest and collaboration is in the field of retinal diseases, particularly diabetic retinopathy and age-related macular degeneration, as well as rapidly emerging field of artificial intelligence (AI) and the application of AI for translational clinical research in ophthalmology, for which we were fortunate to co-author the first editorial in *JAMA* on AI in medicine in 2016, before AI was a household term in the peer-reviewed literature. I also know him from his various senior professional and leadership roles in ophthalmology he has played internationally and in the Asia-Pacific region, such as the Asia Pacific Academy of Ophthalmology and Asia Pacific Vitreo-retinal Society. I also work closely with him as an Editorial Board member of JAMA Ophthalmology, of which I am the Editor in Chief

Tien is a practicing ophthalmologist, retinal specialist and academic leader who has made remarkable contributions to the field of ophthalmology and vision science, not only with the application of AI technology to ophthalmology and vision research, but also in the broader area of medicine and public health over three decades.

Current and Past Position

Over 3 decades, he has also held esteemed senior academic and clinical leadership roles in Singapore, Australia, and now in China throughout his distinguished career.

In 2022, Tien assumed the role of Founding Senior Vice-Chancellor and Chair Professor of Tsinghua Medicine at the prestigious Tsinghua University in Beijing, China. His role in China is to set up a new academic health system that brings together multiple University and healthcare related entities, including Schools of Basic Medicine, Clinical Medicine, Pharmaceutical Sciences, Biomedical Engineering, related research institutes and affiliated hospitals. Such systems, seen at Johns Hopkins and other major US academic medical institutions, are uncommon in China.

From 2014 to 2021, Tien was Arthur Lim Professor of Ophthalmology and Chairman of at the Singapore National Eye Center (SNEC), certainly one of the leading eye hospitals in Asia and possibly globally, with >100 full time ophthalmologists across 10 sub-speciality departments, managing >400,000 outpatient visits yearly. Tien was instrumental to SNEC's international reputation and impact over that period. Tien was also concurrently Vice-Dean and Deputy Group CEO for academic affairs, research and education at the broader SingHealth Duke-NUS Academic Medical Centre, with >30,000 staff across 11 hospitals and healthcare institutions, including Singapore General Hospital (ranked #8 best hospital, https://www.newsweek.com/best-hospitals-2020), and 5 national specialty centers (Cancer, Heart, Neuroscience, Eye, Dental).

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In Singapore, Tien was also previously Executive Director of the Singapore Eye Research Institute (SERI) and Chair of Ophthalmology at National University of Singapore. Prior to these, Tien was Professor and Chair of Ophthalmology at the University of Melbourne, Australia, and Managing Director of the Centre for Eye Research Australia.

Research Contribution in Ophthalmology

Tien is an internationally recognized, outstanding physician-scientist in ophthalmology who has made seminal research contribution to our understanding of a wide range of eye diseases, including diabetic retinopathy, age-related macular degeneration and myopia, three one of the major causes of blindness in the US and worldwide. This has spanned a wide range of epidemiology, clinical and translational research projects in Singapore, Australia, US and elsewhere. He has an extensive publication record, >1500 papers with a notable H-index of over 200. He has published in the best ophthalmology journals as well as in general journals such as the *New England Journal of Medicine, The Lancet, JAMA, Nature Medicine* and *Nature*.

However, two areas of his research are of particular significance from my viewpoint for the Helen Keller Prize

Diabetic Retinopathy: Tien's major research contribution has been on diabetic retinopathy, which he has made two-decade long research covering epidemiology, clinical and translational research, including retinal imaging and clinical trials.

Tien has led international multi-centered epidemiological studies on diabetic retinopathy. In Singapore, Tien initiated and successfully completed three large population-based studies involving 10,000+ Chinese, Indians and Malay subjects in Singapore (Singapore Epidemiology of Eye Disease (SEED) Program) in which he has examined the prevalence and risk factors of DR in Asia. In a major collaborative study, he led a team to document the size and burden of diabetic retinopathy globally; this paper is one of the most highly cited papers in diabetic retinopathy (*Diabetes Care 2010*). In another major paper, he led a multi-centre collaborative meta-analysis including >12,000 persons from three population studies in the US and Australia and showed that retinopathy signs were common in persons without diabetes, challenge the current diagnostic criteria for diabetes itself (*Lancet 2008*). Based on this paper, the *WHO* and *American Diabetes Association* has reviewed the diabetes diagnostic criteria. Based on this research, Tien has led to Singapore's national diabetic retinopathy screening program using telemedicine (*Ophthalmology 2016*). This is a model for other countries in Asia, but also even including the US.

Closely aligned to his epidemiological work in diabetic retinopathy is in the field of novel retinal imaging. He led seminal research that have led to the generation of unique, novel research technique showing "retinal vascular changes" could be useful to understand pathways and key mechanisms in the development of diabetic retinopathy and its related systemic complications, such as stroke and kidney disease. He has shown that identifying and measuring subtle changes in the retinal blood vessels using advanced computer imaging techniques (such as quantifying in micrometers the widening of the retinal venules) may provide signals of early, subclinical stages of DR disease and thus a patient's future risk of DR. His pioneering work on using retinal imaging to predict stroke (*Lancet 2001*), coronary artery disease (*JAMA 2002*), diabetes (*JAMA 2002*), MRI brain disease (*JAMA 2002*) hypertension (*Annals Intern Medicine 2003*), congestive heart failure (*JAMA 2005*) and others have been widely cited and used as basis for many different research programs. This retinal vessel analysis program has also been applied in studies across the US, Australia, Asia and Europe, which have resulted in extensive and seminal papers on retinal vascular imaging published.

Finally, Tien has led many clinical studies and trials on diabetic retinopathy. He has led clinical studies and programs on novel risk factors, and has been a major thought leader on clinical management of diabetic macular edema, including the appropriate use of anti-vascular endothelial growth factor (VEGF) therapy. Tien is the lead for the International Council of Ophthalmology Diabetic Eye Care Guidelines (*Ophthalmology 2018*).

Artificial Intelligence: The second area that I would like to highlight is in the exciting field of AI in ophthalmology that Tien and his team has made in the past 7 years. AI is the now a critical part of the new research platforms at NIH/NEI and globally.

Tien has made substantial progress in Al research particularly for diabetic retinopathy. One of his major contributions has been to develop, validate and more importantly, implement an algorithm to detect diabetic retinopathy (*JAMA 2017*). This algorithm has been tested and validated in multiple populations even in Africa (*Lancet Digital Health 2019*). From this work, Tien set up the world's first national "Al-telemedicine" screening program for diabetic retinopathy in Singapore. More recently, in China, he has led an international consortium to use Al to predict time to progression of diabetic retinopathy, allowing the possibility that screening intervals for screening can be extended to 5 years for some patients (*Nature Medicine 2024*). *This will have major implications for diabetic retinopathy screening programs globally.*

Awards, Honors and Leadership in Global Vision Research

Tien 's remarkable achievements in both research and professional practice have garnered him numerous prestigious awards, highlighting his exceptional contributions to the field. He has been recognized with multiple international awards. I shall highlight a few.

Tien is one of few researchers outside of the US to win the Alcon Research Institute Award, USA. Tien is also one of only 2 ophthalmologists worldwide to receive the Novartis Global Prize in Diabetes for his work on diabetic retinopathy. At different societies, he has been awarded the highest level accolade for these societies. For example, he has been awarded the Arnall Patz Medal from the Macula Society), the Jose Rizal Medal from the Asia Pacific Academy of Ophthalmology (APAO), and Friedenwald Award from ARVO.

At the University and country level, he has been recognized as the top researcher in any research field from two of global Universities: the Outstanding Researcher Award from the National University of Singapore and the Woodward Medal from the University of Melbourne. Tien has also received the highest award for biomedical research from any field in both Australia with the Australian Commonwealth Health Minister's Award for Excellence in Health and Medical Research in 2006 and in Singapore, with the President's Science Award in 2010 and President's Science and Technology Award in 2014.

He is an elected member of the Academia Ophthamological Internationalis (AOI) and the American Ophthalmological Society (AOS). More impressively, Tien is an elected foreign member of the U.S National Academy of Medicine (NAM), one of few ophthalmologists worldwide to be elected into the NAM.

Finally, at the international leadership level, Tien has also contributed to global eyecare and vision health and has served on Boards and Councils of major organizations such as the International Council of Ophthalmology (ICO), the Asia Pacific Academy of Ophthalmology (APAO), the Asia Pacific Vitreo-retinal Society and Macula Society. He was past President of the College of Ophthalmologists Singapore and current President of the Asia-Pacific Ocular Imaging Society (APOIS). He is currently an elected Trustee of ARVO

It is for this reasons that I am pleased and honored to nominate Professor Tien Y Wong for the 2025 Helen Keller Prize for Vision Research

Sincerely,

Neil M Bunten

Neil M. Bressler, MD – Chief, Retina Division (2005 – 2018) – Wilmer Eye Institute Department of Ophthalmology; Johns Hopkins University School of Medicine The James P. Gills Professor of Ophthalmology

Representative Papers on Diabetic Retinopathy

- 1. Wong TY, Klein R, Couper DJ, et al. Retinal microvascular abnormalities and incident clinical strokes. *Lancet* 2001:358:1134-40.
- 2. **Wong TY**, Klein R, Sharrett AR, et al. Retinal arteriolar narrowing and incident coronary heart disease in men and women. *JAMA* 2002; 287:1153-9.
- 3. **Wong TY**, Klein R, Sharrett AR, et al. Retinal arteriolar narrowing and risk of diabetes in middle-aged persons. *JAMA* 2002; 287: 2528-33.
- **4. Wong TY**, Rosamond WR, Chang PP, et al. Retinopathy and risk of congestive heart failure. *JAMA*. 2005 Jan 5; 293(1): 63-9.
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- 9. Wang FH, Liang YB, Zhang F,...**Wong TY**. Prevalence of diabetic retinopathy in rural China: the Handan Eye Study. <u>*Ophthalmology*</u> 2009;116(3):461-7.
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- 12. Wong TY, Cheung CM, Larsen M, Sharma S, Simó R. Diabetic retinopathy. *Nature Review Disease Primers*. 2016 Mar 17;2:16012.
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- 17. **Wong TY**, Tan TE. The Diabetic Retinopathy "Pandemic" and Evolving Global Strategies: The 2023 Friedenwald Lecture. Invest Ophthalmol Vis Sci. 2023 Dec 1;64(15):47.

Representative Papers on Al

- 1. **Wong TY**, Bressler NM. Artificial intelligence with deep learning technology looks into diabetic retinopathy screening. *JAMA* 2016;316(22):2366-2367.
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- 12. Dai L, Sheng B, Chen T,... Wong TY*, Jia W. A deep learning system for predicting time to progression of diabetic retinopathy. <u>Nature Medicine</u>. 2024 Jan 4 [Epub ahead of print]. *Joint last and corresponding author

NAME: Tien Y. Wong

eRA COMMONS USER NAME (credential, e.g., agency login): TIENWO

POSITION TITLE: Chair Professor & Senior Vice Chancellor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
National University of Singapore, Singapore	MBBS	1992	Medicine
Johns Hopkins University, USA	MPH	1997	Public Health
Wilmer Eye Inst, Johns Hopkins Hospital	Fellowship	1997	Ophthalmology
Royal College of Surgeons, Edinburgh, UK	FRCS	1999	Ophthalmology
University of Wisconsin, Madison, WI	Fellowship	2002	Epidemiology
Johns Hopkins University, USA	PhD	2002	Epidemiology
University of Sydney, Australia	Fellowship	2003	Retinal diseases
Royal Australian & NZ College of Ophthalmologists	FRANZCO	2004	Ophthalmology

A. Personal Statement

Professor Tien Wong completed medical school at the National University of Singapore (NUS). He obtained a MPH and PhD from the Johns Hopkins University, USA. In 2022, Tien Wong was appointed Chair Professor and Senior Vice-Chancellor of Tsinghua Medicine, a new academic healthcare system integrating multiple Schools and affiliated teaching hospitals, based at Tsinghua University, Beijing, China; he is concurrently the Vice Provost of Tsinghua University. From 2014 to 2021, Tien Wong was Arthur Lim Professor of Ophthalmology and Medical Director at the Singapore National Eye Center (SNEC). Tien Wong was concurrently Deputy Group CEO (Research and Education) and Vice-Dean at SingHealth Duke-NUS Academic Medical Centre, which comprise 11 hospitals and healthcare institutions. Prior to these, Tien Wong has served in leadership roles as Executive Director of the Singapore Eye Research Institute (SERI), Chair of Ophthalmology at the NUS, and Chair of Ophthalmology at the University of Melbourne, Australia.

Tien Wong is a practicing physician-scientist, and an internationally renowned retinal specialist, with broad clinical expertise and research focused on major retinal diseases, including diabetic retinopathy and age-related macular degeneration. His research includes classic epidemiology, translational ocular imaging studies and clinical trials and studies and, in the past 10 years, digital technology, AI, deep learning, large language models and their applications to ophthalmology. He has published >1600 papers (total citations, >250,000, Google H-index >220, https://scholar.google.com.sg/citations?user=f2XZEZ8AAAAJ&hl=en), with papers in major medical and scientific journals (e.g., New England Journal of Medicine, Lancet, JAMA, Nature and Nature Medicine etc). He is Highly Cited Researcher (2018, 2020, 2021, 2022, 2023, 2024), given >500 invited named, plenary and symposium lectures; and received >US\$100 million in grant funding. He is a two-times recipient of the Singapore Translational Researcher (STaR) Award (2008, 2014), the highest award for the most senior clinician-scientists in Singapore. Tien Wong is on the Editorial Boards of Lancet Digital Health, New England Journal of Medicine-AI and JAMA-Ophthalmology and previously on Boards of American Journal of Ophthalmology, Diabetes Care, Investigative Ophthalmology and Visual Sciences (IOVS) and British Journal of Ophthalmology, amongst many journals. He is an elected Trustee of the Association for Vision and Ophthalmology Research (ARVO), USA, the current President of the Asia-Pacific Ocular Imaging Society (APOIS) and Vice-President of the Asia-Pacific Vitreo-Retinal Society (APVRS). He is Council member of the Asia Pacific Academy of Ophthalmology (APAO) and the Asia-Pacific Teleophthalmology Society (APTOS). He has served on the Executive Committee of the Macula Society, the Board of the International Council of Ophthalmology (ICO), and was past President of the College of Ophthalmologists, Singapore. He was elected as fellow of the Singapore National Acdaemy of Science, an international (foreign) member the U.S. National Academy of Medicine (NAM) and international (corresponding) fellow of the Australian Academy of Health and Medical Sciences.

For his work in medical education development and healthcare services in China, Tien Wong was awarded the Beijing Great Wall Friendship Award in 2024, the highest honor (given once every 3 years) to foreigners who have made significant contribution towards the development of Beijing and China

B. Current Appointments

2022-date Founding Head and Chair Professor, Tsinghua Medicine, Tsinghua University, Beijing, China
2022-date Senior Advisor, Singapore Health Services & Singapore National Eye Centre, Singapore
2023-date Vice Provost, Tsinghua University, Beijing, China
2024-date Senior Vice-Chancellor, Tsinghua Medicine, Tsinghua University, Beijing, China

C. Education & Training

1992	MBBS	National University of Singapore, Singapore
1997	MPH	Johns Hopkins University School of Public Health, USA
1999	MMED	National University of Singapore, Singapore
1999	FRCSE	Royal College of Surgeons of Edinburgh, UK
1999	Fellowship	Research Fellowship, University of Wisconsin-Madison, USA
2002	PhD	Johns Hopkins University School of Public Health, USA
2004	FRANZCO	Royal Australian & New Zealand College of Ophthalmologists, Australia
2019	FRCOphth	Royal College of Ophthalmologists, UK

D. Previous Appointments

- 1992-99 Residency, Ophthalmology, Singapore National Eye Centre, Singapore
- 2001-03 Assistant Professor, Department of Ophthalmology, National University of Singapore, Singapore
- 2004-06 Associate Professor, Department of Ophthalmology, University of Melbourne, Australia
- 2006-08 Professor, Department of Ophthalmology, University of Melbourne, Australia
- 2007-08 Head, Department of Ophthalmology, University of Melbourne, Australia
- 2007-08 Managing Director, Centre for Eye Research Australia, Australia
- 2009-21 Professor, National University of Singapore, Singapore
- 2009-13 Executive Director, Singapore Eye Research Institute, Singapore
- 2010-14 Chair, Department of Ophthalmology, National University of Singapore, Singapore
- 2014-21 Vice-Dean, Duke-NUS Medical School, National University of Singapore, Singapore
- 2014-21 Arthur Lim Professor & Medical Director, Singapore National Eye Centre, Singapore
- 2014-21 Chairman, Board of Directors, Singapore Eye Research Institute, Singapore
- 2018-21 Deputy Group CEO, Research & Education, Singapore Health Services, Singapore

E. Elected Fellowships of Learned Societies

- 2010 Elected Member, Academia Ophthalmologica Internationalis (AOI)
- 2018 Elected Fellow, Singapore National Academy of Science (FSNAS)
- 2019 Elected Member, American Ophthalmological Society (AOS)
- 2020 Elected Member (Foreign/International), US National Academy of Medicine (NAM)
- 2021 Elected Member (Corresponding), Australian Academy of Health and Medical Sciences (FAHMS)

F. Editorial Board Appointments (Selected)

- 2000-05 Editorial Board Member, British Journal of Ophthalmology
- 2007-14 Executive Editor, American Journal of Ophthalmology
- 2009-17 Editorial Board Member, Diabetes Care
- 2005-18 Editorial Board Member, Investigative Ophthalmology and Visual Science
- 2018-date Editorial Board Member, JAMA Ophthalmology
- 2019-date International Advisory Board Member, The Lancet Digital Health
- 2023-date International Advisory Board Member, British Medical Journal
- 2023-date Editorial Board Member, New England Journal of Medicine AI (NEJM AI)

G. Honors and Awards (Selected)

- 1987 The President's Scholarship, Singapore
- 1999 The Scholz Award, Wilmer Ophthalmological Institute, Johns Hopkins University, USA
- 2004 Outstanding Researcher Award, National University of Singapore, Singapore
- 2004 Sandra Daugherty Award, American Heart Association, USA
- 2005 The Woodward Medal for Science and Technology, the University of Melbourne, Australia
- 2005 Fred Hollows Lecture, Australian Ophthalmic and Visual Sciences Meeting, Australia
- 2006 The Commonwealth Minister of Health Award for Excellence in Medical Research, Australia
- 2006 The Alcon Research Institute Award, USA
- 2007 The Australian Society for Medical Research AMGEN Medical Researcher Award, Australia
- 2007 Colin I Johnston Lecture, High Blood Pressure Research Council of Australia, Australia
- 2008 Singapore Translational Researcher (STaR) Award, National Medical Research Council
- 2010 National Outstanding Clinician Scientist Award, Ministry of Health, Singapore
- 2010 De Ocampo Lecture, Asia Pacific Academy of Ophthalmology (APAO)
- 2010 President's Science Award, Singapore
- 2010 Fred Hollows Lecture, Australian Ophthalmic and Visual Sciences Meeting, Australia
- 2013 Eisenhower Fellow, USA
- 2014 Arnall Patz Medal, Macula Society, USA
- 2014 President's Science and Technology Award, Singapore
- 2015 Tano Lecture, Asia Pacific Vitreo-Retinal Society
- 2016 Dawson Lecture, International Society for Clinical Electrophysiology of Vision.
- 2017 Sir Runme Shaw Memorial Lecture, Academy of Medicine Singapore
- 2018 Euretina Lecture, European Society of Retina Specialists
- 2019 Jose Rizal Medal, Asia-Pacific Academy of Ophthalmology (APAO)
- 2019 Norman McAlister Gregg Lecture, Royal Australian & New Zealand College of Ophthalmologists
- 2023 Friedenwald Award, Association for Research in Vision and Ophthalmology (ARVO), USA
- 2023 College Medal, College of Clinician Scientist, Academy of Medicine, Singapore
- 2024 The 16th Beijing Great Wall Friendship Award, City of Beijing, China
- 2024 Changjiang Scholar Award, Ministry of Education, China

H. Memberships of National & International Societies and Committees (Selected)

- 2008-10 Board Member, Ophthalmic Research Institute of Australia, Australia
- 2013-14 Vice-President, Singapore Medical Association, Singapore
- 2014 21 Chair, Clinician Scientist Award (CSA) Panel, National Medical Research Council, Singapore
- 2018 -19 Chair, Clinician Innovator Award Review Panel, National Medical Research Council, Singapore
- 2015 -23 Council Member, Academy of Medicine Singapore
- 2016 -19 Council Member, Singapore Medical Council, Singapore
- 2016 20 President, College of Ophthalmologists, Singapore
- 2016 -21 Council Member, Asia Pacific Tele-Ophthalmology Society
- 2018 20 Executive Committee, Macula Society, USA
- 2018 -20 Board of Trustees, International Council of Ophthalmology
- 2020 -23 Assistant Master (Academic Affairs), Academy of Medicine, Singapore
- 2017 -19 Member, National Health Innovation Centre Oversight Committee, Ministry of Health, Singapore
- 2015 20 Board Member, the Myopia Institute, Australia
- 2016 -20 Member, Global Advisors Committee, American Academy of Ophthalmology
- 2009-date Board Member, National Medical Research Council (NMRC), Singapore
- 2010-date Council Member, Asia Pacific Academy of Ophthalmology (APAO)
- 2017-date Vice President, Asia Pacific Vitreo-Retinal Society (APVRS)
- 2018-date President, Asia-Pacific Ocular Imaging Society (APOIS)
- 2019-date Chair, Singapore Biodesign Steering Committee, Singapore
- 2021-date Advisory Board Member, Saudi National Institute of Health (Saudi NIH)
- 2022-date Elected Board Trustee, Association for Research and Vision in Ophthalmology, USA
- 2023-date Member, Health Human Potential Review Committee, National Research Foundation, Singapore
- 2024-date Member, Subcommittee on International Members, National Academy of Medicine, USA

2024-date Member, Global Strategy Committee, Association for Research and Vision in Ophthalmology, USA

I. Sel	ected Recent Research Grants (Selected, total of >S\$80 million)
2004	National Medical Research Council (NMRC) 0796/2003, Singapore
	PI S\$568,472 1 January 2004– 31 December 2006
	The Singapore Malay Eye Survey (SiMES)
2005	National Health and Medical Research Council (NHMRC) 350448, Australia
	PI A\$208,625 1 January 2005– 31 December 2007
	Early retinal vessel changes in diabetes and the metabolic syndrome
2005	Science, Technology Innovation (STI) Grant, Victoria State Government, Australia
	PI A\$2,000,000 1 July 2005– 30 June 2008
	The Retinal Vascular Imaging Centre (RetVIC)
2008	National Health and Medical Research Council (NHMRC), 475605, Australia
	PI A\$397,863 1 January 2008– 31 December 2010
	Prediction of Microvascular Complications in Type 1 Diabetes Using Novel Retinal Vascular Imaging
2008	Biomedical Research Council (BMRC), 08/1/35/19/550, Singapore
	PI \$\$2,227,000 1 June 2008– 31 May 2012
2000	The Singapore Indian Chinese Cohort Eye Study
2008	National Medical Research Council (NMRC), NMRC/STaR/0003/2008, Singapore
	PI S\$ 8,993,731 1 April 2008–31 March 2013
2000	Retinal Imaging for Disease Prediction: From Bench to Bedside
2009	National Health and Medical Research Council (NHMRC), 52993, Australia
	Translational Clinical Research in Major Eve Diseases (TCR-Eve)
2010	National Health and Medical Research Council (NHMRC), 590212, Australia
2010	$PI = \Lambda \leq 1277$ 375 1 January 2010– 31 December 2013
	Novel Retinal Architectural Vascular Signs and Risk of Cardiovascular Disease: The AusDiah Study
2010	National Medical Research Council (NMRC) Centre Grant 2009 NMRC/CG/SERI/2010 Singapore
2010	Centre Director S\$9 000 000 1 April 2010 – 31 March 2013
	Multi-PlAtform Strategy for EveResearch (MASTER)
2010	National Medical Research Council (NMRC). IRG. R760/044/2010. Singapore
	PI S\$1.472.642 1 July 2010 – 30 June 2014
	The Singapore Malay Eye Study 2 (SiMES-2)
2010	A*STAR, Exploit Technologies Flagship Grant, ETPL/10-FS0001-SERI, Singapore
	PI S\$ 2,277,964 27 August 2010 – 26 August 2013
	Ocular Imaging Techonology
2013	Health Service Development Programme, Ministry of Health, Singapore
	PI \$\$11,825,963 1 April 2013 – 31 March 2022
	The Singapore Integrated Diabetic Retinopathy Programme (SiDRP)
2013	National Medical Research Council, STaR Award, NMRC/STaR/0016/2013, Singapore
	PI \$\$8,000,000 22 October 2013 – 20 April 2019
	Singapore Diabetic Retinopathy Epidemiology, Biomarkers and Imaging (DREAM) Program
2014	National Medical Research Council, CS-IRG, NMRC/CIRG/1371/2013, Singapore
	PI S\$1,499,975 10 January 2014 – 31 January 2018
	The Singapore Indian Eye Study 2 (SINDI-2)
2017	National Medical Research Council, NMRC OF-LCG, NMRC/OFLCG/001c/2017, Singapore
	Theme PI \$\$4,999,850 01 July 2017 – 30 June 2022
	DYNAMO: Diabetes Study on Nephropathy and other microvascular complications
2022	Ministry of Science and Technology, China
	PI KIVIB2,550,000 1 NOVEMBER 2022 – 31 December 2025
	Developing a dynamic prediction model and risk assessment system for common blinding eye diseases by
	compining multimodal imaging and integrating multi-omic data.

J. Contribution to Science

significant contribution to medicine and Tien Wong has made ophthalmology as а pioneering physician-scientist-innovator, clinical ophthalmologist and retinal specialist, and epidemiologist. Of particular significance, he as applied digital technology and artificial intelligence (AI) to develop innovative solutions for the screening, detection and prevention of major eye and systemic diseases via retinal imaging. Over nearly three decades and working in four countries (Singapore, Australia, USA, China), Tien Wong led international, multi-disciplinary teams that combined classic epidemiological studies with translational-implementation studies that applied the latest advances in AI, including machine learning, deep learning and generative AI. His research led to the eventual implementation of an Al-based screening programme in Singapore's public healthcare system, representing one of the world's first country-level adoption of AI technology. This may serve as a model for AI application in other medical and healthcare settings. His major contributions are listed below under 4 Sections: Key Innovation, Foundational Research, Public Health Impact and Implementation.

1. Key Innovation: AI-deep learning algorithms based on retinal images can detect and predict major eye and systemic diseases =

Tien Wong's principal innovation in medical research and practice is in the application of AI and deep learning by developing and applying AI algorithms (SELENA+) to detect diabetic retinopathy, one of the leading causes of blindness globally, from digital retinal images. From 2012 to 2017, his team led the initial development, evaluation and clinical validation of his AI-deep learning algorithm (SELENA+) that could accurately detect diabetic retinopathy (>95%) and related diseases such as macular degeneration and glaucoma. This was then tested and validated using 500,000 images across 10 populations of diverse ethnic groups and countries, including more challenging settings such as Zambia, Africa.^a (**See references**). The SELENA+ algorithm was eventually integrated and implemented in Singapore's public healthcare system. This represents one of the world's first country-level adoption of an AI algorithm under the software-as-a-medical-device (SaMD) solution.^{b c} The development, evaluation and implementation of the SELENA+ algorithm is a case study of how AI can be integrated and adopted into healthcare settings.^d

Tien Wong then demonstrated that such AI-deep learning methods applied to the same digital retinal images can also accurately detect and predict a range of systemic chronic diseases, such as chronic kidney disease, optic disc papilledema and heart disease. For example, screening for kidney disease is a challenge in community and primary care settings, even in high-income countries. Tien Wong developed an AI-deep learning algorithm to accurately detect chronic kidney disease from retinal images. In another example, Tien Wong showed that use of AI-deep learning via retinal imaging allowed accurate detection of optic disc papilledema, which could signify life-threatening brain swelling and brain diseases. Currently, many such life-threatening cases are missed using traditional clinical eye examinations to detect optic disc papilledema.

Tien Wong demonstrated that AI-deep learning applied to retinal images could accurately estimate coronary artery calcium (CAC) levels, which are subclinical markers of heart disease, and a retinal photograph-derived CAC score was comparable to cardiac CT scan-measured CAC in predicting cardiovascular events, and in fact improves on current cardiovascular risk stratification approaches. Using the same approach, he showed that retinal image-based AI-deep learning could detect Alzheimer's disease and dementia, comparable to more expensive brain MRI or PET-scans. These approaches provide opportunities to screen community-based populations for heart disease and dementia without the need for inaccessible and expensive tests such as cardiac CT scans or brain MRI.

Tien Wong's work laid the foundation for a new inter-disciplinary field, now termed "oculomics", where imaging of the eye is a "window" to study and predict systemic cardio-metabolic diseases.^e

2. Foundational Research: Retinal vascular morphology informs on chronic diseases of the brain, heart and kidneys

Tien Wong's underpinning research began in the late-1990s and early-2000s in the early days of digital retinal photography (replacing film-based photography). He conceptualized and led research in digital eye imaging applied to population-based studies to generate a series of hypotheses that the damage seen in the eye blood vessels ("retinal vascular morphology") could inform and provide insights into new pathways (e.g., microvascular, endothelial dysfunction, inflammation) in the development of chronic systemic diseases. He demonstrated through a series of

epidemiological and clinical studies that retinal vascular morphology captured through retinal images was associated with and could predict future risk of major systemic diseases in the brain, heart, diabetes, kidneys, among other organ-systems.

For example, in a prospective, population-based cohort study of 10,000 persons, Tien Wong observed that people with signs of ischemic damage in the retinal vascular morphology were 3-5 times more likely to develop a clinical stroke event in the following 3 years than people with a healthy retina. Using newly developed computer segmentation techniques to measure objective changes in the retinal vascular morphology (e.g., width of retinal vessels), he demonstrated that narrowed retinal blood arteries was predictive of risk of coronary heart disease, with stronger association in women than men, confirming a long-standing but difficult to proof hypothesis that women were more susceptible to "microvascular pathways" in development of heart disease. In a multi-population-based study, he demonstrated that classic retinal vascular morphology signs of diabetic damage were detectable in people without clinical diabetes, proving that the eye provided early warning of metabolic disease. In another series of multi-centre studies conducted on patients with acute stroke in Singapore, Melbourne and Sydney, Tien Wong showed that detailed analysis of retinal vascular morphology could allow differentiation of stroke sub-types (e.g., small versus large blood vessel stroke), which has implications for treatment decisions for acute stroke (e.g., surgery versus use of blood anticoagulation). Subsequent studies led by Tien Wong and his team in patients with dementia showed that retinal vascular morphology could also allow differentiation of major dementia subtypes (e.g., Alzheimer's disease vs vascular dementia), which again has significant implications for treatment (e.g. new therapies for Alzheimer's disease vs control of vascular risk factors).

3. Public Health Impact: Improving the understanding and defining the epidemiology of major eye diseases in multi-ethnic populations

Concurrently, in the early-2000s, Tien Wong initiated a series of population-based studies to document the major causes of vision loss and common eye diseases across different populations. In Singapore, he conceived a unique population-based study (the Singapore Epidemiology of Eye Disease (SEED) program), which involved 10,000+ Chinese, Indians and Malay subjects, covering the 3 major ethnic groups in Asia. The SEED study is now in its 20th year with more than 10 years of follow-up, and has resulted in >500 papers covering all major eye and systemic diseases, including the prevalence and incidence, systemic and genetic risk factors, and the burden and impact of many eye and systemic disease.

Tien Wong then started and led several international consortia to systematically organize individual-level meta-analysis to accurately document the prevalence and projected burden of major eye diseases, including diabetic retinopathy **(16)**, age-related macular degeneration, glaucoma and others. These systematic meta-analyses provided vital data for many international agencies to formulate policies, guidelines and strategies to tackle blindness and visual impairment around the world. Based on these studies, Tien Wong then prioritised the application of SELENA+ and related AI-based systems on tackling diabetes and its complications.

4. Implementing: Screening of diabetic eye and systemic diseases using AI and retinal imaging.

To integrate and implement SELENA+ and other AI-deep learning algorithms into the healthcare system, Tien Wong led a series of critical implementation efforts. First, he conceptualized and started Singapore's first national "telemedicine" screening programme for diabetic retinopathy, referred to as the Singapore Integrated Diabetic Retinopathy Programme (SiDRP). This programme screened persons with diabetes across a network of primary care clinics in Singapore using digital retinal photographs which were centrally read by trained humans technicians.^f Then, to demonstrate the value and impact of integrating and applying AI-deep learning to SiDRP, he led economic modelling studies to show that incorporating the SELENA+ algorithm to the screening programme is cost saving for the country and the healthcare system. He demonstrated that AI-based retinal imaging to screen for eye ad systemic diseases required no additional equipment beyond retinal cameras (which are widely available, portable and inexpensive) nor required specialized skills training (retinal photography can be easily performed by technicians, nurses, and community optometrists/opticians). The SELENA+ algorithm has since obtained regulatory approvals in multiple countries, including Singapore's Health Science Authority (HSA), European Union CE Mark, Australian's Therapeutics Goods Administration (TGA) and others. Since Singapore-wide adoption in September 2020, >200,000 cases have been screened for diabetic retinopathy using the SELENA+ system. The 20-year journey of SELENA+ is now a business case study for the implementation and application of AI in healthcare.^g

More recently, Tien Wong developed a new AI-deep learning method to predict a person's future risk of diabetic retinopathy, accurately up to 5 years, allowing for "personalized screening intervals" for diabetes patients, with 30% of patients now needing screening only once every 4 or 5 years instead of annually. He has also gone on to further explore newer models of healthcare based on AI, particularly useful in low resource healthcare settings. For example, his team developed the world's first integrated vision-large language model (vision-LLM) which assists primary care providers not only with an accurate diagnosis, but with individualized diabetes management guidance to patients. This has a major impact on screening programmes in low resource settings which lack well-trained primary care providers to provide the specific diabetes management advice that is needed.

Tien Wong has outlined a roadmap for the evolution of future medical AI models, moving from the current disease-centric uni-modality models towards models which needs to integrate a physician's "intuition, wisdom and experience" and transiting models towards "maintaining health" rather than on "treating diseases", a concept referred to as Universal Health AI (UHAI).

References (a to g)

^a Bellemo V et al. Artificial intelligence using deep learning to screen for referable and vision-threatening diabetic retinopathy in Africa: a clinical validation study. *Lancet Digit Health* 2019 May;1(1):e35-e44.

^bTa AWA, et al. Two Singapore public healthcare AI applications for national screening programs and other examples. Health Care Sci. 2022 Aug 19;1(2):41-57. <u>Two Singapore public healthcare AI applications for national screening programs and other examples</u> (sciopen.com)

^c Ministry of Health (Singapore). "Efficacy of the SELENA+ system," July 5, 2021. MOH | News Highlights

^d Gunasekeran V...Wong TY. National Use of Artificial Intelligence for Eye Screening in Singapore. *NEJM AI* 2024;1(12) DOI: 10.1056/AIcs2400404

^e Insights into Systemic Disease through Retinal Imaging-Based Oculomics | TVST | ARVO Journals

^f Nguyen et al. Cost-effectiveness of a National Telemedicine Diabetic Retinopathy Screening Program in Singapore. <u>Ophthalmology</u>. 2016 Dec;123(12):2571-2580.

^g <u>Tracing the twenty-year evolution of developing AI for eye screening in Singapore: A master chronology of SiDRP, SELENA+ and EyRis (smu.edu.sg)</u>