Publications

1. Vennam S, **Georgoulas S**, Khawaja A, Chua S, Strouthidis NG, Foster PJ. Heavy metal toxicity and the aetiology of glaucoma. Eye (Lond). 2020 Jan;34(1):129-137. **Joint first authorship**.
2. Khawaja AP, Chua S, Hysi PG, **Georgoulas S**, Currant H, Fitzgerald TW, Birney E, Ko F, Yang Q, Reisman C, Garway-Heath DF, Hammond CJ, Khaw PT, Foster PJ, Patel PJ, Strouthidis N; UK Biobank Eye and Vision Consortium. Comparison of Associations With Different Macular Inner Retinal Thickness Parameters in a Large Cohort: The UK Biobank. Ophthalmology. 2020 Jan;127(1):62-71..
3. Gatzioufas Z, Panos GD, Gkaragkani E, **Georgoulas S** and Angunawela R. Recurrence of keratoconus after deep anterior lamellar keratoplasty following pregnancy. Int J Ophthalmol. 2017; 10(6): 1011–1013. PMID: 28730097
4. Khaw P, Lockwood A, **Georgoulas S**, Dahlmann-Noor A, Brocchini S. (2015). Future Strategies. Glaucoma: Second Edition. 2. 932-938. 10.1016/B978-0-7020-5193-7.00095-9.
5. **Georgoulas, S** & Dahlmann-Noor, Annegret & Brocchini, Steve & Khaw, Peng. (2010). Wound-healing responses to glaucoma surgery. Ocular Disease: Mechanisms and Management. 214-222. 10.1016/B978-0-7020-2983-7.00028-0.
6. Khaw PT, **Georgoulas S**, Dahlmann A, Ru Q, Martin Martin B, Brocchinin S. 'Future Strategies in Wound Healing Modification' in Textbook of Glaucoma. Eds Sharaawy T Hitchings RA Sherwood MB Crowston J Elsevier 2009
7. Khaw PT, **Georgoulas S**, Dahlmann AH, Mireskandari K, Bailly M, Daniels J, Limb GA and Brocchini S. Chapter 15: Tissue Repair and Regeneration. Book: Ocular Therapeutics Eye on New Discoveries 2008, Pages 333-366 doi:10.1016/B978-012370585-3.50017-0
8. **Georgoulas S**, Dahlmann-Noor A, Brocchini S, Khaw PT. Modulation of wound healing during and after glaucoma surgery. Prog Brain Res. 2008;173:237-54. PMID: 18929113.

9. **Georgoulas S**, Dahlmann-Noor A, Brocchini S, Khaw PT. Chapter 28: Wound healing responses to glaucoma surgery in Ocular Disease: Mechanisms and Management. Eds: Levin and Albert Elsevier 2008
10. **Georgoulas S**, Limb GA, Bailly M, Brocchini S, Khaw PT. Wound Healing Modification during and after glaucoma surgery - the state of the art. Chapter 9. p 65-81 in Glaucoma: State of the Art Therapy Eds: Grieshaber Orgul Flammer Elsevier 2008 ISBN 97B 3 9523474 0 9

Publication in management

1. SA Hill, S **Georgoulas**. Internal corporate venturing. Handbook of Research on Corporate Entrepreneurship, edited by Zahra, S.A., Hayton, J., Neubaum, D.O., published in 2016, Edward Elgar Publishing Ltd.

Important Presentations

1. Agorogiannis G, **Georgoulas S**, Vlavianos A, Clarke J. 1-year Outcome of Combined Phacoemulsification and Insertion of an *Ab Interno* Implanted Trabecular Micro-Bypass in Patients with Ocular Hypertension or Glaucoma: Efficacy, Complications and Visual Outcomes. Investigative Ophthalmology & Visual Science June 2020, Vol.61, 3154.
2. Saurabh Goyal, H. Ho, J. Ho, **S. Georgoulas**, M. Parnell, R. Lim, C. Yu-Wai-Man.Outcomes of Baerveldt glaucoma implant & trabeculectomy with mitomycin C in patients with advanced glaucoma with high risk of primary Trabeculectomy failure. Ophthalmology, St. Thomas' Hospital. ARVO 2019. Vol.60, 6639
3. Khawaja AP, **Georgoulas S**, Chua S, Ko FS, Muthy Z, Reisman C, Yang Q, Khaw PT, Foster PJ, Patel P, Strouthidis N. Differential Associations with Macular Nerve Fiber Layer and Ganglion Cell Complex Thickness in a Large Cohort. American Academy of Ophthalmology 2018. FIRST PRIZE
4. Gkaragkani E, Da Costa P, Mitry D, Aiello F, **Georgoulas S**, Gatzioufas Z., V. Saw. Outcomes of therapeutic penetrating keratoplasty for microbial keratitis. Poster Presentation ESCRS 2017

5. **S Georgoulas**, F Sabatino, V Maurino. Outcomes of IOL Exchange Surgery in a Tertiary Referral Centre. ASCRS 2015 Oral presentation.
6. **Georgoulas S**; Sim DA; Keane PA; Egan CA. Comparison of the National Institute of Clinical Excellence with the Royal College of Ophthalmologists guidelines on the treatment of Diabetic Macular Oedema. Poster Presentation at the World Ophthalmology Research Meeting 2014
7. **Georgoulas S**, Ru Q, Brocchini S, and Khaw PT. A Novel Single Application Prolonged Release MMP Inhibitor Is Superior to Mitomycin in Preventing Scarring After Experimental Glaucoma Surgery. Oral Presentation at the ARVO World Ophthalmology Research Meeting 2009. E-3178. **FIRST GLAUCOMA PRIZE**
8. Ru Q, **Georgoulas S**, Li CT, Brocchini S, and Khaw PT. Modelling Prolonged *in vitro* Release of 5-Fluorouracil From Tablets Using a Flow Chamber. Poster Presentation at the ARVO World Ophthalmology Research Meeting 2009. E-4538.
9. **Georgoulas S**, Ru Q, Paull D, Murray L, Brocchini S, and Khaw PT. The Effects of Serum Amyloid P on Experimental Glaucoma Filtration Surgery. Poster Presentation at the ARVO World Ophthalmology Research Meeting 2009. E-3908.

PhD Thesis 2010
University of London (UCL Institute of Ophthalmology and UCL School of Pharmacy).

NOVEL METHODS FOR MODULATION OF WOUND HEALING AFTER GLAUCOMA FILTRATION SURGERY

Dr Stylianos (Stelios) Georgoulas

Supervisors:
Professor Sir Peng Tee Khaw
Professior Stephen Brocchini

Examiners:
Mr Sheng Lim
Professor Keith Martin

During the period of my PhD I designed and performed 5 different studies, 4 of which were in collaboration with pharmaceutical companies (Astra Zenaca, Promedior PLC, Daniolabs and QUARK PLC) and one funded by the UCL Institute of Ophthalmology and the UCL School of Pharmacy. I received a 3 years Scholarship from the UCL School of Pharmacy.

1. **Antiscarring subconjunctival tablet.**

This innovative project constitutes to the best of our knowledge the first attempt to develop a prolonged release formulation against scarring after glaucoma filtration surgery. The sterile (after gamma radiation) ilomastat tablet, which was created for first time during this PhD by Stelios Georgoulas, meets the criteria of the European and the US pharmacopoeia for the lack of degradation after radiation. The irradiated ilomastat was shown to inhibit the contraction of gels in vitro ocular antiscarring models. The irradiated ilomastat tablet significantly inhibited scarring and enhanced bleb survival compared to the positive and negative controls in 2 in vitro studies. As the positive control (MMC) used in this experiment is the currently used anti-scarring treatment after glaucoma filtration surgery, this work indicates that the ilomastat tablet may offer enhanced therapeutic effect in the attempts to inhibit scarring after glaucoma filtration surgery, and subsequently the increase in IOP and potential blindness. Detailed histopathology studies of the ocular tissue were performed on the ocular tissues harvested by the in vivo experiment by Stelios Georgoulas, which supported these findings.

2. **Testing of 4 Matrix Metalloproteinase Inhibitors on their effectiveness on an ocular scarring model**

During the three years of work that is presented in my thesis, we sought new matrix mettaloproteinase inhibitors in order to test their effectiveness against scarring. This included a collaboration with AstraZeneca was created, which had developed many MMP inhibitors, which have never been tested against ocular scarring.

All four MMPis from AstraZeneca were found to be effective against contraction in our in vitro model of scarring (collagen I gels populated with Human Tenon's Fibroblasts –HTFs-) over seven days. The compounds were also observed to inhibit the elongation of HTFs. In particular, compound 4 was shown to be more effective than ilomastat, which is known to effectively inhibit MMPs and contraction in vitro and in vivo). Based on these preliminary results, we believe that these compounds warrant further study.

3. **Serum Amyloid P**

The work that has been done during the last decade by the Ocular Repair and Regeneration Biology Unit at the UCL Institute of Ophthalmology has focused on examining scarring as a function in which the local fibrocytes, transformed into myofibroblasts, play the dominant role. By testing the effects of Serum Amyloid P (SAP) in the inhibition of scarring, a broader picture of the mechanisms of wound healing after glaucoma filtration surgery was examined. Many scientific groups have suggested that nonactivated fibroblasts (fibrocytes) circulating in the blood participate in the mechanism of scarring. Several studies provided evidence that myofibroblasts do not originate from tissue fibroblasts, but from a bone-marrow-derived precursor. It was suggested that these cells enter the wound area after tissue damage and, by

expressing cytokines and chemokines, cleave the existing ECM and promote angiogenesis, to produce new ECM and to promote contraction.
In vitro and in vivo studies were designed in order to evaluate the role of SAP in ocular antiscarring models. As SAP does not target Tenon's Fibroblasrs, it was not effective in in vitro antiscarring models. Regarding the results from the in vivo experiment, our observations indicate that SAP has managed to inhibit macroscopically the scarring of the bleb significantly more compared to the negative, but also the positive control. The positive control used in this experiment is the currently used treatment in humans for scarring inhibition after glaucoma filtration surgery, which is the reason why this finding is very important. This result presents similarities with the study performed by Naik-Mathuria et al. (2008) in skin wounds.
Histological analysis of the treated eyes of the in vivo experiment revealed lower collagen deposition in the SAP treated groups compared to the controls. Lower collagen deposition in SAP treated animals has also been reported by Kisseleva et al (2006), who found that Serum amyloid P reduces scarring deposition in a bile duct ligation model.
Regarding the immunohistochemistry results, the results from our in vivo study are contradictory compared to other published studies that examined fibrosis in other tissues. It was found in our studies that the +αSMA fibroblasts in the rabbit bleb area were slightly increased in the SAP treatment groups compared to the negative control group and reduced compared to the positive control group.

4. **SiRNA against MMP-1, -2, -3, -8 and -9.**

Based on the observations of the in vitro experiments, it is suggested by this thesis that SiRNAs against MMP-1,-2,-3,-8 and -9 may manage to inhibit contraction. The in vitro results indicate that some of the siRNA treatment groups (the siRNA 100nM with and without lipofectamine and the siRNA 30nM groups) inhibit the contraction of Human Tenon's Fibroblasts populated collagen I gels significantly more than the negative control.
The same treatment groups were found to be also more effective in inhibiting contraction of the collagen I gels (in vitro contraction model) than the positive control (ilomastat 100uM), although the end result between these groups and the ilomastat group was not different.
Although the in vitro results indicate that the five siRNA molecules against MMPs may be effective against scarring, they failed to produce any statistically significant effect on the in vivo ocular scarring model in our lab.

5. **IOP lowering effect drops to be tested on in vivo models.**

In the initial experiment performed in the Ocular Repair and Regeneration Biology Unit at the UCL Institute of Ophthalmology in co-operation with DanioLabs PLC, compounds developed by Daniolabs were tested for their effectiveness in reducing intraocular pressure in normotensive rabbits. Other compounds (Abbott compound 19C and Latanoprost 0.005%.) were used in this study as controls.
The effectiveness of both the one drop studies and of the three drops /day for five days regimen was not significant in lowering the IOP and no reproducibility was shown in the two studies.