# **BIOGRAPHICAL SKETCH**

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. DO NOT EXCEED FIVE PAGES.

#### NAME: Peter Luke Santa Maria

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

POSITION TITLE: Assistant Professor, Otolaryngology Head & Neck Surgery Stanford University School of Medicine

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Stanford University, Stanford, USA	Instructorship	06/2015	Otology and Neurotology
Sir Charles Gairdner Hospital, Perth, Western Australia	Fellowship	06/2012	Otology and Neurotology
Royal Australian College of Surgeons, Perth, Western Australia	Residency	11/2011	Otolaryngology, Head and Neck Surgery
University of Western Australia,Perth, Western Australia	PhD	03/2012	Medicine / Surgery
Royal Australian College of Surgeons Western Australia, Perth, Western Australia		12/2005	Basic Surgical Training
University of Western Australia, Perth, Western Australia	MBBS	01/2002	Medicine / Surgery

#### A. Personal Statement

I am an early career clinician scientist and I have dedicated my career to helping those with hearing loss. As part of my clinical practice in otology, including through outreach clinics to the indigenous children of northern Australia, I experienced firsthand the clinical implications of chronic suppurative otitis media. This compelled me to find a way to help patients through my clinical practice and scientific research. I began by developing a foundation to do this by completing a combined Otolaryngology Residency and PhD in Australia. I then concentrated my research efforts around tympanic membrane wound healing and middle ear infectious disease. I am currently Associate Director of Stanford SPARK where I facilitate over 20 therapeutic translational projects every year. I have had two projects graduate from the program. Through my role I have the ability to collaborate with Dr Bollyky (expert in pseudomonas biofilms) and the many Stanford SPARK mentors to drive my research into chronic suppurative otitis media using a novel animal model I created. My previous work in tympanic wound healing includes a regenerative treatment that has been licensed to Astellas Pharmaceuticals and has entered phase I trials in 2020. I have another two therapeutics currently undergoing diligence with pharma companies. I have been seed funded to develop novel ideas on developing adjuvant therapies for chronic suppurative otitis media model and have received close mentorship by Stanford SPARK advisors who have been invaluable in helping to develop our lab's ideas on nanoparticle antibiotic adjuvants. If this work is successful I have an emerging record in translation as highlighted through the following publications:

- 1. **Santa Maria, PL.** Gottlieb, P. Santa Maria, C. Kim, S. Yang, YP. Puria, S. Functional Outcomes of Heparin Binding Epidermal Growth Factor Like Growth Factor Treatment for Chronic Tympanic Membrane Perforations Tissue Eng Part A. 2017:436-444. PMID 28142401.
- 2. **Santa Maria PL**, Kim S, Yang YP. No systemic exposure of transtympanic heparin-binding epidermal growth factor like growth factor. Drug Chem Toxicol. 2016;18:1-4. 26887920

### **B.** Positions and Honors

#### **Positions and Employment**

 2011-2012 Fellow, Otology & Neurotology, Sir Charles Gairdner Hospital, Perth, Australia
2012-2015 Instructor, Otology & Neurotology, Stanford University, Stanford, CA
2015-2017 Associate Professor, The University of Western Australia, Perth, Australia
2014-present Founder, Chief of Scientific Advisory Board, Auration Biotech (Pharmaceutical start-up), Burlingame, CA
2014- present Founder, , Chief of Scientific Advisory Board, Flotherm (Medical device start-up), Palo Alto, CA

2017-present Assistant Professor, Stanford University, Stanford, CA

#### Other Experience and Professional Memberships

2000	Council Member, The University of Western Australia, Faculty of Medicine Curriculum
2000	Council member, Australian Medical Association of Western Australia
2000	President, President of the Western Australian Medical Students Society
2002-2005	Council member, Australian Medical Association of Western Australia Doctors in Training
2007	Council Member, Western Australian Surgical Trainees Committee
2007-2008	Vice President and Board Member, Youth Media Society / Groove Radio
2011-2012	Committee member, ESIA Centre for Ear Nose and Throat Education and Research, Curriculum
	development
2015 – 2017	Committee member, Ear Science Institute of Australia Research Committee
2014 – 2016	Committee member, American Academy of Otolaryngology, Head and Neck Surgery Skull Base
	Surgery
2015 – 2016	Committee member, American Academy of Otolaryngology, Head and Neck Surgery
	Implantable Devices Committee
2015 – 2016	Committee member, American Academy of Otolaryngology, Head and Neck Surgery Hearing
	Committee
2015-2017	Board Member, Lions Hearing Foundation Western Australia
2016- 2018	Director, SPARK Co-Lab (Not for profit education in medical research), Perth, Australia
2004-present	Member, Royal Australian College of Surgeons
2011-present	Member, American Academy of Otolaryngology, Head and Neck Surgery
2012-present	Member, American Auditory Society
2012-present	Member, North American Skull Base Society
	Editorial board, Journal of Laryngology and Otology (Aus Supplement)
2018-present	Associate Director, Stanford SPARK, Stanford, USA

#### <u>Honors</u>

2017	40 under 40 award, Western Australia and overall winner of small business / start up category
2015	Robert Howard Next Step Award in Medical Technology Innovation, Stanford CA
2014	William E. Eaglestein Award for Excellence in SPARK, Stanford CA
2014	Neurotology Fellow Award at American Neurotology Society Meeting, Orlando, FL
2008	The University of Western Australia Local Travel Award, Perth AUS
2005	William Allnutt & May G Saw Medical Research Scholarship, Perth AUS
2000	Simon Seow Memorial Prize in Public Health, Perth AUS

#### C. Contribution to Science

#### 1. Understanding tympanic membrane wound healing

Chronic tympanic membrane perforations are a significant cause of hearing loss, especially in the developing world where access to surgery is limited. Unfortunately, when I began to research this area, I found that there was very little known about tympanic membrane wound healing. There was some potential treatments for the condition, but there was not an available animal model to progress these through to the clinic. Before an animal model could be developed, there needed to be a comprehensive understanding of tympanic membrane wound healing. To obtain this understanding I performed research that thoroughly documented the histological and post transcriptome response to tympanic membrane perforation in a rodent model over two weeks. With this foundation, I was able to inhibit wound healing to create an animal

model for future therapeutic testing. This research was initially performed within my PhD and then this transitioned to work where I served as the primary investigator.

- a. **Santa Maria PL**, Atlas MD, Ghassemifar R. Chronic tympanic membrane perforation: a better animal model is needed. Wound Repair Regen. 2007;15(4):450-8. PMID: 17650087
- b. **Santa Maria PL**, Redmond SL, Atlas MD, Ghassemifar R. Histology of the healing tympanic membrane following perforation in rats. Laryngoscope. 2010;120(10):2061-70. PMID: 20824636
- c. Santa Maria PL, Redmond SL, Atlas MD, Ghassemifar R. The role of epidermal growth factor in the healing tympanic membrane following perforation in rats. J Mol Histol. 2010;41(6):309-14. PMID: 20967565
- d. **Santa Maria PL**, Redmond SL, McInnes RL, Atlas MD, Ghassemifar R. Tympanic membrane wound healing in rats assessed by transcriptome profiling. Laryngoscope. 2011;121(10):2199-213. doi: 10.1002/lary.22150. Epub 2011 Sep 14. PMID: 21919009

# 2. Development of animal models for chronic tympanic membrane perforation and chronic suppurative otitis media

Through the work above, I was able to create a novel animal model for chronic tympanic membrane perforation that has served as a basis for in vivo testing of therapeutics in this area, including my own. Previously attempts at creating a suitable animal model were unsuccessful, too destructive preventing their use in further wound healing treatment studies, would create a wound not comparable to the real life situation or could not be replicated. Research in this field had therefore relied on testing on acute perforations. Since one hundred per cent of laboratory created perforations heal spontaneously, it was always argued that the perforations would have healed naturally without the intervention. I created three animal models to mimic the human condition including a model for dry perforation, a model that involves Eustachian tube occlusion and another that involves a pseudomonas aeruginosa chronic suppurative otitis media. Having reproducible and available chronic animal models provides researchers with an in vivo tool to test their therapies for treating chronic perforations. This inhibitor is also now the basis of another potential therapeutic under development. It is currently being tested in vivo, in a new delivery form, for the potential for maintaining a perforation in the clinical setting.

- a. Santa Maria PL, Santa Maria C, Kim S, Yang YP. Single Administration of a sustained release formulation of KB-R7785 inhibits tympanic membrane regeneration in an animal model. 2016. J Adv Otol. 2016: 12; 237-40. PMID: 28031154
- b. (Provisional patent) PCT/US2014/033536 Modulation of heparin binding epidermal growth factor activity for tympanic membrane healing
- c. Davidoss, NH. Varsak, YK. Santa Maria, PL. Animal Models of Acute Otitis Media A Review with Practical Implications for Laboratory Research. 2018. Eur Ann Otorhinolaryngol Head Neck Dis. 2018: 135: 3; 183-190. PMID: 29656888.
- d. Varsak YK, **Santa Maria PL**. Mouse model of experimental Eustachian tube occlusion: a surgical technique. Acta Otolaryngol. 2016;136(1):12-7. PMID 26381832.

# 3. A growth factor therapy for regeneration of tympanic membranes

After creating the chronic perforation animal model I undertook work to test out some potential therapeutics for tympanic membrane regeneration. After a few failures, one of my discoveries led to successful animal proof of concept studies that had the potential to remove the need for surgery. Since then I translated this, by working on drug delivery, safety and showing non-toxicity first in the academic setting at Stanford and then in partnership with industry. This then led to its license to a major pharmaceutical company, Astellas that is aiming to manufacture it and take it to clinical trials in two years. I served as the primary investigator throughout all of the development.

- a. **Santa Maria, PL.** Gottlieb, P. Santa Maria, C. Kim, S. Yang, YP. Puria, S. Functional Outcomes of Heparin Binding Epidermal Growth Factor Like Growth Factor Treatment for Chronic Tympanic Membrane Perforations Tissue Eng Part A. 2017:436-444. PMID 28142401.
- b. **Santa Maria PL**, Kim S, Yang YP. No systemic exposure of transtympanic heparin-binding epidermal growth factor like growth factor. Drug Chem Toxicol. 2016;18:1-4. PMID 26887920
- c. Santa Maria PL, Varsak KY, Kim S, Yang YP. Heparin Binding Epidermal Growth Factor Like Growth Factor for Regeneration of Chronic Tympanic Membrane Perforations in Mice. Tissue Eng Part A. 2015;21(9-10):1483-94. PMID 26908042.

d. **Santa Maria PL**, Weierich K, Kim S, Yang YP. Heparin Binding Epidermal Growth Factor-Like Growth Factor Heals Chronic Tympanic Membrane Perforations With Advantage Over Fibroblast Growth Factor 2 and Epidermal Growth Factor in an Animal Model. Otol Neurotol. 2015;36(7):1279-83. PMID: 26075672.

# 4. Repurposing growth factor therapy for oral wound healing

Additionally, as I had worked to translate a growth factor treatment for tympanic membrane regeneration I also looked at other areas where it could be repurposed, knowing that this growth factor was likely non toxic and able to be formulated. This led to new understanding of how the oral cavity heals after tonsillectomy. Previously, it was thought that a fibrin clot or eshar fell off and led to secondary hemorrhage. My created the new hypothesis that secondary hemorrhage was a result of poor epithelialization which lifts off during a period of muscle contraction and neoangionesis in the underlying muscle bed. Through a growth factor treatment that can accelerate and thicken epithelialization in this setting and reduce epithelial separation during wound contraction, there is a potential for a therapeutic to reduce post tonsillectomy secondary hemorrhage.

a. Beswick, DM. Santa Maria C. Ayoub NF. Capasso, R. Santa Maria PL. Epithelial separation theory for post-tonsillectomy secondary hemorrhage: evidence in a mouse model and potential heparin-binding epidermal growth factor-like growth factor therapy. Eur Arch Otorhinolaryngol. 2018; 275(2): 569-578. PMID 29188436.

# 5. Clinical research into chronic suppurative otitis media outcomes

To complement my basic science work in the field, I continue to critically evaluate the literature and conduct clinical research into the surgical treatments for chronic perforations and the surgical microbiology. This complements the work performed in the basic science.

- Tan, HE. Santa Maria, PL. Eikelboom, RH. Anandacoomaraswamy, KS. Atlas, MD. Type I Tympanoplasty Meta-Analysis: A Single Variable Analysis. Otol Neurotol. 2016;37:838-46.
  PMID: 27273405
- Buth MB, Tan BY, Santa Maria PL, Atlas MD. Unique microbiology of chronically unstable canal wall down tympanomastoid cavities: considerations for surgical revision. J Laryngol Otol. 2013;127(5):458-62. PMID: 23552343.
- c. **Santa Maria PL**, Oghalai JS. Is office-based myringoplasty a suitable alternative to surgical tympanoplasty? Laryngoscope. 2014;124(5):1053-4. PMID: 24114573.

# Complete List of Published Work in MyBibliography:

https://www.ncbi.nlm.nih.gov/myncbi/1rWMus5xmNv/bibliography/public/

# D. Research Support

# **Ongoing Research Support**

Stanford Neuroscience Translate Grant 02/01/20- 02/01/21 To develop and test clinically a prototype vertigo event monitor Role: co-PI

Stanford SPADA Seed grant 04/20/20-04/19/20 Role: Co-PI To optimize the design of a prototype vertigo event monitor Role: co-PI

Center for Dental, Oral & Craniofacial Tissue and Organ Regeneration, Interdisciplinary Translational Project Program U24 DE026914 (National Institute of Dental & Craniofacial Research) 07/01/19- 06/30/20 To develop HB-EGF as a therapy for radiation induced oral mucositis. Role: PI

Pre - Stanford Coulter Translational Grant 05/16/19- 05/15/20 To develop a drug device combination to delivery steroids to the middle meatus in the nasal cavity Role: co-PI Stanford Coulter Translational Grant 5/16/2019 - 5/15/2020 To develop a Eustachian tube opening device Role: co-PI Stanford SPARK / Stanford Child Health Research Institute Grant 01/01/19-01/01/21 Novel nanoparticle antibiotic adjuvant therapy for chronic suppurative otitis media. Role: Co-PI Stanford SPARK / Stanford Child Health Research Institute Grant 01/01/19-01/01/21 Synthetic Antimicrobial Peptoid therapy for chronic suppurative otitis media. Role: Co-PI Faculty Start-Up Grant, Stanford University 06/01/17-06/01/19 The goal of this project is to develop animal models for chronic suppurative otitis media for the identification of therapeutic targets. Role: PI **Completed Research Support** Center for Dental, Oral & Craniofacial Tissue and Organ Regeneration. Interdisciplinary Translational Project Program U24 DE026914 (National Institute of Dental & Craniofacial Research) 07/01/18-06/30/19 The goal of this project is to develop HB-EGF as a therapy for radiation induced oral mucositis. Role: PI Pilot Research Grant, Action on Hearing Loss – Translational Research Initiative for Hearing Grant 11/12017-11/1/2018 Provides seed funding to characterize a mouse model of pseudomonas chronic suppurative otitis media. Role: PI Stanford SPARK / Stanford Child Health Research Institute Grant 07/01/17-01/01/19 To test the proof of concept and develop a delivery method for preventing post tonsillectomy secondary hemorrhage Role: Co-PI Stanford SPARK / Stanford Child Health Research Institute Grant 01/01/14-30/06/15 The goal of this project was to further develop animal proof of concept, safety and non-toxicity of a growth factor therapy for tympanic membrane wound healing through preclinical phase Role: PI Stanford SPECTRUM – Innovation Accelerator Seed Grant Award 01/01/14-30/06/15 (Supported by UL1 TR001085) The goal of this project was to conduct a first in human clinical study of a prototype device for maintaining perioperative normothermia. Role: PI Garnett Passe and Rodney Williams Memorial Foundation – Principal Surgeon Scientist 01/01/12-30/06/15

The goal of this project was to develop novel therapies for regenerating tympanic membranes including the development of novel models of chronic tympanic membrane perforation and chronic suppurative otitis media Role: PI