

令和6年4月30日

令和5年度共同研究講座活動実績報告書

共同研究講座名：感覚器未来医療学

所属長：木下 茂

1 共同研究講座の目的

眼疾患のアンメットニーズを克服する新規治療薬の開発
眼科領域におけるアンメットニーズとして、マイボーム腺機能不全の本質的な改善薬、緑内障視神経障害の阻止薬、小児の近視進行の抑制薬、眼精疲労の治療薬、角膜内皮障害の治療薬などの開発が待たれている。本共同研究では、これらについての研究開発を行う。候補となる薬剤およびデバイスの目 途は立っている。

2 報告年度に係る取組状況

マイボーム腺機能不全の治療薬の開発を目的として、主として、若年者と高齢者の健常者ならびにマイボーム腺機能不全患者のマイボーム腺の構造的変化、機能的変化についてのベースラインデータを取得した。眼精疲労の評価につて、赤外線オプトメータを用いた解析方法を検討した。さらに、治療薬剤の可能性のある数種を同定した。

3 報告年度における著書、論文、学会発表、講演、研究助成等の実績

1. Ueta M, Nishigaki H, Komai S, Mizushima K, Tamagawa-Mineoka R, Naito Y, Katoh N, Sotozono C, Kinoshita S. Positive regulation of innate immune response by miRNA-let-7a-5p. *Front Genet.* 2023 Jan 6;13:1025539.
2. Ban Y, Yoshida Y, Aziza Y, Kinoshita S, Sotozono C. Strengthening of the barrier function in human telomerase reverse transcription (hTERT) immortalized corneal and conjunctival epithelium by double-stranded RNA. *Exp Eye Res.* 2023 Feb;227:109357.

3. Ikeda Y, Mori K, Maruyama Y, Ueno M, Yoshii K, Yamamoto Y, Imai K, Omi N, Sato R, Sato F, Nakano M, Hamuro J, Tashiro K, Sotozono C, Kinoshita S. Novel Vertical Cup-to-Disc Classification to Identify Normal Eyes that Maintain Non-Glaucoma Status: A 10-Year Longitudinal Study. *J Glaucoma*. 2023 Feb 1;32(2):127-132
4. Hamuro J, Yamashita T, Otsuki Y, Hiramoto N, Adachi M, Miyatani T, Tanaka H, Ueno M, Kinoshita S, Sotozono C. Spatiotemporal Coordination of RPE Cell Quality by Extracellular Vesicle miR-494-3p Via Competitive Interplays With SIRT3 or PTEN. *Invest Ophthalmol Vis Sci*. 2023 May 1;64(5):9.
5. Ueno M, Yoshii K, Yamashita T, Sonomura K, Asada K, Ito E, Fujita T, Sotozono C, Kinoshita S, Hamuro J. The Interplay Between Metabolites and MicroRNAs in Aqueous Humor to Coordinate Corneal Endothelium Integrity. *Ophthalmol Sci*. 2023 Mar 16;3(3):100299.
6. Tomioka Y, Kitazawa K, Fukuoka H, Ueno M, Koizumi N, Sotozono C, Kinoshita S. Twelve-year outcome of Rho-associated protein kinase inhibitor eye drop treatment for Fuchs endothelial corneal dystrophy: A case study. *Am J Ophthalmol Case Rep*. 2023 Mar 31;30:101839.
7. Yoshikawa Y, Ueta M, Kinoshita S, Kida T, Sotozono C. Long-Term Benefits of Tear Exchangeable Limbal-Rigid Contact Lens Wear Therapy in Stevens-Johnson Syndrome Cases. *Eye Contact Lens*. 2023 Jun 1;49(6):247-253.
8. Matsumoto K, Ueta M, Inatomi T, Fukuoka H, Mieno H, Tamagawa-Mineoka R, Katoh N, Kinoshita S, Sotozono C. Topical Betamethasone Treatment of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis with Ocular Involvement in the Acute Phase. *Am J Ophthalmol*. 2023 May 12;253:142-151.
9. Komai S, Ueta M, Nishigaki H, Mizushima K, Naito Y, Kinoshita S, Sotozono C.

Differences in gene regulation by TLR3 and IPS-1 signaling in murine corneal epithelial cells. *Sci Rep.* 2023 May 16;13(1):7925.

10. Ueta M, Inoue C, Nakata M, Sotozono C, Kim MK, Wakamatsu T, Jongkhajornpong P, Saeed H, Rauz S, Ma DH, Yoon KC, Puangsricharern V, Bouchard C, Ahmad S, Seo KY, Joo CK, Gomes JAP, Chodosh J, Kinoshita S, Teramukai S. Severe ocular complications of SJS/TEN and associations among pre-onset, acute, and chronic factors: a report from the international ophthalmology collaborative group. *Front Med (Lausanne).* 2023 Jun 22;10:1189140.
11. Deguchi H, Tanioka H, Watanabe M, Horiuchi N, Fukuoka H, Hieda O, Inatomi T, Kinoshita S, Sotozono C. Identification and Analysis of Primary Cilia in the Corneal Endothelial Cells of Patients with Bullous Keratopathy. *Curr Eye Res.* 2023 Sep 14:1-6.
12. Aziza Y, Imai K, Itoi M, Yoshioka H, Komai S, Kitazawa K, Sitompul R, Ueta M, Fukuoka H, Inatomi T, Kinoshita S, Sotozono C. Strategic combination of cultivated oral mucosal epithelial transplantation and postoperative limbal-rigid contact lens-wear for end-stage ocular surface disease: a retrospective cohort study. *Br J Ophthalmol.* 2023 Nov 2:bjoo-2023-323617.
13. Morales-Mancillas NR, Velazquez-Valenzuela F, Kinoshita S, Suzuki T, Dahlmann-Noor AH, Dart JKG, Hingorani M, Ali A, Fung S, Akova YA, Doan S, Gupta N, Hammersmith KM, Tan DTH, Paez-Garza JH, Rodriguez-Garcia A. Definition and Diagnostic Criteria for Pediatric Blepharokeratoconjunctivitis. *JAMA Ophthalmol.* 2023 Dec 21 on line
14. Kato H, Yokoi N, Watanabe A, Komuro A, Sonomura Y, Sotozono C, Kinoshita S. Effect of Punctal Occlusion on Blinks in Eyes with Severe Aqueous Deficient Dry Eye. *Diagnostics (Basel).* 2023 Dec 19;14(1):3.
15. Komuro A, Yokoi N, Sotozono C, Kinoshita S. Effectiveness of Single-Dose Oral

Pilocarpine Administration in Patients with Sjögren's Syndrome. *Diagnostics* (Basel).
2023 Dec 30;14(1):91.

特別講演

1. Kinoshita S. Dr. Harold Stein Innovator Lecture. Toward corneal regenerative medicine, Canadian Ophthalmological Society Annual Meeting and Exhibition 2023 (COS2023), Quebec, Canada, June 17, 2023.
2. Kinoshita S. Gregg Lecture. Toward corneal regenerative medicine Royal Australian and New Zealand College of Ophthalmologist (RANZCO), Perth, Australia, October 21, 2023.

招聘講演

3. Kinoshita S. Toward Corneal Regenerative Medicine, Plenary Lecture, Asan Medical Center for Professor Hungwon Tchah's 35-year Service, Seoul, South Korea, February 5, 2023.
4. Kinoshita S. The Present Status of CHCEC-Injection Therapy for Corneal Endothelial Failure, Canadian Ocular Regenerative Society, Quebec, Canada, June 17, 2023.
5. Kinoshita S. The Quality Control of Cultured Human Corneal Endothelial Cells, Canadian Ocular Regenerative Society, Quebec, Canada, June 17, 2023.
6. Kinoshita S. Cultivated Oral Mucosal Epithelial Transplantation for Stevens-Johnson Syndrome, Canadian Ocular Regenerative Society, Quebec, Canada, June 17, 2023.

教育講演

7. Kinoshita S. WEB Presentation. Will EK go extinct? AAO Webinar, January 13, 2023.

シンポジウム

8. Kinoshita S. 21st Century Epithelium, The 15th Moorfields International Glaucoma

Symposium, London, January 28, 2023.

9. Kinoshita S. Corneal Endothelial Health in Glaucoma. The 15th Moorfields International Glaucoma Symposium, London, January 29, 2023.
10. Kinoshita S. The Biological Aspects of Human Corneal Endothelial Cells in Health and Disease. ISER2023, Gold Coast, Australia, February 23, 2023.
11. Kinoshita S. Inhibition of ROCK Signaling-- What it Means for Regenerative Therapies in FECD, Fuchs VIII Symposium, Miami, USA, April 1, 2023.
12. Kinoshita S. Update on Endothelial Cell-based Therapy, What's New in Cornea, APACRS, Singapore, June 8, 2023.
13. Kinoshita S. WEB presentation. Update on Endothelial Keratoplasty, Update on Keratoplasty Symposium, APAO-IrSO Satellite Congress, Tehran, Iran, June 19, 2023.
14. Kinoshita S. WEB presentation. Lifetimes learnings on "endothelial cell culture and clinical application". EKLG2023, June 25, 2023.
15. Kinoshita S. Endothelium Cell Injection: Long-Term Outcome, Regenerative Medicine in Ophthalmology, The Joint Meeting of Chulalongkorn University and KPUM, Bangkok, Thailand, August 11, 2023.
16. Kinoshita S. Ocular Surface Reconstruction in Stevens-Johnson Syndrome. CorneaFocus, London, UK, September 20, 2023.
17. Kinoshita S. WEB presentation. In Pathological Alteration in Corneal Endothelial Cells due to Microenvironment in Aqueous Humor, ARVO SIG, September 29, 2023.

18. Kinoshita S. Toward Corneal Regenerative Medicine. 4th International Ocular Regeneration Symposium, Boston, USA, October 5, 2023.
19. Kinoshita S. One thought about meibomian gland dysfunction and its inflammation. Clinical Controversies, Royal Australian and New Zealand College of Ophthalmologist (RANZCO), Perth, Australia, October 23, 2023.
20. Kinoshita S. The Advanced Medical and Surgical Management of Ocular Surface Disorders, AAO Instruction course 244, November 4, 2023.
21. Kinoshita S. New Therapies for Corneal Endothelial Diseases, AAO Instruction course 264, November 4, 2023.
22. Kinoshita S. Seeds and Soil in Corneal Transplantation. Asia Cornea Society Session: Update diagnosis and treatment of Corneal Disease, KERACON 2023, India, November 8, 2023.
23. Kinoshita S. Understanding Science and Technology Underpinning Corneal Endothelial Cell Transplantation, ECLA Session, KERACON 2023, India, November 8, 2023.

研究費

1. 木下茂. AMED Cicle研究費
【研究課題名】
世界初のイントラクライン機構を介したマイボーム腺機能不全治療薬の開発
2. 木下茂. 日本学術振興会 科学研究費 基盤B
【研究課題名】
培養ヒト角膜内皮細胞注入療法から発するリバーストランスレーショナルリサーチ

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