SINGAPORE EYE RESEARCH INSTITUTE

Medical Technology Innovation: From clinic to bench, and back again

Dr. Danny Belkin
Technology Development and Commercialization Director, SERI

SINGAPORE EYE RESEARCH INSTITUTE

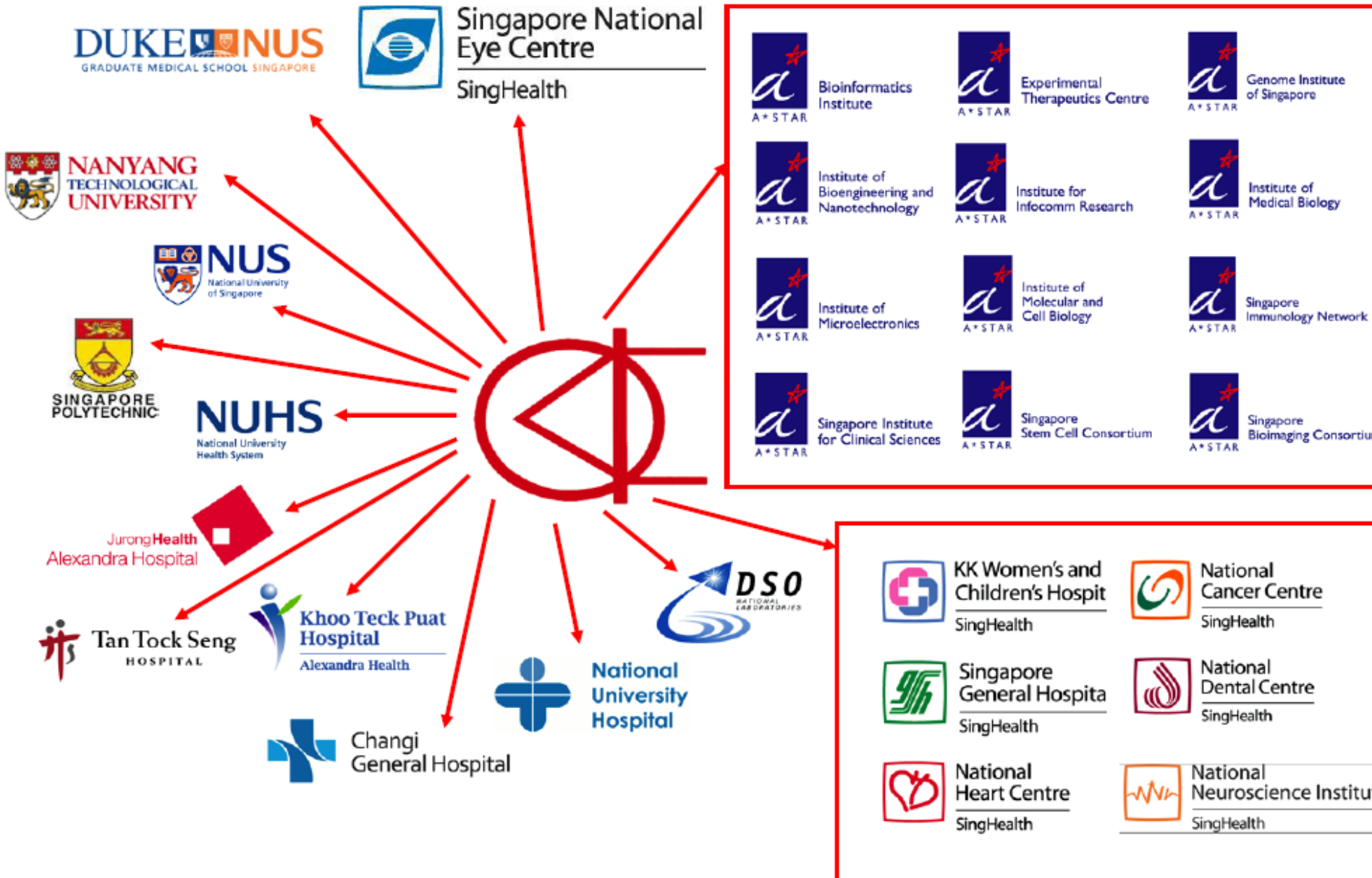
Medical Technology Innovation: From clinic to bench, and back again

1. **About SERI**
2. **Medical Technology Innovation**
   - ❑ Why?
   - ❑ How
   - ❑ Examples : devices, startups and industrial collaborations

About SERI

- SERI is Singapore's national institute for ophthalmology research, the research arm of SNEC
- Affiliated to National University of Singapore
- Recognized as the pioneer of eye research in Singapore, and as one of the foremost eye research institutes in the world
- 220 staff (+128 adjunct)
- >160 Students
- >2,100 Scientific Papers

Local Collaborations



A Spectrum of Our International/ Industry Collaborations

GLOBAL ACADEMIC COLLABORATIONS

- **Aravind Eye Care System**, India
- **Aston University**, Birmingham
- **Australian National University School of Biological Sciences**, Australia
- **Center for Eye Research Australia, University of Melbourne**
- **Centre for Vision Research, University of Sydney**
- **CHUV-Lausanne University Hospital, Lausanne**, Switzerland
- **City University London**
- **Cornea Research Foundation of America**
- **Doshisha University**, Kyoto, Japan
- **Duke University Eye Centre**, USA
- **East Valley Ophthalmology**, USA
- **Erasmus University Medical Center**, Rotterdam, Netherlands
- **Ho Chi Minh Eye Hospital**, Vietnam
- **Hospital Kuala Lumpur**, Malaysia
- **Indiana University School of Medicine**, USA
- **Institute of Ophthalmology, Moorfields Eye Hospital**, London, United Kingdom
- **Johns Hopkins University**, Baltimore, USA
- **King Khaled Eye Specialist Hospital**, Saudi Arabia
- **Kirchhoff-Institute for Physics, University of Heidelberg**
- **Kyoto Prefectural University of Medicine**, Japan
- **Lions Eye institute,** Australia
- **Max Planck Institute**, Germany
- **Narayana Nethralaya Foundation**, India
- **Oregon Health & Science University**, USA
- **St. George's University**, USA
- **Stanford University**, USA
- **Tel Aviv University**, Israel
- **The First Affiliated Hospital of Chongqing Medical University**, China
- **Queen's University Belfast**, Canada
- **The University of Wisconsin-Madison**, USA
- **The Weizmann Institute of Science**, Israel
- **University of Aberdeem**, Scotland
- **University of New South Wales**, Australia
- **University of Pennysylvania**, USA
- **University of Wisconsin**, USA
- **Vietnam National Institute of Ophthalmology**
- **West Virginia University Eye Institute**
- **Zhongshan Ophthalmic Centre, Sun Yat-Sen University**, China

INDUSTRY COLLABORATIONS

- AcuFocus
- Advanced Medical Optics
- Advanced Medical Technologies
- Alcon
- Allergan
- Angioblast Systems
- AqueSys
- AYOXXA
- Bausch & Lomb
- Bayer
- Canon
- Capital Optical
- Carl Zeiss
- Ceepro
- Celgene
- Ellex
- Essilor
- Eyedetec Medical
- Frontier FMC
- GlaxoSmithKline
- i-Optics
- Johnson & Johnson
- Kendle International
- Keravision
- Laserex
- Lenticor
- Mandarin Opto-Medic
- Menicon
- Merlion Pharma
- Network Medical
- Neurovision
- Northern Lipids
- Novartis
- Ocular Therapeutix
- Oculex Asia
- Optique Paris Miki
- ORA
- Oxigene
- PARAXEL International
- Patsnap
- Pfizer
- Pharmacia & Upjohn
- Quark Pharmaceuticals
- Quintiles
- Roche
- Santen Pharmaceutical
- SATA CommHealth
- SkinEthic
- Technolas
- VisionEx
- Welch Allyn

Industry Collaboration Models @ SERI

Collaboration tracks:

- Strategic input into ophthalmology strategy
- Technology co-development (IP sharing, licensing option)
- Licensing of SERI-developed technology
- Fee-for-service (non-, pre-clinical & clinical research)
- Development and/or use of animal models

Industrial collaborations:

- Early and late stage
- Small and large companies
- Devices, pharmaceuticals, software and diagnostics

SERI Technology Development and Commercialization Office

Est. 2012

Mission:

To proactively pursue the development and commercialization of **SERI's technologies** as well as enhance current, and create new, **partnerships with industry**

Ocular Disease Screening
Drug Delivery
Stem Cell Research
Proteomics
Point of Care Diagnostics
Preclinical Models

Surgical Devices
Tissue Engineering
Ophthalmic Imaging
Genetics
Software

Ophthalmic Biomarkers
Cell Culture Devices
Antimicrobials
Light Therapy
Wearable Devices

Medical Technology Innovation

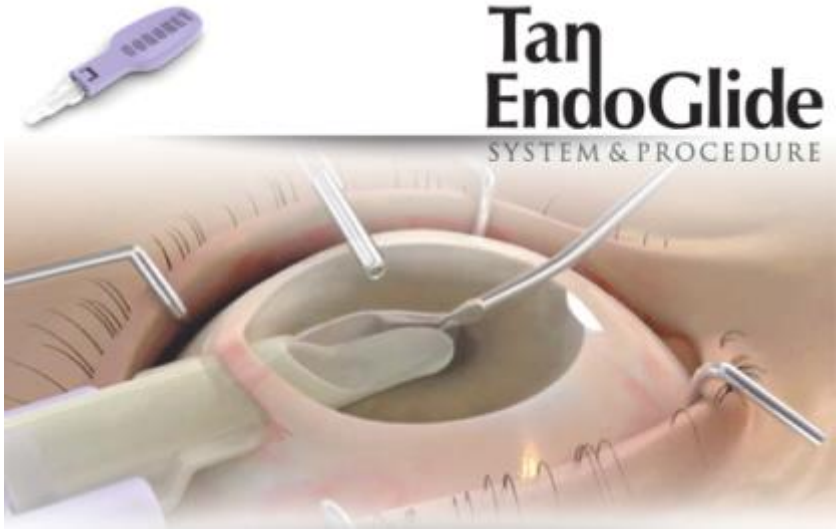
Why?

The Role of Medical Technology Innovation

Medicine is the only profession that labors incessantly to destroy the reason for its existence

Why Be a Medical Technology Inventor?

Clinical need → Solution → Patients



Why Be a Medical Technology Inventor?

- Help large numbers of patients (more than one at a time)
- Innovation / novelty
- Publications: academic track -> Professorship
- Economic impact (startups)
- Financial: monetary reward
- Prestige/ recognition
- Exciting and enjoyable
- Self-fulfillment

Why Be a Medical Technology Inventor?

Singapore/SERI Advantages

- Strong public research funding
- One of the world's top eye research institutes
- High quality research personnel and facilities available
- Access to top world eye researchers and clinicians
- Support platform for technology development and commercialization
  - Strong ophthalmic domain specialty
  - Constant 'on the ground' presence
  - Established relationship and trust with clinicians and researchers
  - Strong network with large and small companies in ophthalmic domain
  - Network of domain-specific advisors

However…

- I don’t have enough time
- I’m working too hard as it is
- I will make enough money in my future practice
- I don’t know much about product development, patents and translational medicine
- I don’t have the patience to face committees, bureaucracy, businessmen and lawyers

Medical technology Innovation

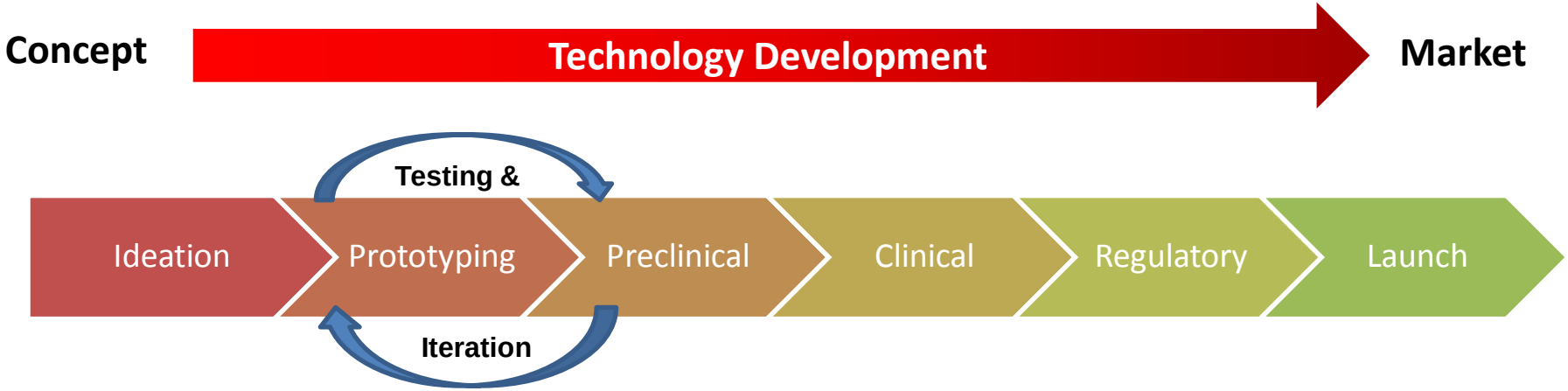
How?

Types of New Medical Technologies

- ***Sustaining/ incremental*** – Linear improvement of existing technology. Most innovations in a given industry are of this type
  - e.g. bottles -> single unit drops

- ***Disruptive*** – Introduction of completely new approaches that have a transformative potential
  - Revolutionary innovations (IOL, Phacoemulsification, anti-VEGF)
  - Evolutionary – formed by the convergence of previously separate research areas (LASIK, slow release drugs)

Technology Development Pathway



Preliminary Research	Viability Assessment	Opportunity Development	Preparing for Commercialization
	• Patent Analysis • Market Analysis • Competitive Analysis	•Initial Product Development and Testing •IP Development •Business Model Development •High level regulatory assessment	• Advanced Product Development and Testing • Regulatory and quality Considerations • Further Funding • Licensing or Start-up?

Licensing vs. Start-ups

- **Licensing to an established industrial party**
  - **Less hassle**: relatively hands-off
  - Reduced personal & financial **exposure and risk**
  - **Reduced return** vs. successful start-up
  - Reduced **control**
  - Reduced **emotional link**

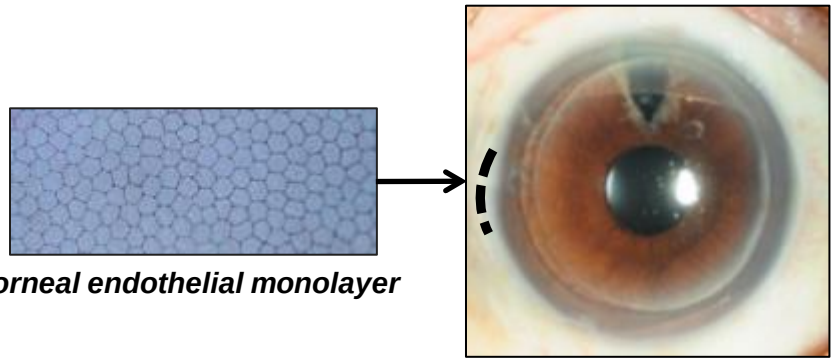
VS.

- **Spinning off a company**
  - **Maximum** potential for **gain**
  - High level of **involvement and some control**
  - Possible to see invention **from conception to final widespread utilization**
  - Increased **risk**
  - Substantial **time dedication** required
  - Likely to demand **working adjustment**

Medical technology Innovation

Example:
The Endoglide Story

Clinical Need: Drawbacks of Corneal Transplantation Technique



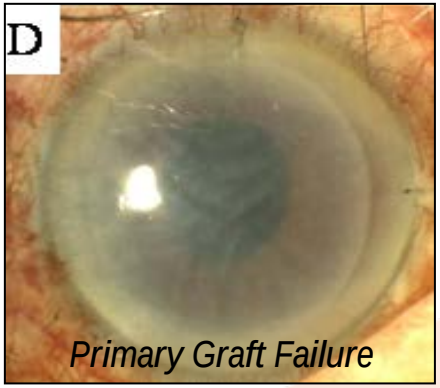
Corneal endothelial monolayer

Key Surgical Challenge:

How can we get a thin (150um) donor tissue, which measures about 9mm in diameter, through a 4mm opening, without touching or damaging the inner endothelial cell monolayer?

Standard "Taco Folding" graft Insertion Technique:

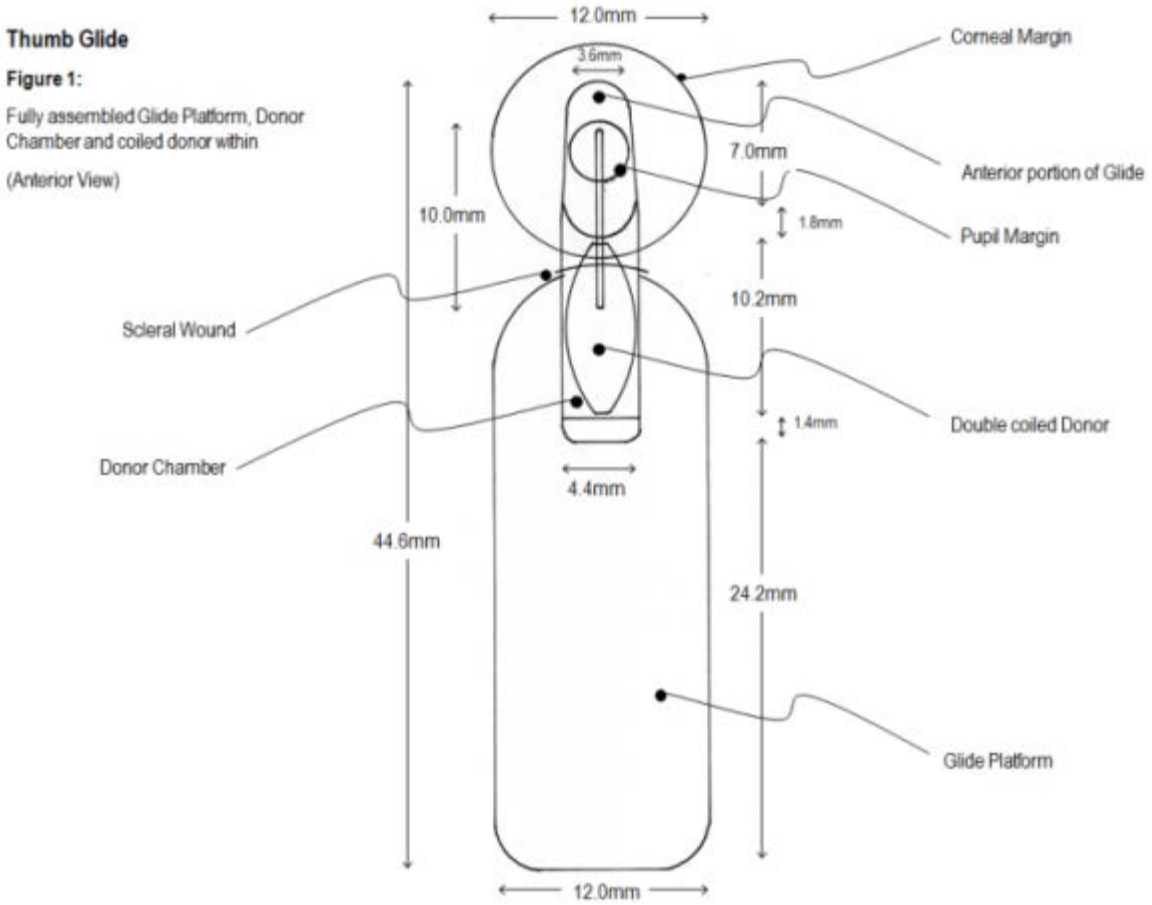
- Donor Grant Dislocation: **mean: 14%** (range 0%-82%, 16 studies)
- Primary Graft Failure: **mean: 5%** (range 0%-29%, 14 studies)
- Endothelial Cell Loss: **29-35% loss at 6-12 months**
- **Asian eyes (Japan, Singapore: 60% cell loss)**



Primary Graft Failure

Tan Endoglide: Concept and Early Sketches

- Donor tissue lies coiled up inside a Glide Capsule
- Design concept: Simplicity, "Thumbdrive in a USB port"



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Tan Endoglide: Concept and Early Sketches

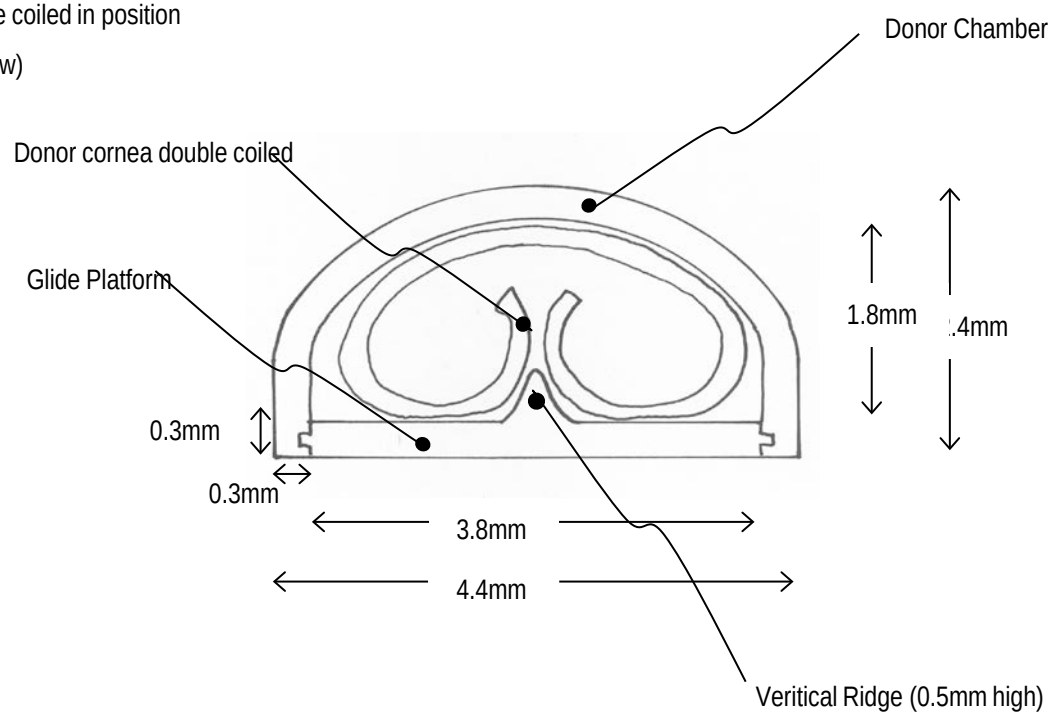
Thumb Glide

Figure 3:

Donor Chamber with Glide Platform in place

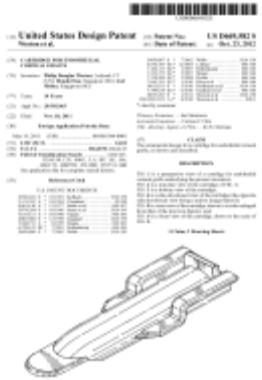
Donor cornea double coiled in position

(Cross Sectional View)



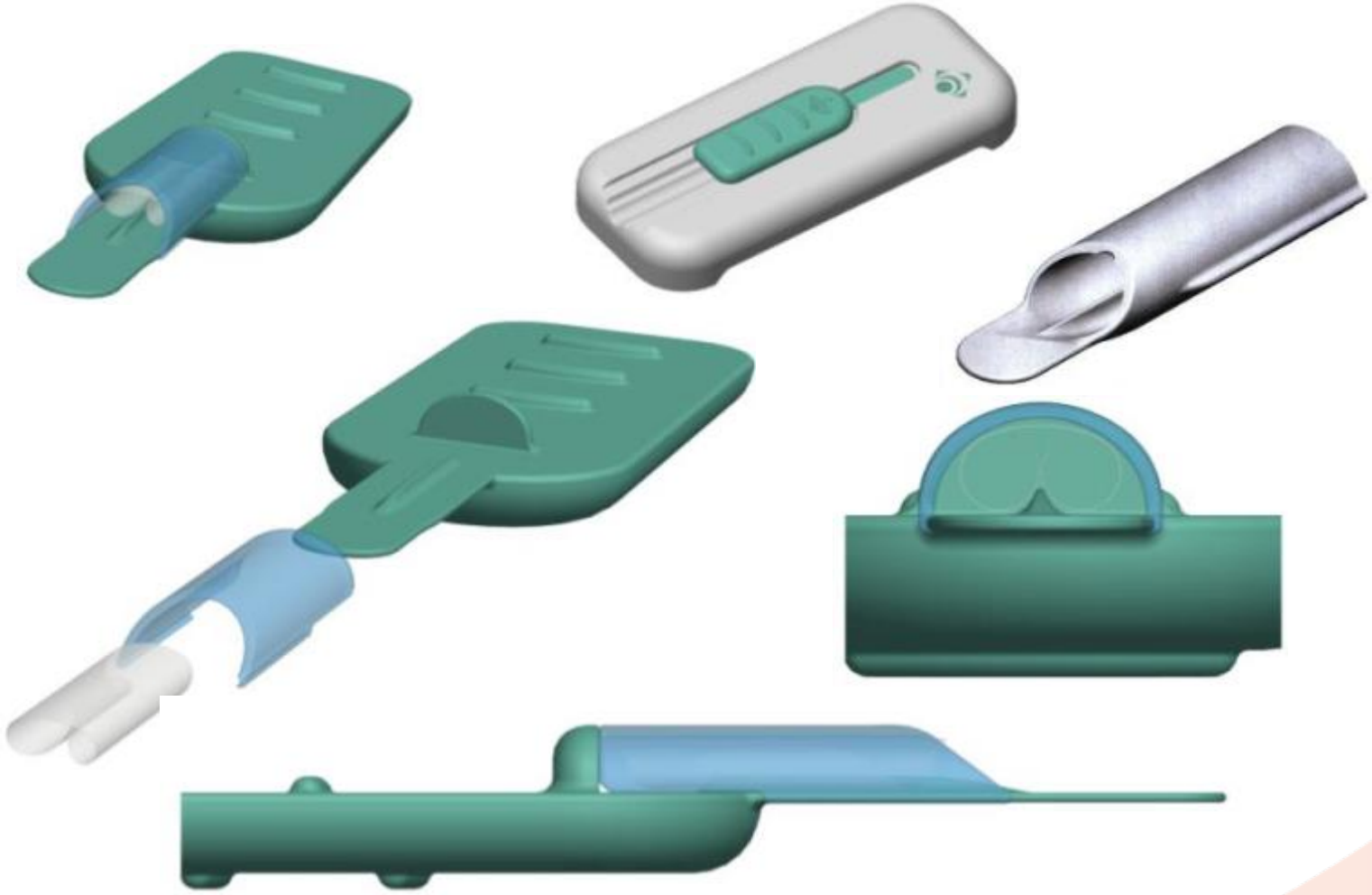
IP and Development Strategy

- "Thumbdrive" patent filed by SHIP – 16 Oct 2008; further patents filed

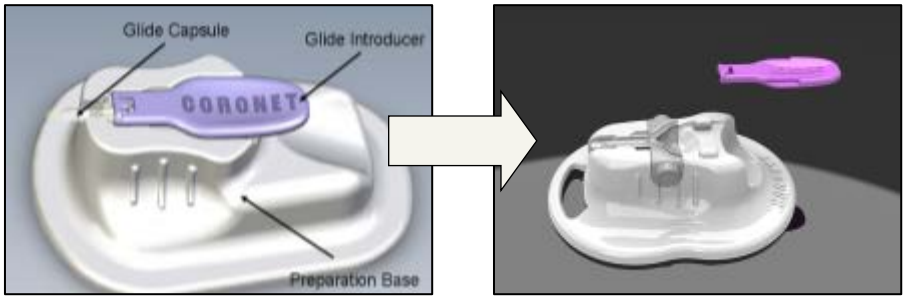


- Several Ophthalmic instrument companies approached
- Network Medical Products (UK)
  - Small UK company super-specializing in corneal surgery; hungry for new products to license
  - Small and nimble – direct negotiation with CEO
  - Links to UK network of device development expertise

Tan Endoglide: Early CAD version



Tan EndoGlide: Summary



EndoGlide Classic ***EndoGlide Ultrathin***

- First disposable donor corneal tissue inserter
- FDA Class 1 medical device, CE Mark
- Lowest endothelial cell loss to date (best in class)
- Clinical data: up to 5 years follow-up
- Can be used for wide range of tissue thickness (20-200 um)
- >10 clinical studies – Singapore, UK, Brazil, Japan, Greece, Poland
- >15,000 devices sold in 31 countries

Tan EndoGlide: Lessons Learned

- The path to Innovation in ophthalmic medical devices can be rewarding to both clinician inventors and patients

- How to handle the development process:
  - Focus and define the appropriate clinical challenge to be solved ***(bedside)***
  - Understand the gaps in the technology, and devise how solve these
  - Evaluate these solutions and determine the optimal one ***(bench)***
  - Find the right commercial pathways, and ways to move fast ***(commercialization)***
  - Implement the innovation in the clinic, to patients' benefit ***(back to the bedside)***

The Next Generation of Devices at SERI

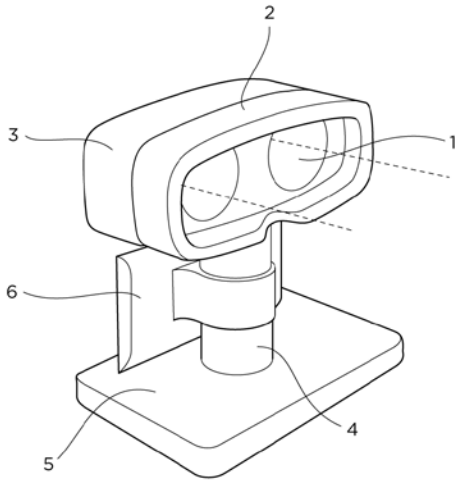


Fig 1.

Medical technology Innovation

Examples:

Startups and Commercial Collaborations

TCR Ocular Drug Delivery spinoff: Peregrine Ophthalmic

Global pharma firms interested in local startup's new glaucoma treatment

By Claire Huang
huangjy@sph.com.sg
@ClaireHuangBT

Singapore

"FIRST you have my interest, now you have my attention."

And that is what local biotech startup Peregrine Ophthalmic managed to do, in the words of associate professor Tina Wong, who was describing how a new glaucoma drug delivery solution developed by her 15-month-old startup has attracted inquiries from the world's top five pharmaceutical companies.

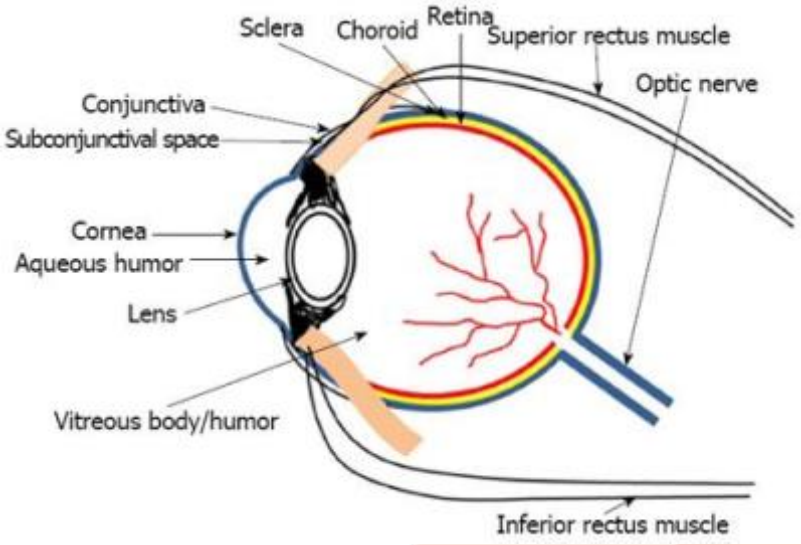
Clinical Need

Currently, only eye drops are approved for glaucoma

- Patient compliance issues (in Singapore 20% prescription refill rate)
- Side effects of eye drops
- Daily administration
- Bioavailability, drug wastage

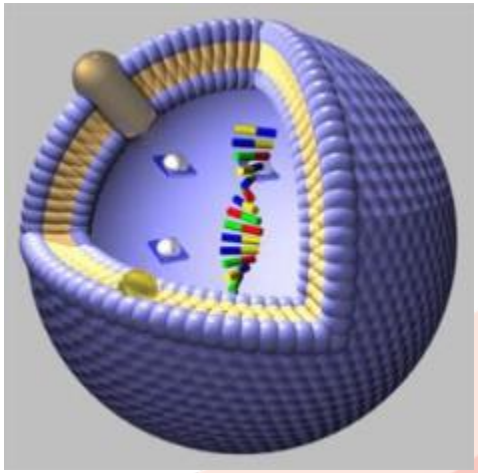
Sustained- and localized release solutions can:

- *Solves patient compliance problem*
- *Effects sustained over a few months*
- *Bioavailability increased, less wastage of drug*
- *Increased efficacy*
- *Fewer side effects*



Development of Liposomal Latanoprost ("Lipolat"): @ Bench

- **Funding** from TCR grant and SNEC HREF
- Extensive ***in vitro*** **bench testing** for 2 years to find best fit **drug delivery platform** for latanoprost (most common glaucoma drug, now off-patent)
- Prolonged **efficacy and safety studies in animals** (2 species, rabbit and monkey) for 2 years
- Preclinical **toxicology studies** for preparation for Phase 1B in Singapore
- Drug development by OEM in Canada to provide **stability and validation of process and cGMP product for FiM**
- Completion of **FiM** July 2013
- **IP licensed** from SingHealth and NTU in Aug 2013



Peregrine Ophthalmic: The Company

- Local, experienced angel investor sole private investor
- Spring Singapore providing additional funding support
- Focus now on further development of product towards **next clinical trial in major target markets**
  - Next major milestone before larger fundraising efforts commence

TCR AMOP spinoff: SinSa Labs

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Technology

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SinSa Labs inks licencing pact with Singapore Health Services and ETPL for new class of antibiotics

Montreal
Monday, January 12, 2015, 14:00 Hrs [IST]

SinSa Labs announced the signing of a licence agreement with Singapore Health Services and ETPL, A* STAR's technology transfer arm, regarding a technology developed at the Singapore Eye Research Institute (SERI) and Bioinformatics Institute (BII), A* STAR that deters the development of antibiotic resistance. This agreement provides SinSa Labs with a technology platform leading to a new class of antibiotics that kill bacteria quickly at a low dose and deters antibiotic resistance.

- *December 2014: licensing agreement with SingHealth and Exploit signed*

SinSa Labs: Press

BioCentury

PRODUCT DEVELOPMENT | EMERGING COMPANIES | POLITICS, POLICY & LAW | FINANCE

EMERGING COMPANY PROFILE

EYEING NEW ANTIBIOTICS

BY STEPHEN PARMLEY, SENIOR WRITER

Traditional antibiotics kill bacteria by inhibiting protein, DNA, or cell wall synthesis but require multiplying cells to be effective. SinSa Laboratories Inc.'s peptide antibiotics kill slow- and fast-growing bacteria by direct disruption of the cell membrane, and could have reduced risk of susceptibility to resistance mechanisms compared with existing antibiotics for antibiotic-resistant eye infections.

SinSa's antimicrobial peptides were created with its SpearHead technology, which incorporates positively charged amino acids and lipophilic groups to specifically disrupt negatively charged bacterial cell membranes regardless of their growth state.

According to CSO Robert Beuerman, "It doesn't make any difference whether the cells are in log or stationary phase, we see rapid killing." Beuerman also is senior scientific director of the Singapore Eye Research Institute (SERI), from which SinSa has exclusive rights to the SpearHead technology, plus antimicrobial compounds AM218 and B2088.

Beuerman said another benefit of the therapeutic dose you see a terrible amount of inflammation," he said.

In 2012 the SERI team reported preclinical data

SINSA LABORATORIES INC.
Montreal, Quebec

Technology: Synthetic peptide antimicrobials that target pathogen membranes

Disease focus: Infectious

Clinical status: Preclinical

Founded: 2014 by Roger Beuerman, Magnus Precht and Urban Olson

University collaborators: Singapore Eye Research Institute (SERI)

Corporate partners: None

Number of employees: 2

Funds raised: Not disclosed

Investors: Not disclosed

CEO: Magnus Precht

Patents: 5 issued covering small molecules, peptides and pharmaceutical antimicrobial compositions

The combination of B2088 with gatifloxacin was more effective than gatifloxacin alone at treating an existing *P. aeruginosa* corneal infection in mice. In a rabbit corneal wound-healing model, topical application of B2088 did not interfere with wound closure and showed no clinical signs of toxicity.

President and CEO Magnus Precht said SinSa has started manufacturing B2088 and will combine it with fixed doses of gentamicin — a combination the company calls Dorzidin — to treat antibiotic-resistant *Pseudomonas* eye infections that lead to keratitis in contact lens wearers.

The company's second candidate is AM218, a SpearHead antimicrobial that was synthesized by modifying a hydrophobic xanthone core with cationic arginine and lipophilic isoprenyl groups. Data published in the *Journal of Medicinal Chemistry* last month showed AM218 killed a wide range of Gram-positive bacteria. In studies similar to those performed on B2088, AM218 killed *Staphylococcus aureus* with a MIC of 0.5 µg/mL, lysed red blood cells with an EC50 of 277 µg/mL and showed less resistance than generic gatifloxacin or norfloxacin.

SinSa Labs: Overview

- Technology includes **small peptides and small organic molecules** that kill bacteria and fungi significantly faster than current antibiotics

- **Previous R&D funding**:
  1. **TRIOS TCR grant at SERI** (AMOP theme), together with **A*Star - BII**
  2. **Flagship grant** from ETPL/A*Star
  3. **Two NMRC CBRG** grant spinoffs and a spinoff project in the **SNEC incubator**

- SinSa is dedicated to **developing effective pharmacological therapies for communicable disease** and substantially reducing the dramatic negative effects such diseases have in the developing and developed world

- The first product will be directed to treating **resistant Gram negative infections** in **ophthalmology** and **otolaryngology**

- **Main staff:**
  - Magnus Precht (CEO): 30+ years leadership positions in pharmaceuticals and biotech
  - Roger Beuerman (CSO)
  - Urban Olsen (Counsel), substantial experience on IP and general legal affairs

SinSa Labs: Current Status

- Currently raising **series A**
- Held meetings with VCs at **JP Morgan healthcare summit** in San Francisco (January), as well as at Montreal **Biotech cluster** to establish first site
- The company aims to **reach clinical studies and marketing by the fastest route**, this approach being facilitated by priority given to such potentially impactful projects by regulatory authorities
- Positive background meeting with the **MPA in Sweden**, one of the three **regulatory bodies** in Europe that deals with ophthalmology to discuss plans going forward

Strategic Collaboration with Santen Pharmaceutical

Santen Pharmaceutical Co., Ltd. and the Singapore Eye Research Institute Collaborate to Develop New Ophthalmology Therapeutics

Nov 14 14

Santen Pharmaceutical Co. Ltd. and the Singapore Eye Research Institute have announced a multi-year collaboration to develop new therapeutics in ophthalmology, with a focus on diseases prevalent in Asia.

Strategic Collaboration with Santen Pharmaceutical

- **Strategic, multi-year collaboration to co-develop new therapeutics in ophthalmology** by bringing together the two parties' capabilities in ophthalmic R&D, with a special focus on diseases prevalent in Asia.
- Multiple long term **R&D programmes** combining Santen's asset portfolio and experience in drug development, and SERI's novel technologies and proven translational research capabilities
- Oversight by **high level SERI-Santen Joint Research Committee**
- R&D activities span a **variety of domains** within ophthalmology and **involve researcher teams from both sides**, with the goal of **establishing a robust pipeline of therapeutics** which Santen will be able to bring to market to the benefit of patients

Collaboration with AYOXXA Biosystems GmbH

european pharmaceutical review

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AYOXXA and SERI to collaborate on protein biomarker detection

3 February 2015 • Source: AYOXXA Biosystems / SERI

AYOXXA, an international biotech company with headquarters in Cologne, has signed an agreement with the Singapore Eye Research Institute (SERI), one of the leading international eye research institutes. AYOXXA and SERI will work together on validating the company's multiplexing technology platform for protein biomarker detection, as part of an expanded collaboration for developing ophthalmic diagnostic tools.

Related pharma topics

- AYOXXA Biosystems
- Biomarkers
- SERI

Related stories

HOX genes: HOX transcription factors as biomarkers in cancer

Targeted therapy in metastatic melanoma

Discovery and validation

Collaboration with AYOXXA Biosystems GmbH

- SERI and AYOXXA (NUS spinoff biotech company, HQ'd in Cologne, Germany) working together on validating the company's **protein multiplexing technology platform** for **cytokine biomarker detection** as a therapy monitoring diagnostic tool
- Part of an **expanded planned collaboration for developing ophthalmic diagnostics**
- **Clinical validation** of technology via access to very low-volume samples from the eye
- Technology can potentially be used for **diagnostic applications in the treatment of AMD, and in the future for additional diseases**
- Can potentially also **help better assess patients** and **more objectively steer their treatment**, as well as potentially assist in **development of new treatments**.

- **AYOXXA Management team visit and discussions** on diagnostics in ophthalmology on **27th April** (open to local stakeholders and industry)

AYOXXA BIOSYSTEMS

SINGAPORE EYE RESEARCH INSTITUTE

Medical technology Innovation

Summary

Summary

Development of innovative medical technology at local hospitals has great potential to:

- Create **new, impactful treatments** for our patients
- Help develop a **new generation of clinician inventors** within the public healthcare sector
- Help **retain these rare individuals** within the public sector
- Potentially **close the loop** and get funds flowing back into research
- Push forward the **med-tech sector** in Singapore
- Establish Singapore as the **Asian medical technology innovation hub**

Summary

However

- Resources **sorely needed on the ground** to support medical technology development: national frameworks are beneficial complementary elements, but **not sufficient on their own**
- Importance of individuals/teams with a **high level of domain expertise and broad domain-specific network**, in close & frequent contact with innovators for **successful cultivation and execution** of development programs and commercialization thereof
- **Strategic alignment** throughout the public healthcare sector on the importance of entrepreneurship in medical technology needs to be improved

Summary


Proteomics
Clinical Trials
Startups
Pharmaceutical Companies
Stem Cell Research
Point of Care Diagnostics
Diagnostics
Ophthalmic Imaging
Ophthalmic Imaging
Stem Cell Research
Therapeutics
Therapeutics
Clinical Trials
Surgical Devices
Cel Culture Devices
Tissue Engineering
Diagnostics
Preclinical Models
Light Therapy
Incubator
Co Development
Antimicrobials
Ophthalmic Biomarkers
Co Development
Antimicrobials
Pharmaceutical Companies
Ocular Disease Screening
Genetics
Ophthalmic Imaging
Software
Drug Delivery
Ocular Disease Screening
Surgical Devices
Point of Care Diagnostics
Incubator
IP Licensing
Surgical Devices
Cel Culture Devices
IP Licensing
Stem Cell Research
Preclinical Models
Pharmaceutical Companies
Drug Delivery
Therapeutics
Light Therapy
Co Development
Wearable Devices
Cel Culture Devices
Clinical Trials
Software
Clinical Trials
Preclinical Models
Tissue Engineering
Startups
Light Therapy
Drug Delivery
Wearable Devices
Wearable Devices
Ophthalmic Biomarkers
Wearable Devices
Light Therapy
Startups
Ocular Disease Screening
Proteomics
IP Licensing
Ocular Disease Screening