



25 | In Pursuit
of Research
Excellence
1990 – 2015

**Research Papers
with Clinical Impact**

A clear vision for the future – building on a strong foundation



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The Singapore National Eye Centre (SNEC) was set up in 1990 with a vision to spearhead the development of ophthalmology and provide cost-effective, best-in-class clinical eye care for all Singaporeans.

In the early days, research was sporadic, inadequately funded and involved only a small proportion of the clinical faculty. 25 years later, research is one of the three missions of SNEC and the foundation for which innovations impact on clinical care and clinical service delivery.

How did this happen? Professor Arthur Lim, SNEC's founding Medical Director, took an early 'bet' on one of SNEC's young ophthalmologists, Associate Professor Chew Sek Jin, who had a passion for research and was willing to be adequately trained. He went on to become one of Singapore and SNEC's first MD-PhDs in the 1990s. Today, we have more than 20 MD-PhDs among our residents and faculty.

To harness the growth of research, the Singapore Eye Research Institute (SERI) was conceived in 1997 as the research arm of SNEC, but with a national mission to bring together a critical mass of clinicians, clinician-researchers, and scientists all over Singapore, including those at the National University of Singapore. SERI's mandate was to develop a translational research programme in ophthalmology and the visual sciences.

Since then, SERI's faculty has been fully committed to translating basic science into clinical applications for the benefit of patients. Professor Lim, who was also SERI's first chairman, had envisioned the seamless integration of cutting-edge basic research to clinical care, a mission which we still hold to today.

Why do we do research? As clinicians, we often ask questions like: How can we do better for our patients? What are gaps in the current treatment? How do we better diagnose a condition? Research provides a means to scientifically answer these questions and the framework to bridge the gaps in clinically important challenges. Research therefore makes all of us better doctors and provides patients with hope for better outcomes. In the process, we build a better healthcare ecosystem for our population.

What have we achieved? Beyond publications, grants and awards, SERI's research has led to discoveries that have helped improved clinical care, enhanced standards of diagnosis and treatment, restored sight and improved the quality of life to our patients.

We are pleased to present you this summary highlighting 25 of our research projects commemorating the 25th anniversary of the SNEC. These landmark research projects have come to define eye research and have helped establish SNEC/SERI as a global innovator in clinically applicable science. They range from developing pioneering surgical techniques for intractable eye conditions, to understanding the genetic basis for Asian eye diseases, and innovations in drug delivery.

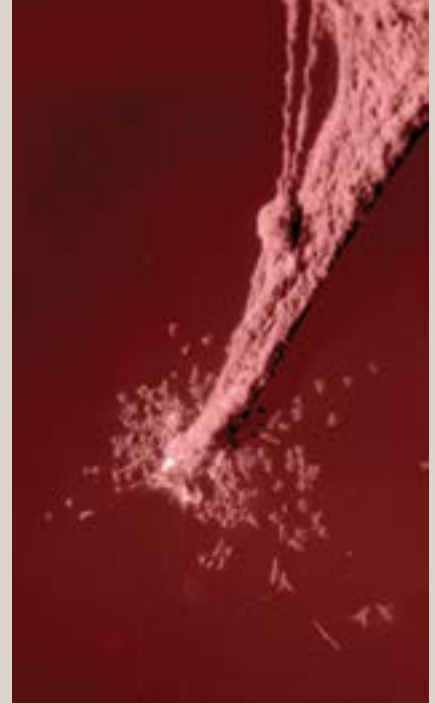
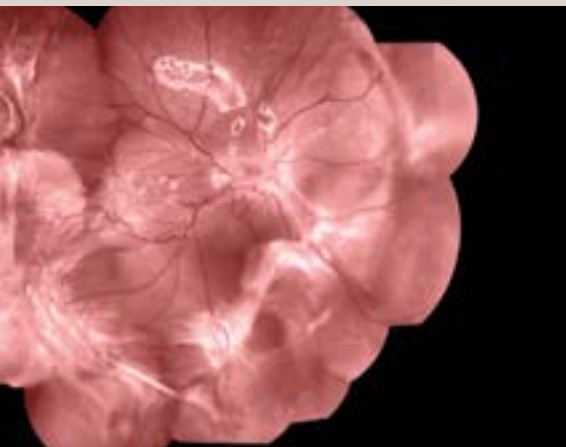
Selecting just 25 projects conducted over the span of 25 years has been difficult, but they are a testament to the considerable momentum we have gained over the years. We will continue on this upward trajectory in the years to come, setting our sights on being one of the top eye centres and research institutes worldwide.

We congratulate and thank all at SNEC and SERI who have contributed to these 25 projects. Please enjoy!



Contents

- pg 04** Overview
- 06** Clinical audits provide evidence for LASIK's safety
- 07** From cradle to grave: tracking the myopia epidemic
- 08** A gold standard for pterygium surgery
- 09** Pioneering techniques in corneal transplantation
- 10** A tooth for an eye
- 11** Improved understanding and diagnosis of Asian glaucoma
- 12** Averting a global blindness outbreak
- 13** Discovery of a new 'natural' antibiotic
- pg 14** Bringing to patients innovative, evidenced-based glaucoma treatment
- 15** A paradigm shift in management of the 'inflamed eye'
- 16** Finally, a treatment for myopia!
- 17** Tracking vascular damage from hypertension and stroke with retinal imaging
- 18** The state of the nation's eye health
- 19** Leading global consortiums to identify major risk factors of eye diseases
- 20** Searching for the best treatment options for the Asian subtype of age-related macular degeneration
- 21** Goodbye, daily eye drops!
- 22** FDA-approved: Tan Endoglide
- 23** Want better eyesight? Just ReLEx!
- 24** The gene hunters
- pg 25** An eye image is worth a thousand words
- 26** Diabetes and the eye: from biomarker studies to a national screening programme
- 27** Transforming how corneal dystrophy is tested
- 28** A new biomarker for Alzheimer's disease
- 29** Safe & successful cataract surgeries
- 30** Stem cell therapy
- 31** Our research milestones



Overview

The Singapore National Eye Centre (SNEC) is the designated national centre for ophthalmology and one of the largest eye centres in Asia-Pacific, with a faculty of close to 80 ophthalmologists and more than 500 staff. In 2014, SNEC had 300,000 patient visits and performed more than 27,000 surgeries.

The Singapore Eye Research Institute (SERI) was set up in 1997 as Singapore's national research institute for ophthalmic and vision research. It is the research arm of SNEC, and affiliated to the National University of Singapore (NUS) and the Duke-NUS Graduate Medical School, as part of the SingHealth-Duke-NUS Academic Medical Centre.

Over the years, SERI has invested considerable resources into our research infrastructure and in the training of the next generation of clinician-scientists, clinician-researchers and scientists. The returns on our investment have been tremendous. In two decades, SERI has grown from a team of 5 to over 220 staff, with more than 100 distinguished adjunct faculty members to become the largest eye research institute in the Asia-Pacific region.

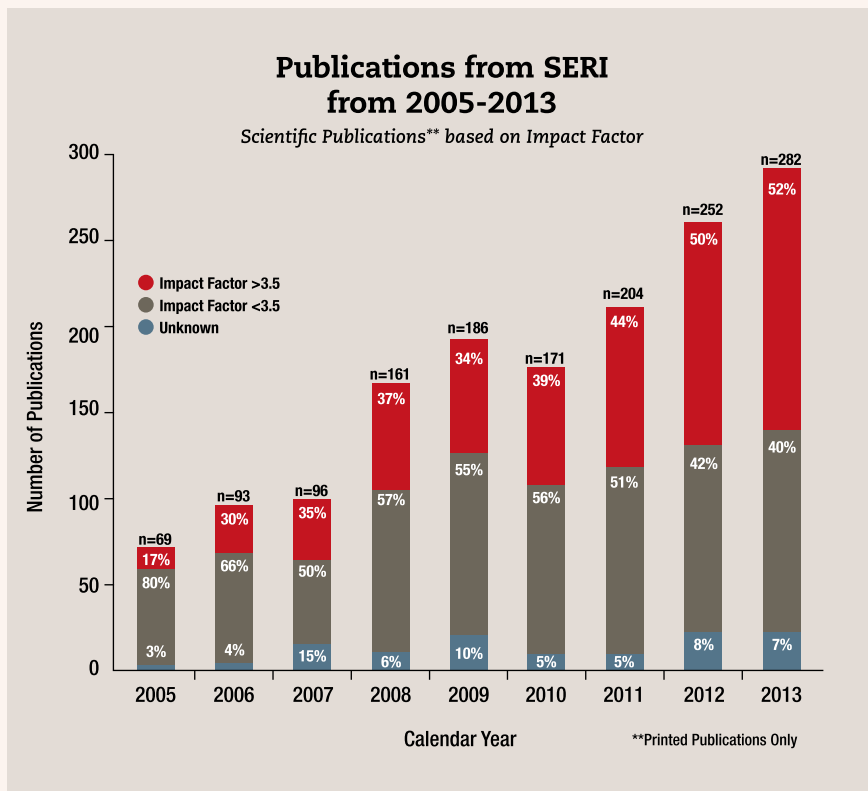
Collectively, our clinician-scientists and researchers have published more than 2,000 peer-reviewed papers supported by nearly S\$200 million in competitive research grants. SERI has trained

more than 150 current and past graduate students; many of our alumni now work in hospitals, industry, academic institutions, at A*STAR institutes and in major institutions overseas.

Today, SERI is recognised as a pioneering centre for high quality eye research in Asia, with breakthrough discoveries such as the low-dose atropine eye drop as a treatment for myopia.

We have been granted more than 105 international patents: the Tan Endoglide, the first disposable inserter to be approved by the U.S. Food and Drug Administration, is an example of a project that was successfully commercialised. Our faculty has also started spin-off companies, such as SinSa Laboratories and Peregrine Ophthalmic.

Research at SERI has translated to actual patient success stories and significant improvements in clinical eye care management. All of these achievements would not have been possible without the commitment and passion that have come to define the SERI research community.



Our Mission

To be Asia's global centre of excellence in eye and vision research, renowned internationally for translating basic science to clinical applications for the prevention and treatment of sight threatening disorders.

Our Vision

To conduct innovative and world leading basic science, clinical and translational eye and vision research.

Our Values

- SUCCESS** : Our success stories validate SERI's legacy as a trailblazer of eye research
- INNOVATION** : Our research is innovative, out-of-the-box and constantly challenging new boundaries
- GLOBAL** : We stand tall among global heavyweights in eye research due to our impactful research
- HEAL** : We seek to heal and strive towards a cure for blindness & vision disorders
- TRANSLATION**: Our research is geared towards tangible outcomes (from bench-bedside-population)



220 STAFF

+105 ADJUNCT FACULTIES



> 2,190

SCIENTIFIC PAPERS



> 1,098 STUDIES

ON ALL ASPECTS OF
EYE RESEARCH



> 320 AWARDS

NATIONAL & INTERNATIONAL



> \$198 MILLION

IN GRANT FUNDING SECURED



> 105 PATENTS



> 165 STUDENTS

MASTERS, PhD & POST-DOCTORAL

1993 & 2010

Clinical audits provide evidence for LASIK's safety

Impact:

In the early 90s, SNEC introduced excimer laser surgery in Singapore to treat myopia and established a robust clinical audit system to track and monitor outcomes. Since then, SNEC's refractive laser programme has been instrumental in testing new laser treatments and technologies to ensure that they are both safe and effective for Singaporeans. Our paper reporting on almost 38,000 cases of LASIK surgery is one of the world's largest studies to date. This study shows that LASIK significantly improved visual acuity and was safe, demonstrating the value of the clinical audit in continually improving the testing of new surgical techniques over the last two decades.

EXCIMER LASER PHOTOREFRACTIVE KERATECTOMY IN SINGAPORE - A NEW TREATMENT MODALITY FOR MYOPIA

V Balakrishnan, A S M Lim, C H Low, C P Lee, P S F Tseng, W K Chan, T K Chan, J Tan, D Tan

Background: Myopia is a national epidemic in Singapore. Photorefractive keratectomy (PRK) for the treatment of myopia using the Argon Fluoride Excimer Laser commenced in January 1993 at the Singapore National Eye Centre.
Objective: An open, prospective, non-randomised clinical audit to assess the efficacy, predictability, stability, and safety of PRK for the correction of myopia between -1.0 to -8.0 dioptres.
Results: The hospital and clinic sites of one hundred and thirty-five patients underwent PRK between January and September 1993, of which sixty-one had completed at least six months of follow-up. Twenty-nine of the thirty-one patients (93%) achieved an unaided visual acuity of at least 6/6. Post-operative patients (95%) were within 1 dioptre of emmetropia. There was no lathet over-correction in all patients which required a placebo of another three or four months. Corneal haze did not pose a significant problem. These patients had stable refractions, and another hundred and thirty-eight had stable refractions in the amblyopic eye.
Conclusion: Excimer Laser Photorefractive Keratectomy is a safe, effective, and stable modality for the treatment of myopia.

A 10-Year Prospective Audit of LASIK Outcomes for Myopia in 37 932 Eyes at a Single Institution in Asia

Lanman JF, Tan, MD, MPH,¹ Wang Kang Chen, FRCOphth, FRCSEd,² Joo Kah, Ah, Dip. Sc., (St),³ Jullian S. Mehta, FRCOphth, FRCSEd,⁴ Donald T. Tan, FRCOphth, FRCSEd,^{1,2} for the SingLasik Research Group⁵

Purpose: This study evaluated the efficacy, predictability and safety of LASIK surgery as a treatment for myopia performed as part of a large-scale, prospective clinical audit spanning 10 years in an Asian study population and to evaluate the outcomes and trends.

Design: Prospective, nonrandomized, single-center, multicenter study.

Participants: We included 37 932 eyes of 19 753 patients that underwent myopic LASIK at the Singapore National Eye Centre between 1998 and 2007.

Methods: All eyes underwent LASIK as a treatment for myopia. Pre- and postoperative refractions, unaided visual acuity (UCVA), and best-corrected visual acuity (BCVA) were documented.

Main Outcome Measures: Safety, efficacy, refractive predictability, treatment trends, retreatment rates, and complications for mild, moderate, and high myopia according to spherical equivalence (SE) of less than -3.00 diopters (D), -3.00 D or more to less than -10.0 D, and -10.00 D or more, respectively.

Results: Patients' median age was 33 years (mean, 33.0±7.9 years); there were 6802 males (24.8%) and 12 501 females (35.2%). Patients were predominantly ethnic Chinese (90.5%). Mean follow-up time was 68.8 months. The mean spherical error corrected was -5.90±2.57 D (median, -5.625 D), and outcomes were 90% since onset into low, moderate, or high myopia. The UCVA achieving ≥20/40 has been consistently above 90% since 2003, with 72.8% achieving ≥20/30. More than 80.0% of eyes achieved within ±1.00 D target in the last 4 years. An improvement in safety was observed since the start of the study, with the best retreatment rate was 3.8% (91% of retreated eyes achieved UCVA of ≥20/30). Between 1998 and 2007, there was a significant improvement in postoperative UCVA and BCVA (P<0.001).

Conclusions: Myopic LASIK performed in Asian eyes within a comprehensive LASIK clinical program with appropriate clinical audit governance can be safe and effective, with high refractive predictability. Improvements in the refractive program to prevent undercorrection and to compensate for myopic regression have led to better efficacy after LASIK, with an increasing percentage of patients achieving 20/15 visual acuity postoperatively.

Financial Disclosures: Proprietary or commercial disclosures may be found after the references.

Optphthalmology 2010;117:1236-1244 © 2010 by the American Academy of Ophthalmology

¹Group members listed online in Appendix 1 (available at <http://aopjournal.org>)

LASIK is among most common ophthalmic procedures in the world. However, due to popularity, its safety, efficacy, quick visual recovery, and minimal patient discomfort.¹⁻³ As a result, millions of patients worldwide undergo this procedure each year, making the safety and efficacy of LASIK a significant public health issue.⁴

LASIK audits have been initiated at Singapore National Eye Centre (SNEC) since 1998, at a similar time when the first excimer laser was approved by the United States Food and Drug Administration (FDA) for use in LASIK for myopia.⁵ The aim of this study was to evaluate refractive outcomes and trends on safety, efficacy, and predictability of myopic LASIK in Singapore, spanning 10 years with a complete 100% data capture. To our

knowledge this is the largest refractive series reported in the literature.

Materials and Methods

Patient Population

In this prospective study, informed consent was obtained from 19 753 patients after they received a detailed description of LASIK, a thorough review of its known risks, all patients underwent and a thorough review of the Singapore National Eye Centre (SNEC) myopic LASIK at the Singapore National Eye Centre (SNEC) between February 14, 1998, and December 31, 2007. Patients returned for 1 day, 1 week, 1 month, and 3 months follow-up after the initial procedure. Patient demographics are given in Table 1, &

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¹ Balakrishnan V, Lim AS, Low CH, Lee CP, Tseng PS, Chan WK, Chan TK, Tan J, Tan D. Excimer laser photorefractive keratectomy in Singapore - a new treatment modality for myopia. *Singapore Med J*. 1993 Aug;34(4):309-12.

² Yuen LH, Chan WK, Koh J, Mehta JS, Tan DT; SingLasik Research Group. A 10-year prospective audit of LASIK outcomes for myopia in 37,932 eyes at a single institution in Asia. *Ophthalmology*. 2010 Jun;117(6):1236-1244.

2000 & 2001

From cradle to grave: tracking the myopia epidemic



Other key publications:

1. Saw SM, Nieto FJ, Katz J, Schein OD, Levy B, Chew SJ. Factors related to the progression of myopia in Singaporean children. *Optom Vis Sci.* 2000 Oct;77(10):549-54.
2. Seet B, Wong TY, Tan DT, Saw SM, Balakrishnan V, Lee LK, Lim AS. Myopia in Singapore: taking a public health approach. *Br J Ophthalmol.* 2001 May;85(5):521-6.
3. Pan CW, Zheng YF, Anuar AR, Chew M, Gazzard G, Aung T, Cheng CY, Wong TY, Saw SM. Prevalence of refractive errors in a multiethnic Asian population: the Singapore epidemiology of eye disease study. *Invest Ophthalmol Vis Sci.* 2013 Apr 9;54(4):2590-8.
4. Zheng YF, Pan CW, Chay J, Wong TY, Finkelstein E, Saw SM. The economic cost of myopia in adults aged over 40 years in Singapore. *Invest Ophthalmol Vis Sci.* 2013 Nov 13;54(12):7532-7.

Impact:

Myopia is a disease of epidemic proportions not only in Singapore but all across Asia. Since the early signals of this epidemic was observed in Singapore in the 1990s, SNEC/SERI has systematically documented and tracked the myopia epidemic, uncovering key risk factors at all stages of life. Our research showed that both 'nature' (parents with myopia) and 'nurture' (excessive near-work activity, inadequate outdoor activities) contribute to myopia in children. In the elderly, our population-based studies identified risk factors for myopia.

These studies have informed the Ministry of Health's National Myopia Prevention Programme, culminating in a series of strategies that have resulted in a downward trend of myopia and associated healthcare costs for Singapore.

¹ Saw SM, Hong CY, Chia KS, Stone RA, Tan D. Nearwork and myopia in young children. *Lancet.* 2001 Feb 3;357(9253):390.

² Wong TY, Foster PJ, Hee J, Ng TP, Tielsch JM, Chew SJ, Johnson GJ, Seah SK. Prevalence and risk factors for refractive errors in adult Chinese in Singapore. *Invest Ophthalmol Vis Sci.* 2000 Aug;41(9):2486-94.

A gold standard for pterygium surgery



Other key publications:

1. Tan DT, Lim AS, Goh HS, Smith DR. Abnormal expression of the p53 tumor suppressor gene in the conjunctiva of patients with pterygium. *American Journal of Ophthalmology* 1997 Mar; 123 (3): 404-405.
2. Jap A, Chan C, Lim L, Tan DT. Conjunctival rotation autograft for pterygium: An alternative to conjunctival autografting. *Ophthalmology*. 1999 Jan;106(1):67-71.
3. Ti SE, Chee SP, Dear KB, Tan DT. Analysis of variation in success rates in conjunctival autografting for primary and recurrent pterygium. *Br J Ophthalmol*. 2000 Apr;84(4):385-9.
4. Ang M, Li X, Wong W, Zheng Y, Chua D, Rahman A, Saw SM, Tan DT, Wong TY. Prevalence of and racial differences in pterygium: a multiethnic population study in Asians. *Ophthalmology*. 2012 Aug;119(8):1509-15.

Impact:

Pterygium is a growth of the conjunctiva which can, in some cases, grow large enough to cover the central cornea and cause vision loss. In the early 1990s, pterygium surgery was very basic and outcomes were poor as surgery was limited by high recurrence rates of the disease. We pioneered a new procedure—the conjunctival autograft procedure—which resulted in a far safer and more effective surgical procedure which we demonstrate in a clinical trial. Today, this new procedure is considered the gold standard in Singapore and around the world. Concomitantly, we conducted epidemiological studies that showed a high prevalence of pterygium in Asia, and our laboratory studies have identified biomarkers which helped us understand why some pterygia are more aggressive and recur rapidly after surgery.

¹ Tan DT, Chee SP, Dear KB, Lim AS. Effect of pterygium morphology on pterygium recurrence in a controlled trial comparing conjunctival autografting with bare sclera excision. *Archives of Ophthalmology*. 1997 Oct;115 (10):1235-40.

2008 & 2012

Pioneering techniques in corneal transplantation



Other key publications:

1. Anshu A, Lim LS, Htoon HM, Tan DT. Postoperative risk factors influencing corneal graft survival in the Singapore Corneal Transplant Study. *Am J Ophthalmol.* 2011 Mar;151(3):442-8.e1.
2. Anshu A, Parthasarathy A, Mehta JS, Htoon HM, Tan DT. Outcomes of therapeutic deep lamellar keratoplasty and penetrating keratoplasty for advanced infectious keratitis: a comparative study. *Ophthalmology.* 2009 Apr;116(4):615-23.
3. Ang M, Mehta JS, Sng CC, Htoon HM, Tan DT. Indications, outcomes, and risk factors for failure in tectonic keratoplasty. *Ophthalmology.* 2012 Jul;119(7):1311-9.
4. Ang M, Mehta JS, Lim F, Bose S, Htoon HM, Tan D. Endothelial cell loss and graft survival after Descemet's stripping automated endothelial keratoplasty and penetrating keratoplasty. *Ophthalmology.* 2012 Nov;119(11):2239-44.
5. Han DC, Mehta JS, Por YM, Htoon HM, Tan DT. Comparison of Outcomes of Lamellar Keratoplasty and Penetrating Keratoplasty in Keratoconus. *Am J Ophthalmol.* 2009 Nov;148(5):744-751.e1.

Impact:

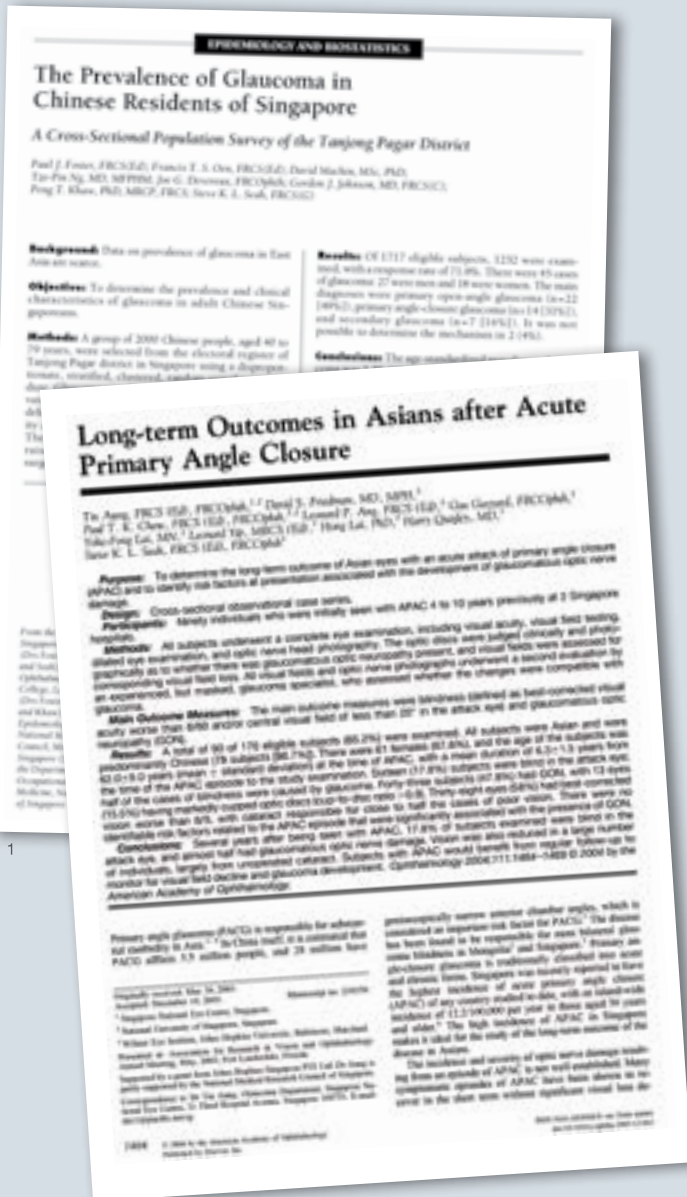
The Singapore Corneal Transplant Study (SCTS) is the largest Asian corneal transplant database tracking over 4,000 transplants performed in SNEC since the early 1990s. Instead of the standard full thickness corneal transplant, we introduced the partial thickness (lamellar) method to Asia, which has resulted in lower transplant rejection rates and much fewer complications. Success rates for our transplants are now extremely high (95-98%), leading to a paradigm shift in the types of transplants we now perform.

¹ Tan DT, Janardhanan P, Zhou H, Chan YH, Htoon HM, Ang LP, Lim LS. Penetrating keratoplasty in Asian eyes: the Singapore Corneal Transplant Study. *Ophthalmology.* 2008 Jun;115(6):975-982.

² Tan DT, Dart JK, Holland EJ, Kinoshita S. Corneal transplantation. *Lancet.* 2012 May 5;379(9827):1749-61.

2000 & 2004

Improved understanding and diagnosis of Asian glaucoma



Other key publications:

1. Kumar RS, Baskaran M, Chew PT, Friedman DS, Handa S, Lavanya R, Sakata LM, Wong HT, Aung T. Prevalence of plateau iris in primary angle closure suspects an ultrasound biomicroscopy study. *Ophthalmology*. 2008 Mar;115(3):430-4.
2. Nongpiur ME, He M, Amerasinghe N, Friedman DS, Tay WT, Baskaran M, Smith SD, Wong TY, Aung T. Lens vault, thickness, and position in Chinese subjects with angle closure. *Ophthalmology*. 2011 Mar;118(3):474-9.
3. Foo LL, Nongpiur ME, Allen JC, Perera SA, Friedman DS, He M, Cheng CY, Wong TY, Aung T. Determinants of angle width in Chinese Singaporeans. *Ophthalmology*. 2012 Feb;119(2):278-82.
4. Lavanya R, Baskaran M, Kumar RS, Wong HT, Chew PT, Foster PJ, Friedman DS, Aung T. Risk of acute angle closure and changes in intraocular pressure after pupillary dilation in Asian subjects with narrow angles. *Ophthalmology*. 2012 Mar;119(3):474-80.
5. Yong KL, Gong T, Nongpiur ME, How AC, Lee HK, Cheng L, Perera SA, Aung T. Myopia in Asian subjects with primary angle closure: implications for glaucoma trends in East Asia. *Ophthalmology*. 2014 Aug;121(8):1566-71.

Impact:

Glaucoma is a major blinding disease globally, but Asian patients more commonly present with a different form of the disease known as narrow angle or angle closure glaucoma. Our studies have documented the burden of this condition in the population and its risk factors. Other studies have provided long-term data on how this condition evolves over time and the outcomes of treatment. This information is now widely used to identify high risk patients, and to design screening programmes in Asia to improve clinical outcomes.

¹ Foster PJ, Oen FT, Machin D, Ng TP, Devereux JG, Johnson GJ, Khaw PT, Seah SK. The prevalence of glaucoma in Chinese residents of Singapore: a cross-sectional population survey of the Tanjong Pagar district. *Arch Ophthalmology*. 2000 Aug;118(8):1105-11.

² Aung T, Friedman DS, Chew PTK, Ang LP, Gazzard G, Lai YF, Yip L, Lai H, Quigley H, Seah SK. Long-term outcomes in Asians after acute primary angle-closure. *Ophthalmology*. 2004 Aug;111(8):1464-9.

Averting a global blindness outbreak



Other key publications:

1. Saw SM, Ooi PL, Tan DT, Khor WB, Fong CW, Lim J, Cajucom-Uy HY, Heng D, Chew SK, Aung T, Tan AL, Chan CL, Ting S, Tambyah PA, Wong TY. Risk factors for contact lens-related fusarium keratitis: a case-control study in Singapore. *Arch Ophthalmol*. 2007 May;125(5):611-7.

Impact:

In 2005, SNEC clinicians observed a spike in patients presenting with corneal ulcers (infectious keratitis), a blinding condition that is difficult to treat. We quickly convened an inter-disciplinary taskforce, and working with infectious disease experts, we uncovered a global outbreak of *Fusarium* (a type of fungus) keratitis that was associated with soft contact lens wear. We linked this outbreak to the use of a certain brand of contact lens cleaning solution. Our publication in *JAMA* resulted in the worldwide withdrawal of the contact lens product. An FDA review of the standards in contact lens care solutions later led to new international standards. This timely intervention resulted in a dramatic drop in cases of keratitis, potentially preventing thousands of cases of corneal blindness globally.

¹ Khor WB, Aung T, Saw SM, Wong TY, Tambyah PA, Tan AL, Beuerman R, Lim L, Chan WK, Heng WJ, Lim J, Loh RS, Lee SB, Tan DT. An outbreak of *Fusarium* keratitis associated with contact lens wear in Singapore. *JAMA*. 2006 Jun 28;295(24):2867-73.

2007

Discovery of a new ‘natural’ antibiotic



Other key publications:

- Li J, Raghunath M, Tan D, Lareu RR, Chen Z, Beuerman RW. Defensins HNP1 and HBD2 stimulation of wound-associated responses in human conjunctival fibroblasts. *Invest Ophthalmol Vis Sci.* 2006 Sep;47(9):3811-9.

Impact:

Defensins are small proteins secreted by the body which act as ‘natural’ antibiotics, targeting a broad spectrum of bacteria, fungi and viruses. SERI was one of the first labs to study defensins in patients, and our researchers have identified and developed new defensin-based treatments. The research has led to the formation of a spin-off company—SinSa Laboratories—which has a pipeline of natural anti-microbial drugs that are a platform for multiple infectious conditions beyond those invading the eye.

¹ Verma C, Seebah S, Low SM, Zhou L, Liu SP, Li J, Beuerman RW. Defensins: antimicrobial peptides for therapeutic development. *Biotechnol J.* 2007 Nov;2(11):1353-9.

2009 & 2015

Bringing to patients innovative, evidenced-based glaucoma treatment



Other key publications:

1. Aung T, Seah SK. Glaucoma drainage implants in Asian eyes. *Ophthalmology*. 1998 Nov;105(11):2117-22.
2. Aung T, Wong HT, Yip CC, Leong JY, Chan YH, Chew PT. Comparison of the intraocular pressure-lowering effect of latanoprost and timolol in patients with chronic angle closure glaucoma: a preliminary study. *Ophthalmology*. 2000 Jun;107(6):1178-83.
3. How AC, Kumar RS, Chen YM, Su DH, Gao H, Oen FT, Ho CL, Seah SK, Aung T. A randomised crossover study comparing bimatoprost and latanoprost in subjects with primary angle closure glaucoma. *Br J Ophthalmol*. 2009 Jun;93(6):782-6.
4. Husain R, Gazzard G, Aung T, Chen Y, Padmanabhan V, Oen FT, Seah SK, Hoh ST. Initial management of acute primary angle closure: a randomized trial comparing phacoemulsification with laser peripheral iridotomy. *Ophthalmology*. 2012 Nov;119(11):2274-81.
5. Wong MH, Husain R, Ang BC, Gazzard G, Foster PJ, Htoon HM, Wong TT, Oen FT, Khaw PT, Seah SK, Aung T. The Singapore 5-fluorouracil trial: intraocular pressure outcomes at 8 years. *Ophthalmology*. 2013 Jun;120(6):1127-34.

Impact:

When it comes to deciding whether a new experimental treatment is suitable for patients, clinical trials provide the best level of evidence. SNEC/SERI is the leader in ophthalmologic clinical trial execution in Asia. Over the last 25 years, we have performed many pivotal glaucoma clinical trials. These include trials on the latest surgical techniques such as laser trabeculectomy, lens extraction and glaucoma drainage implants. The Singapore 5-fluorouracil (5-FU) trial was the first and largest randomised clinical trial on glaucoma surgery performed in Asia. It showed that the anti-fibrotic agent 5-FU was safe to use in low-risk East Asian patients. Valuable information gleaned from these trials has informed the management of our glaucoma patients.

¹ Wong TT, Khaw PT, Aung T, Foster PJ, Htoon HM, Oen FT, Gazzard G, Husain R, Devereux JG, Minassian D, Tan SB, Chew PT, Seah SK. The Singapore 5-Fluorouracil Trabeculectomy Study - Effects on Intraocular Pressure Control and Disease Progression at 3 Years. *Ophthalmology*. 2009 Feb;116(2):175-84.

² Narayanaswamy AK, Leung CK, Istantoro DV, Perera SA, Ho CL, Nongpiur ME, Baskaran M, Htoon HM, Wong TT, Goh D, Su DH, Belkin M, Aung T. Efficacy of Selective Laser Trabeculoplasty in Primary Angle Closure Glaucoma- A Randomized Controlled Trial. *JAMA Ophthalmol*. 2015 Feb;133(2):206-12.

2007 & 2008

A paradigm shift in management of the 'inflamed eye'



Other key publications:

1. Anshu A, Chee SP, Mehta JS, Tan DT. Cytomegalovirus endotheliitis in Descemet's stripping endothelial keratoplasty. *Ophthalmology*. 2009 Apr;116(4):624-30.
2. Chee SP, Jap A. Cytomegalovirus anterior uveitis: outcome of treatment. *Br J Ophthalmol*. 2010 Dec;94(12):1648-52.
3. Chee SP, Jap A. Immune ring formation associated with cytomegalovirus endotheliitis. *Am J Ophthalmol*. 2011 Sep;152(3):449-453.
4. Li J, Ang M, Cheung CM, Vania M, Chan AS, Waduthantri S, Yang H, Chee SP. Aqueous cytokine changes associated with Posner-Schlossman syndrome with and without human cytomegalovirus. *PLoS One*. 2012;7(9):e44453.
5. Chee SP, Jap A, Ling EC, Ti SE. Cytomegalovirus-positive corneal stromal edema with keratic precipitates after penetrating keratoplasty: a case-control study. *Cornea*. 2013 Aug;32(8):1094-8.

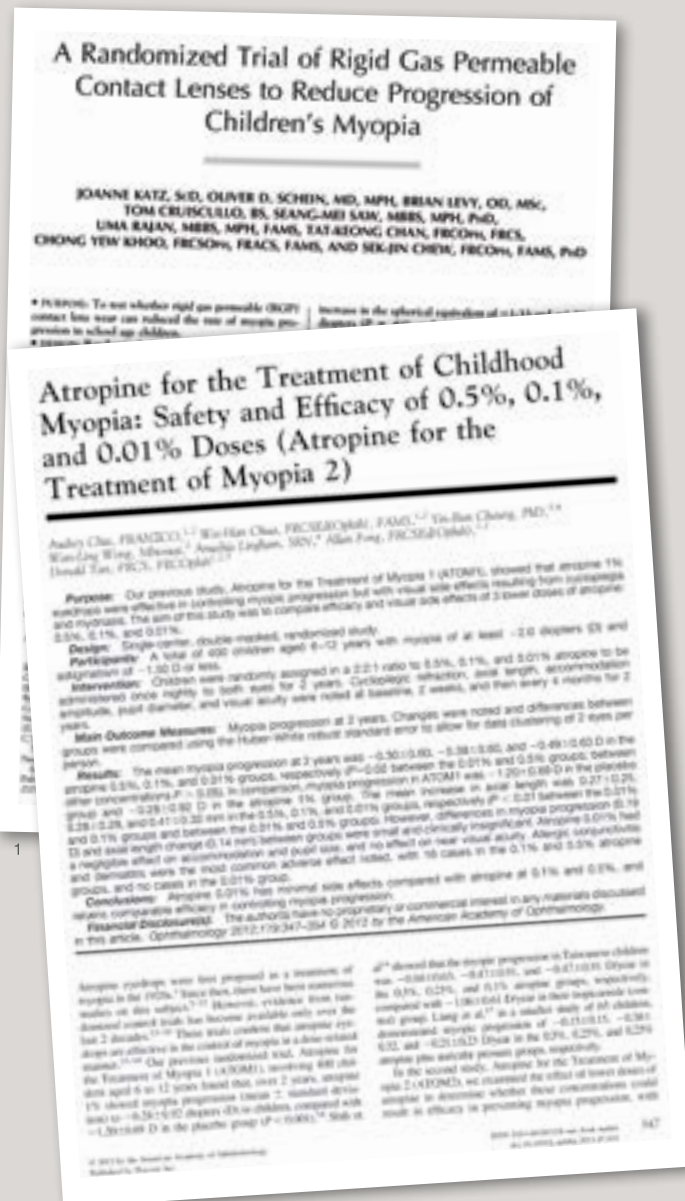
Impact:

SNEC was among the first to discover and describe the link between cytomegalovirus (CMV) and inflammation in the cornea (corneal endotheliitis), a condition which often results in a need for corneal transplantation to restore vision in patients. Our landmark paper published in 2007 led to the worldwide use of antiviral therapy to treat this condition, restoring sight to many patients without the need for corneal transplantation. In 2008, we also published a paper that linked CMV to uveitis in immunocompetent patients. Our findings led to a paradigm shift in the treatment of uveitis. Today, antiviral treatment is now used prevent blindness, progressive glaucoma and corneal swelling.

¹ Chee SP, Baska K, Jap A, Se-Thoe SY, Cheng CL, Tan BH. Corneal Endotheliitis Associated with Evidence of Cytomegalovirus Infection. *Ophthalmology*. 2007 Apr;114(4):798-803.

² Chee SP, Baska K, Jap A, Se-Thoe SY, Cheng CL, Tan BH. Clinical Features of Cytomegalovirus Anterior Uveitis in Immunocompetent Patients. *Am J Ophthalmol*. 2008 May;145(5):834-40.

Finally, a treatment for myopia!



Other key publications:

1. Chua WH, Balakrishnan V, Chan YH, Tong L, Ling Y, Quah BL, Tan D. Atropine for the treatment of childhood myopia. *Ophthalmology*. 2006 Dec;113(12):2285-91.
2. Tong L, Huang XL, Koh AL, Zhang X, Tan DT, Chua WH. Atropine for the treatment of childhood myopia: effect on myopia progression after cessation of atropine. *Ophthalmology*. 2009 Mar;116(3):572-9.
3. Chia A, Chua WH, Wen L, Fong A, Goon YY, Tan D. Atropine for the treatment of childhood myopia: changes after stopping atropine 0.01%, 0.1% and 0.5%. *Am J Ophthalmol*. 2014 Feb;157(2):451-457.e1.

Impact:

Since the observation of the myopia epidemic in the 1990s, SERI has conducted extensive clinical trials into treatments that may prevent the development and progression of myopia. SERI is now the first in the world to fine-tune the dosage of atropine eye drops from the 1% available in market to a new 0.01%, an optimal dose that balances between efficacy and safety. In the five-year trial, daily application of this low-dose 0.01% atropine eye drops was shown to slow the progression of childhood myopia by as much as 60% over a two-year period. For some children, progression of myopia even ceased. Based on this research, atropine could reduce the cost of myopia by approximately \$500 million each year.

¹ Katz J, Schein OD, Levy B, Cruiscullo T, Saw SM, Rajan U, Chan TK, Yew Khoo C, Chew SJ. A randomized trial of rigid gas permeable contact lenses to reduce progression of children's myopia. *Am J Ophthalmol*. 2003 Jul;136(1):82-90.

² Chia A, Chua WH, Cheung YB, Wong WL, Lingham A, Fong A, Tan D. Atropine for the treatment of childhood myopia: safety and efficacy of 0.5%, 0.1%, and 0.01% doses (Atropine for the Treatment of Myopia 2). *Ophthalmology*. 2012 Feb;119(2):347-54.

2004 & 2011

Tracking vascular damage from hypertension and stroke with retinal imaging



Other key publications:

1. Wong TY. Is retinal photography useful in the measurement of stroke risk? *Lancet Neurol*. 2004 Mar;3(3):179-83.
2. De Silva DA, Liew G, Wong MC, Chang HM, Chen C, Wang JJ, Baker ML, Hand PJ, Rochtchina E, Liu EY, Mitchell P, Lindley RI, Wong TY. Retinal vascular calibre and extracranial carotid disease in patients with acute ischemic stroke: the Multi-Centre Retinal Stroke (MCRS) study. *Stroke*. 2009 Dec;40(12):3695-9.
3. Ong YT, De Silva DA, Cheung CY, Chang HM, Chen CP, Wong MC, Wong TY, Ikram MK. Microvascular structure and network in the retina of patients with ischemic stroke. *Stroke*. 2013 Aug;44(8):2121-7.
4. Cheung CY, Tay WT, Ikram MK, Ong YT, De Silva DA, Chow KY, Wong TY. Retinal microvascular changes and risk of stroke: the Singapore Malay Eye Study. *Stroke*. 2013 Sep;44(9):2402-8.
5. Cheung CY, Ikram MK, Sabanayagam C, Wong TY. Retinal microvasculature as a model to study the manifestations of hypertension. *Hypertension*. 2012 Nov;60(5):1094-103.

Impact:

The arteries of the retina are the only blood vessels directly observable from outside the body and can be measured from non-invasive retinal imaging. Our research in this field demonstrates the strong interrelationship between early damage in the blood vessels of the eye and brain. With such information, we can better predict adverse outcomes such as a stroke by observing hypertensive damage in retinal blood vessels. Retinal imaging could also help to sub-classify patients who suffer an acute stroke into 'large' or 'small artery' stroke and thus help to improve their management.

¹ Wong TY, Mitchell P. Hypertensive retinopathy. *N Engl J Med*. 2004 Nov 25;351(22):2310-7.

² De Silva DA, Manzano JJ, Liu EY, Woon FP, Wong WX, Chang HM, Chen C, Lindley RI, Wang JJ, Mitchell P, Wong TY, Wong MC; Multi-Centre Retinal Stroke Study Group. Retinal microvascular changes and subsequent vascular events after ischemic stroke. *Neurology*. 2011 Aug 30;77(9):896-903.

2008 & 2013

The state of the nation's eye health



Other key publications:

1. Zheng Y, Lamoureux EL, Chiang PP, Cheng CY, Anuar AR, Saw SM, Aung T, Wong TY. Literacy is an independent risk factor for vision impairment and poor visual functioning. *Invest Ophthalmol Vis Sci.* 2011 Sep 29;52(10):7634-9.
2. Tan AC, Tay WT, Zheng YF, Tan AG, Wang JJ, Mitchell P, Wong TY, Lamoureux EL. The impact of bilateral or unilateral cataract surgery on visual functioning: when does second eye cataract surgery benefit patients? *Br J Ophthalmol.* 2012 Jun;96(6):846-51.
3. Chiang PP, Zheng Y, Wong TY, Lamoureux EL. Vision impairment and major causes of vision loss impacts on vision-specific functioning independent of socioeconomic factors. *Ophthalmology.* 2013 Feb;120(2):415-22.
4. Cheung CM, Li X, Cheng CY, Zheng Y, Mitchell P, Wang JJ, Wong TY. Prevalence, racial variations, and risk factors of age-related macular degeneration in Singaporean Chinese, Indians, and Malays. *Ophthalmology.* 2014 Aug;121(8):1598-603.
5. Wang X, Lamoureux E, Zheng Y, Ang M, Wong TY, Luo N. Health burden associated with visual impairment in Singapore: the Singapore epidemiology of eye disease study. *Ophthalmology.* 2014 Sep;121(9):1837-42.

Impact:

In 2004, SERI initiated a series of major epidemiological studies on the prevalence, causes and impact of vision loss and major eye diseases involving more than 10,000 Singaporeans—the Singapore Epidemiology of Eye Disease (SEED) studies. SEED is the largest and most comprehensive population-based study of its kind globally, and has resulted in more than 300 publications. As a result of Singapore's unique and diverse racial makeup, findings from these studies have provided key data on the risk factors and impact of vision-threatening eye diseases affecting the three major ethnic groups (Chinese, Indians and Malays) in Asia. These data have also been used by the International Council of Ophthalmology and the Ministry of Health for preparing professional and clinical guidelines, as well as for the planning of eye care services for Singapore and Asia.

¹ Zheng Y, Cheng CY, Lamoureux EL, Chiang PP, Rahman Anuar A, Wang JJ, Mitchell P, Saw SM, Wong TY. How Much Eye Care Services Do Asian Populations Need? Projection from the Singapore Epidemiology of Eye Disease (SEED) Study. *Invest Ophthalmol Vis Sci.* 2013 Mar;54(3):2171-7.

² Wong TY, Chong EW, Wong WL, Rosman M, Aung T, Loo JL, Shen S, Loon SC, Tan DT, Tai ES, Saw SM; Singapore Malay Eye Study Team. Prevalence and causes of low vision and blindness in an urban Malay population: the Singapore Malay Eye Study. *Arch Ophthalmol.* 2008 Aug;126(8):1091-9.

2011 & 2012

Leading global consortiums to identify major risk factors of eye diseases



Other key publications:

1. Kawasaki R, Yasuda M, Song SJ, Chen SJ, Jonas JB, Wang JJ, Mitchell P, Wong TY. The prevalence of age-related macular degeneration in Asians: a systematic review and meta-analysis. *Ophthalmology*. 2010 May;117(5):921-7.
2. Pan CW, Ikram MK, Cheung CY, Choi HW, Cheung CM, Jonas JB, Saw SM, Wong TY. Refractive errors and age-related macular degeneration: a systematic review and meta-analysis. *Ophthalmology*. 2013 Oct;120(10):2058-65.
3. Tham YC, Li X, Wong TY, Quigley HA, Aung T, Cheng CY. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. *Ophthalmology*. 2014 Nov;121(11):2081-90.

Impact:

SERI clinician-scientists have been actively contributing and leading global meta-analysis studies of major eye diseases. For example, the Meta-Analysis for Eye Disease (META-EYE) study group published the first global estimate of diabetic retinopathy (DR), the leading cause of blindness among working-aged adults around the world. The study found that 35% of people with diabetes had some form of DR. It also identified three major modifiable risk factors for DR. SERI has also contributed to global public health by providing the data to international agencies such as the World Health Organisation (WHO) and the annual Global Burden of Disease (GBD) Study funded by the Bill & Melinda Gates Foundation.

25 Research Papers with Clinical Impact

¹ Yau JW, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, Chen SJ, Dekker JM, Fletcher A, Grauslund J, Haffner S, Hamman RF, Ikram MK, Kayama T, Klein BE, Klein R, Krishnaiah S, Mayurasakorn K, O'Hare JP, Orchard TJ, Porta M, Rema M, Roy MS, Sharma T, Shaw J, Taylor H, Tielsch JM, Varma R, Wang JJ, Wang N, West S, Xu L, Yasuda M, Zhang X, Mitchell P, Wong TY; Meta-Analysis for Eye Disease (META-EYE) Study Group. Global prevalence and major risk factors of diabetic retinopathy. *Diabetes Care*. 2012 Mar;35(3):556-64.

² Wong WL, Su X, Li X, Cheung CM, Klein R, Cheng CY, Wong TY. Global prevalence of age-related macular degeneration and disease burden projection for 2020 and 2040: a systematic review and meta-analysis. *Lancet Glob Health*. 2014 Feb;2(2):e106-16.

2012 & 2014

Searching for the best treatment options for the Asian subtype of age-related macular degeneration



Other key publications:

1. Laude A, Cackett PD, Vithana EN, Yeo IY, Wong D, Koh AH, Wong TY, Aung T. Polypoidal choroidal vasculopathy and neovascular age-related macular degeneration: same or different disease? *Prog Retin Eye Res*. 2010 Jan;29(1):19-29.
2. Lim LS, Mitchell P, Seddon JM, Holz FG, Wong TY. Age-related macular degeneration. *Lancet*. 2012 May 5;379(9827):1728-38.
3. Cheung CM, Li X, Mathur R, Lee SY, Chan CM, Yeo I, Loh BK, Williams R, Wong EY, Wong D, Wong TY. A prospective study of treatment patterns and 1-year outcome of Asian age-related macular degeneration and polypoidal choroidal vasculopathy. *PLoS One*. 2014 Jun 30;9(6):e101057.
4. Ng WY, Tan GS, Ong PG, Cheng CY, Cheung CY, Wong DW, Mathur R, Chow KY, Wong TY, Cheung GC. Incidence of myocardial infarction, stroke, and death in patients with age-related macular degeneration treated with intravitreal anti-vascular endothelial growth factor therapy. *Am J Ophthalmol*. 2015 Mar;159(3):557-64.e1.
5. Wong CW, Cheung CM, Mathur R, Li X, Chan CM, Yeo I, Wong E, Lee SY, Wong D, Wong TY. Three-year results of polypoidal choroidal vasculopathy treated with photodynamic therapy: Retrospective Study and Systematic Review. *Retina*. 2015 Feb 24.

Impact:

Age-related macular degeneration (AMD) is a leading cause of vision loss, and increasingly so in Asia, as its population rapidly ages. In the early 2000s, it was observed that Asians with AMD do not respond to standard treatment. In particular, SERI studies have helped identify a subtype of AMD called polypoidal choroidal vasculopathy (PCV), which appears to be more common in Asian populations and may behave differently from traditional AMD in Western populations. Since then, SERI has conducted many studies on Asian AMD, to show how these patients are different and how they should be best managed. This has led to major trials being conducted in Singapore and other parts of Asia to improve the treatment of Asian AMD.

¹ Cheung CM, Tai ES, Kawasaki R, Tay WT, Lee JL, Hamzah H, Wong TY. Prevalence of and risk factors for age-related macular degeneration in a multiethnic Asian cohort. *Arch Ophthalmol*. 2012 Apr;130(4):480-6.

² Cackett P, Yeo I, Cheung CM, Vithana EN, Wong D, Tay WT, Tai ES, Aung T, Wong TY. Relationship of smoking and cardiovascular risk factors with polypoidal choroidal vasculopathy and age-related macular degeneration in Chinese persons. *Ophthalmology*. 2011 May;118(5):846-52.

1999 & 2012

Goodbye, daily eye drops!



Other key publications:

1. Tan DT, Chee SP, Lim L, Theng J, Van Ede M. Randomized clinical trial of Surodex steroid drug delivery system for cataract surgery: anterior versus posterior placement of two Surodex in the eye. *Ophthalmology*. 2001 Dec;108(12):2172-81.
2. Narayanaswamy AK, Lee K, Zhen M, Chua J, Chai SM, Boey PY, Zheng C, Aung T, Venkatraman S, Wong TT. Randomized, controlled trial of a sustained delivery formulation of 5-fluorouracil for the treatment of falling blebs. *Ophthalmology*. 2012 Feb;119(2):314-20.
3. Liu YC, Peng Y, Lwin NC, Venkatraman SS, Wong TT, Mehta JS. A biodegradable, sustained-released, prednisolone acetate microfilm drug delivery system effectively prolongs corneal allograft survival in the rat keratoplasty model. *PLoS One*. 2013 Aug 5;8(8):e70419.
4. Natarajan JV, Darwita A, Barathi VA, Ang M, Htoon HM, Boey F, Tam KC, Wong TT, Venkatraman SS. Sustained drug release in nanomedicine: a long-acting nanocarrier-based formulation for glaucoma. *ACS Nano*. 2014 Jan 28;8(1):419-29.
5. Wong TT, Novack GD, Natarajan JV, Ho CL, Htoon HM, Venkatraman SS. Nanomedicine for glaucoma: sustained release latanoprost offers a new therapeutic option with substantial benefits over eyedrops. *Drug Deliv Transl Res*. 2014 Aug;4(4):303-9.

Impact:

Eyedrops are the standard method to deliver medication for eye diseases, but this often requires frequent (sometimes three times a day) and long-term use, affecting both patient quality-of-life and treatment compliance. In the 1990s, SNEC and SERI researchers developed Surodex, a biodegradable polymeric nanoparticle formulation of dexamethasone, for post-cataract surgery eye care. Suradex, which was eventually acquired by Allergan, was the first-ever drug approved by Singapore regulatory authorities that did not have any prior approval elsewhere. More recently, in collaboration with the Nanyang Technological University, we developed a novel liposomal nano-formulation of latanoprost for glaucoma treatment, which is now in clinical trials. A single injection of liposomal latanoprost lowered intraocular pressure in animal models for up to 90 days.

¹ Tan DT, Chee SP, Lim L, Lim AS. Randomized clinical trial of a new dexamethasone delivery system (Surodex) for treatment of post-cataract surgery inflammation. *Ophthalmology*. 1999 Feb;106(2):223-31.

² Natarajan JV, Ang M, Darwita A, Chattopadhyay S, Wong TT, Venkatraman SS. Nanomedicine for glaucoma: liposomes provide sustained release of latanoprost in the eye. *Int J Nanomedicine*. 2012;7:123-31.

2008 & 2013

FDA-approved: Tan Endoglide



Other key publications:

1. Khor WB, Mehta JS, Tan DT. Descemet stripping automated endothelial keratoplasty with a graft insertion device: surgical technique and early clinical results. *Am J Ophthalmol*. 2011 Feb;151(2):223-32.e2.
2. Khor WB, Teo KY, Mehta JS, Tan DT. Descemet stripping automated endothelial keratoplasty in complex eyes: results with a donor insertion device. *Cornea*. 2013 Aug;32(8):1063-8.
3. Ang M, Saroj L, Htoon HM, Kiew S, Mehta JS, Tan D. Comparison of a donor insertion device to sheets glide in Descemet stripping endothelial keratoplasty: 3-year outcomes. *Am J Ophthalmol*. 2014 Jun;157(6):1163-1169.e3.
4. Ang AY, Liu YC, Tan DT, Mehta JS. Descemet stripping automated endothelial keratoplasty with the EndoGlide Ultrathin graft insertion device. *Expert Rev Med Devices*. 2014 Nov;11(6):573-9.

Impact:

The Tan Endoglide, a patent-protected device developed at SNEC and SERI, is used to deliver donor corneal tissues to treat endothelial dysfunction. Glide insertion was shown to significantly reduce cell loss during corneal transplant surgery from 60% to a mere 15%, and increase transplant success rates to over 95% at the one-year mark, compared to conventional 'taco' fold insertion. The first disposable inserter to be FDA-approved, the Tan Endoglide has since been used in 31 countries for more than 14,000 transplants. SNEC now performs the largest number of these selective tissue transplants in Asia and is one of the leading transplant centres worldwide, largely due to the EndoGlide device.

¹ Mehta JS, Por YM, Poh R, Beuerman RW, Tan D. Comparison of donor insertion techniques for descemet stripping automated endothelial keratoplasty. *Arch Ophthalmol*. 2008 Oct;126(10):1383-8.

² Khor WB, Han SB, Mehta JS, Tan DT. Descemet stripping automated endothelial keratoplasty with a donor insertion device: clinical results and complications in 100 eyes. *Am J Ophthalmol*. 2013 Oct;156(4):773-9.

2011

Want better eyesight? Just ReLEx!



1

Other key publications:

- Ang M, Chaurasia SS, Angunawela RI, Poh R, Riau A, Tan D, Mehta JS. Femtosecond lenticule extraction (FLEx): clinical results, interface evaluation, and intraocular pressure variation. *Invest Ophthalmol Vis Sci.* 2012 Mar 15;53(3):1414-21.
- Angunawela RI, Riau AK, Chaurasia SS, Tan DT, Mehta JS. Refractive lenticule re-implantation after myopic ReLEx: a feasibility study of stromal restoration after refractive surgery in a rabbit model. *Invest Ophthalmol Vis Sci.* 2012 Jul 26;53(8):4975-85.
- Riau AK, Angunawela RI, Chaurasia SS, Lee WS, Tan DT, Mehta JS. Reversible femtosecond laser-assisted myopia correction: a non-human primate study of lenticule re-implantation after refractive lenticule extraction. *PLoS One.* 2013 Jun 24;8(6):e67058.

¹ Riau AK, Angunawela RI, Chaurasia SS, Lee WS, Tan DT, Mehta JS. Early corneal wound healing and inflammatory responses after refractive lenticule extraction (ReLEx). *Invest Ophthalmol Vis Sci.* 2011 Aug 5;52(9):6213-21.

- Lim CH, Riau AK, Lwin NC, Chaurasia SS, Tan DT, Mehta JS. LASIK following small incision lenticule extraction (SMILE) lenticule re-implantation: a feasibility study of a novel method for treatment of presbyopia. *PLoS One.* 2013 Dec 11;8(12):e83046.
- Rosman M, Hall RC, Chan C, Ang A, Koh J, Htoon HM, Tan DT, Mehta JS. Comparison of efficacy and safety of laser in situ keratomileusis using 2 femtosecond laser platforms in contralateral eyes. *J Cataract Refract Surg.* 2013 Jul;39(7):1066-73.
- Riau AK, Poh R, Pickard DS, Park CH, Chaurasia SS, Mehta JS. Nanoscale helium ion microscopic analysis of collagen fibrillar changes following femtosecond laser dissection of human cornea. *J Biomed Nanotechnol.* 2014 Aug;10(8):1552-62.
- Ang M, Mehta JS, Chan C, Htoon HM, Koh JC, Tan DT. Refractive lenticule extraction: transition and comparison of 3 surgical techniques. *J Cataract Refract Surg.* 2014 Sep;40(9):1415-24.
- Mohamed-Noriega K, Riau AK, Lwin NC, Chaurasia SS, Tan DT, Mehta JS. Early corneal nerve damage and recovery following small incision lenticule extraction (SMILE) and laser in situ keratomileusis (LASIK). *Invest Ophthalmol Vis Sci.* 2014 Mar 25;55(3):1823-34.

Impact:

LASIK is the most common refractive surgical procedure performed worldwide. Over the past decade, femtosecond (FS) laser technology has enabled a breakthrough: the first potentially reversible refractive surgery called refractive lenticule extraction (ReLEx). In 2011, SNEC/SERI performed animal studies showing that the ReLEx procedure led to better wound healing and nerve repair compared to conventional LASIK procedures, especially at high refractive correction. Follow up studies in human patients showed that LASIK can still be performed after lenticule reimplantation. The team is currently exploring whether discarded lenticules could be used in intracorneal presbyopia implants.

2006, 2012 & 2015

The gene hunters



Other key publications:

1. Vithana EN, Morgan PE, Ramprasad V, Tan DT, Yong VH, Venkataraman D, Venkataraman A, Yam GH, Nagasamy S, Law RW, Rajagopal R, Pang CP, Kumaramanickevel G, Casey JR, Aung T. SLC4A11 mutations in Fuchs endothelial corneal dystrophy. *Hum Mol Genet.* 2008 Mar 1;17(5):656-66.
2. Lu Y et al. Genome-wide association analyses identify multiple loci associated with central corneal thickness and keratoconus. *Nat Genet.* 2013 Feb;45(2):155-63.
3. Hysi PG et al. Genome-wide analysis of multi-ancestry cohorts identifies new loci influencing intraocular pressure and susceptibility to glaucoma. *Nat Genet.* 2014 Oct;46(10):1126-30.
4. Aung T et al. A common variant mapping to CACNA1A is associated with susceptibility to exfoliation syndrome. *Nat Genet.* 2015 Apr;47(4):387-92.

Impact:

Starting in the mid-2000s, SERI has embarked on an ambitious research programme focused on discovery of the genetic basis of Asian eye diseases. In 2006, SNEC/SERI researchers discovered seven mutations in the *SLC4A11* gene associated with autosomal recessive congenital hereditary endothelial dystrophy (CHED), a common corneal disease that requires transplanation. In 2012, another study in collaboration with A*STAR's Genome Institute of Singapore (GIS) revealed three new susceptibility loci for primary angle closure glaucoma (PACG), a disease with largely unresolved causal mechanisms. More recently, we identified new genetic loci conferring AMD susceptibility in East Asians, showing that some loci are shared with Europeans but others have a distinct genetic signature. These studies, involving large consortiums around the world, have been published in top-flight journals *Nature Genetics* and *Nature Communications*. The findings may enable the development of a clinically useful genetic profile for the identification and treatment of patients with these eye diseases.

¹ Vithana EN et al. Mutations in sodium-borate cotransporter SLC4A11 cause recessive congenital hereditary endothelial dystrophy (CHED2). *Nat Genet.* 2006 Jul;38(7):755-7.

² Vithana EN et al. Genome-wide association analyses identify three new susceptibility loci for primary angle closure glaucoma. *Nat Genet.* 2012 Oct;44(10):1142-6.

³ Cheng CY et al. New loci and coding variants confer risk for age-related macular degeneration in East Asians. *Nat Commun.* 2015 Mar 30;6:6817.

2008 & 2010

An eye image is worth a thousand words



Other key publications:

1. Sakata LM, Lavanya R, Friedman DS, Aung HT, Gao H, Kumar RS, Foster PJ, Aung T. Comparison of gonioscopy and anterior segment ocular coherence tomography in detecting angle closure in different quadrants of the anterior chamber angle. *Ophthalmology*. 2008 May;115(5):769-74.
2. Cheung CY, Thomas GN, Tay W, Ikram MK, Hsu W, Lee ML, Lau QP, Wong TY. Retinal vascular fractal dimension and its relationship with cardiovascular and ocular risk factors. *Am J Ophthalmol*. 2012 Oct;154(4):663-674.e1.
3. Nongpiur ME, Haaland BA, Friedman DS, Perera SA, He M, Foo LL, Baskaran M, Sakata LM, Wong TY, Aung T. Classification algorithms based on anterior segment optical coherence tomography measurements for detection of angle closure. *Ophthalmology*. 2013 Jan;120(1):48-54.
4. Cheng J, Liu J, Xu Y, Yin F, Wong DW, Tan NM, Tao D, Cheng CY, Aung T, Wong TY. Superpixel classification based optic disc and optic cup segmentation for glaucoma screening. *IEEE Trans Med Imaging*. 2013 Jun;32(6):1019-32.
5. Baskaran M, Ho SW, Tun TA, How AC, Perera SA, Friedman DS, Aung T. Assessment of circumferential angle-closure by the iris-trabecular contact index with swept-source optical coherence tomography. *Ophthalmology*. 2013 Nov;120(11):2226-31.

Impact:

Over the past 15 years, SNEC/SERI, along with key collaborators from the NUS School of Computing and A*STAR's Institute of Infocomm Research (I²R), has been at the forefront of eye imaging research, including studies on the cornea, glaucoma, optic disc, cataract and the retinal vasculature. SERI and NUS have jointly developed a new computer software, the Singapore I Vessel Analyzer (SIVA), which allows quantitative measurement of the retinal vasculature and has now been licensed to more than 20 institutions, hospitals and industry partners worldwide.

¹ Lavanya R, Foster PJ, Sakata LM, Friedman DS, Kashiwagi K, Wong TY, Aung HT, Alfred T, Gao H, Ee AG, Seah SK, Aung T. Screening for narrow angles in the Singapore population: evaluation of new noncontact screening methods. *Ophthalmology*. 2008 Oct;115(10):1720-7, 1727.e1-2.

² Cheung CY, Hsu W, Lee ML, Wang JJ, Mitchell P, Lau QP, Hamzah H, Ho M, Wong TY. A New Method to Measure Peripheral Retinal Vascular Caliber over an Extended Area. *Microcirculation*. 2010 Oct;17(7):495-503.

2008 & 2010

Diabetes and the eye: from biomarker studies to a national screening programme



Other key publications:

1. Lamoureux EL, Tai ES, Thumboo J, Kawasaki R, Saw SM, Mitchell P, Wong TY. Impact of diabetic retinopathy on vision-specific function. *Ophthalmology*. 2010 Apr;117(4):757-65.
2. Huang OS, Lamoureux EL, Tay WT, Tai ES, Wang JJ, Wong TY. Glycemic and blood pressure control in an Asian Malay population with diabetes and diabetic retinopathy. *Arch Ophthalmol*. 2010 Sep;128(9):1185-90.
3. Zheng Y, Lamoureux EL, Lavanya R, Wu R, Ikram MK, Wang JJ, Mitchell P, Cheung N, Aung T, Saw SM, Wong TY. Prevalence and risk factors of diabetic retinopathy in migrant Indians in an urbanized society in Asia: the Singapore Indian eye study. *Ophthalmology*. 2012 Oct;119(10):2119-24.
4. Bhargava M, Cheung CY, Sabanayagam C, Kawasaki R, Harper CA, Lamoureux EL, Chow WL, Ee A, Hamzah H, Ho M, Wong W, Wong TY. Accuracy of diabetic retinopathy screening by trained non-physician graders using non-mydriatic fundus camera. *Singapore Med J*. 2012 Nov;53(11):715-9.
5. Ikram MK, Cheung CY, Lorenzi M, Klein R, Jones TL, Wong TY, NIH/JDRF Workshop on Retinal Biomarker for Diabetes Group. Retinal vascular caliber as a biomarker for diabetes microvascular complications. *Diabetes Care*. 2013 Mar;36(3):750-9.

Impact:

Diabetes affects 10% of the Singapore population. Of these people, 1 in 3 will have diabetic retinopathy (DR), and 1 in 10 will develop threatening retinopathy. SERI's research in DR spans understanding the epidemiology, risk factors and impact, to programmes designed to improve screening. The Singapore Integrated Diabetic Retinopathy Programme (SIDRP), established in July 2010 as a partnership between SERI and TTSH, seeks to provide a comprehensive telemedicine screening programme for DR, with 'real-time' assessment of DR from photographs by a centralised team of trained technicians at the SERI Ocular Reading Centre (SORC). This represents a paradigm shift in the way DR screening is carried out, resulting in faster, more accurate and more cost-effective screening.

¹ Wong TY, Cheung N, Tay WT, Wang JJ, Aung T, Saw SM, Lim SC, Tai ES, Mitchell P. Prevalence and risk factors for diabetic retinopathy: the Singapore Malay Eye Study. *Ophthalmology*. 2008 Nov;115(11):1869-75.

² Cheung N, Mitchell P, Wong TY. Diabetic retinopathy. *Lancet*. 2010 Jul 10; 376(9735):124-36.

2011

Transforming how corneal dystrophy is tested



Other key publications:

1. Lakshminarayanan R, Chaurasia SS, Anandalakshmi V, Chai SM, Murugan E, Vithana EN, Beuerman RW, Mehta JS. Clinical and genetic aspects of the TGFBI-associated corneal dystrophies. *Ocul Surf*. 2014 Oct;12(4):234-51.
2. Lakshminarayanan R, Chaurasia SS, Murugan E, Venkataraman A, Chai SM, Vithana EN, Beuerman RW, Mehta JS. Biochemical properties and aggregation propensity of transforming growth factor-induced protein (TGFBIp) and the amyloid forming mutants. *Ocul Surf*. 2015 Jan;13(1):9-25.

Impact:

Personalised medicine is the future of medical care. With just a drop of blood, clinicians can make a precise diagnosis of disease, aiding in long-term prognosis and treatment selection. Working with A*STAR and Duke-NUS, we are setting the pace of development in genetic testing with our POLARIS transforming growth factor-beta induced (*TGFBI*) gene test. We showed that a novel mutation in the TGFβ1p protein may be responsible for the amyloid formation seen in corneal dystrophies (CD). Based on this finding, we developed the POLARIS test, a validated and laboratory-certified test that may aid in the diagnosis and management of stromal CD.

¹ Lakshminarayanan R, Vithana EN, Chai SM, Chaurasia SS, Saraswathi P, Venkataraman A, Rojare C, Venkataraman D, Tan D, Aung T, Beuerman RW, Mehta JS. A novel mutation in transforming growth factor-beta induced protein (TGFβ1p) reveals secondary structure perturbation in lattice corneal dystrophy. *Br J Ophthalmol*. 2011 Oct;95(10):1457-62.

A new biomarker for Alzheimer's disease



Other key publications:

1. Ikram MK, Cheung CY, Wong TY, Chen CP. Retinal pathology as biomarker for cognitive impairment and Alzheimer's disease. *J Neurol Neurosurg Psychiatry*. 2012 Sep;83(9):917-22.
2. Cheung CY, Ong YT, Ikram MK, Chen C, Wong TY. Retinal microvasculature in Alzheimer's disease. *J Alzheimers Dis*. 2014;42 Suppl 4:S339-52.
3. Cheung CY, Ong S, Ikram MK, Ong YT, Chen CP, Venketasubramanian N, Wong TY. Retinal vascular fractal dimension is associated with cognitive dysfunction. *J Stroke Cerebrovasc Dis*. 2014 Jan;23(1):43-50.
4. Cheung CY, Ong YT, Hilal S, Ikram MK, Low S, Ong YL, Venketasubramanian N, Yap P, Seow D, Chen CL, Wong TY. Retinal ganglion cell analysis using high-definition optical coherence tomography in patients with mild cognitive impairment and Alzheimer's disease. *J Alzheimers Dis*. 2015;45(1):45-56.
5. Ong YT, Hilal S, Cheung CY, Venketasubramanian N, Niessen WJ, Vrooman H, Anuar AR, Chew M, Chen C, Wong TY, Ikram MK. Retinal neurodegeneration on optical coherence tomography and cerebral atrophy. *Neurosci Lett*. 2015 Jan 1;584:12-6.

Impact:

The number of dementia patients in Asia is projected to grow to 64.6 million by 2050 and represents a substantial health care burden. There are no good biomarkers for Alzheimer's disease. In recent years, SERI researchers have pioneered the development of new tests to measure changes in microvasculature and nerve layers, thereby providing a glimpse of the pathophysiological processes taking place in the brain. We showed that patients with Alzheimer's disease have an altered microvascular network in the retina, with narrower blood vessels that are also sparser and more tortuous. Such studies show that imaging retinal blood vessels may act as a biomarker for dementia, and provide an indication of disease risk before the onset of cognitive dysfunction symptoms.

¹ Cheung CY, Ong YT, Ikram MK, Ong SY, Li X, Hilal S, Catindig JA, Venketasubramanian N, Yap P, Seow D, Chen CP, Wong TY. Microvascular network alterations in the retina of patients with Alzheimer's disease. *Alzheimers Dement*. 2014 Mar;10(2):135-42.

2014 & 2015

Safe & successful cataract surgeries



Other key publications:

1. Chee SP, Ti SE, Sivakumar M, Tan DT. Postoperative inflammation: extracapsular cataract extraction versus phacoemulsification. *J Cataract Refract Surg.* 1999 Sep;25(9):1280-5.
2. Chee SP. Management of the hard posterior polar cataract. *J Cataract Refract Surg.* 2007 Sep;33(9):1509-14.
3. Chee SP, Jap A. Management of traumatic severely subluxated cataracts. *Am J Ophthalmol.* 2011 May;151(5):866-871.e1.

Impact:

Over 17,000 cataract surgeries are performed every year at SNEC, making it the most common surgery performed in Singapore. SNEC has been instrumental in testing new cataract surgery technologies to ensure that they are safe and effective for Singaporeans. The new technique of femtosecond (FS) laser-assisted cataract surgery was tested by SNEC and shown to have low complication rates. A five-year audit study showed that posterior capsule rupture (PCR) after capsule surgery was extremely low and comparable with centres around the world.

¹ Chee SP, Yang Y, Ti SE. Clinical outcomes in the first two years of femtosecond laser-assisted cataract surgery. *Am J Ophthalmol.* 2015 Apr;159(4):714-719.e2.

² Ti SE, Yang YN, Lang SS, Chee SP. A 5-year audit of cataract surgery outcomes after posterior capsule rupture and risk factors affecting visual acuity. *Am J Ophthalmol.* 2014 Jan;157(1):180-185.e1.

2004 & 2015

Stem cell therapy



Other key publications:

1. Chng Z, Peh GS, Herath WB, Cheng TY, Ang HP, Toh KP, Robson P, Mehta JS, Colman A. High throughput gene expression analysis identifies reliable expression markers of human corneal endothelial cells. *PLoS One*. 2013 Jul;8(7):e67546.
2. Cheong YK, Ngho ZX, Peh GS, Ang HP, Seah XY, Chng Z, Colman A, Mehta JS, Sun W. Identification of cell surface markers glypican-4 and CD200 that differentiate human corneal endothelium from stromal fibroblasts. *Invest Ophthalmol Vis Sci*. 2013 Jul;54(7):4538-47.
3. Ding V, Chin A, Peh G, Mehta JS, Choo A. Generation of novel monoclonal antibodies for the enrichment and characterization of human corneal endothelial cells (hCENC) necessary for the treatment of corneal endothelial blindness. *MAbs*. 2014;6(6):1439-52.
4. Tan TE, Peh GS, George BL, Cajucom-Uy HY, Dong D, Finkelstein EA, Mehta JS. A cost-minimization analysis of tissue-engineered constructs for corneal endothelial transplantation. *PLoS One*. 2014 Jun;9(6):e100563.
5. Yam GH, Yusoff NZ, Kadaba A, Tian D, Myint HH, Beuerman RW, Lei Z, Mehta JS. *Ex vivo* propagation of human corneal stromal "activated keratocytes" for tissue engineering. *Cell Transplant*. 2014 Oct 6.
6. Muhammad R, Peh GS, Adnan K, Law JB, Mehta JS, Yim EK. Micro- and nano-topography to enhance proliferation and sustain functional markers of donor-derived primary human corneal endothelial cells. *Acta Biomater*. 2015 Jun;19:138-148.

Impact:

Stem cell research holds substantial promise. In the face of the global shortage of donor corneal tissues, tissue-engineered stem cell therapy remains a highly attractive option. Since the early 2000s, SNEC/SERI researchers have established a method to use stem cells for ocular surface reconstruction. Our research has highlighted novel cell culture methods developed at SERI to grow and propagate primary human corneal endothelial cells (hCEC), a prerequisite to cultivating sufficient number of cells for cell based therapy. SERI is now conducting preclinical studies with a view to undertaking first-in-man studies.

¹ Tan DT, Ang LP, Beuerman RW. Reconstruction of the ocular surface by transplantation of a serum-free derived cultivated conjunctival epithelial equivalent. *Transplantation*. 2004 Jun 15;77(11):1729-34.

² Peh GS, Chng ZZ, Ang HP, Cheng TY, Adnan K, Seah XY, George BL, Toh KP, Tan DT, Yam GH, Colman A, Mehta JS. Propagation of human corneal endothelial cells – A novel dual media approach. *Cell Transplantation* 2015;24(2):287-304.

Our research milestones

- 1990 SNEC is founded by first Medical Director Professor Arthur Lim.
- 1997 SERI is established by founding Director Professor Arthur Lim and led by Deputy Director Professor Chew Sek Jin.
- 1999 Professor Donald Tan is appointed as SERI's second Executive Director.
- 2001 Two floors dedicated to SERI's clinical and laboratory research is opened at SNEC's Phase 2 tower block.
- 2003 SERI releases encouraging findings from the Atropine in the Treatment of Myopia (ATOM) clinical trial study on children. Atropine is now available as a treatment option for progressive myopia in children at SNEC.
- 2006 SNEC and SERI scientists publish in *Nature Genetics* a study describing a gene that causes congenital corneal hereditary endothelial dystrophy, a severe form of blindness affecting children.
- 2006 SNEC doctors establish causal link between a potentially blinding fungal infection and a multipurpose contact lens solution that led to its worldwide recall, halting a potential epidemic. The paper is published in *JAMA*, and team later receives the inaugural Minister for Health Award.
- 2007 ASIA-ARVO meeting is held in Singapore.
- 2008 Professor Wong Tien Yin is appointed as SERI's third Executive Director.
- 2008 An international publication ranks Singapore (with 90% of the authors from SNEC/SERI) as having published the highest number of eye research publications per capita in the world.
- 2008 SERI is awarded a \$25 Million Translational Clinical Research Flagship Grant for the Translational Research Innovations in Ocular Surgery (TRIOS), a five-year programme focusing on two major causes of global blindness, corneal disease and glaucoma.
- 2009 Professor Donald Tan and team design the Tan Endoglide™ endothelium insertion system for corneal transplantation.
- 2011 SERI is officially admitted as a full member of the International Agency for the Prevention of Blindness (IAPB), which leads a worldwide effort in blindness prevention.
- 2012 SERI partners with Tan Tock Seng Hospital to introduce the Singapore Integrated Diabetic Retinopathy Programme (SiDRP), a national diabetic retinopathy screening programme conducted at polyclinics.
- 2012 SERI launches its inaugural annual fund raising gala dinner, The EYE Ball.
- 2013 SERI's \$25 million TCR programme is renewed with the introduction of the Surgery and Innovative Technologies (EyeSITE) programme.
- 2013 SERI scientists discover three genes linked to primary angle closure glaucoma (PACG), a leading cause of blindness in Chinese people, and publish their findings in the prestigious *Nature Genetics* journal.
- 2014 Professor Aung Tin is appointed as SERI's fourth Executive Director.
- 2014 Launch of Arthur Lim Professorship in Ophthalmology, which is conferred on Professor Donald Tan.
- 2015 SNEC celebrates 25th anniversary.

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