All English Web Live Seminar 2022

主催：千寿製薬株式会社

All English Web Live Seminar 2022

Date : Wednesday, Jun. 29, 2022 18:30～20:00

Venue: Web（Zoom Webinar）

Sponsor: SENJU Pharmaceutical Co., Ltd.

Chairman: Prof. Kimura（Yamaguchi Univ.）

Opening : 18:30～

Chairman : Prof. Kimura (Yamaguchi Univ.)

Sessions I 18:35:～19:05

Organizer: ①Prof. Nakazawa (Tohoku Univ.)
②Prof. Aihara (Tokyo Univ.)
③Prof. Nishida (Osaka Univ.)

Speakers:

① Yuka Suimon (Hokkaido Univ.)
「The mechanism underlying low radiation sensitivity in some cases of MALT lymphoma」
Discussant : Prof. Sonoda (Kyushu Univ.)

② Naoki Kiyota (Tohoku Univ.)
「Constitutively active Ras promotes protection and axon regeneration in retinal ganglion cells after optic nerve injury」
Discussant : Prof. Inatani (Fukui Univ.)

③ Ai KIdo（Kyoto Univ.)
「Anti-inflammatory Treatment After Intravitreal Injection of Brolucizumab 2020-2021: A Nationwide Population-Based Cohort Study」
Discussant : Prof. Hori (Toho Univ.)

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SessionsⅡ　19:05～19:35

Organizer: ④Prof. Tsujikawa (Kyoto Univ.)
⑤Prof. Kondo (Mie Univ.)
⑥Prof. Kimura (Yamaguchi Univ.)

Speakers:

④ Kazuma Saito (Gunma Univ.)

「Maternal hypothyroidism causes M-opsin developmental delay in neonatal mice」

Discussant : Prof. Suzuma (Kagawa Univ.)

⑤ Nobuhiko Shiraki (Osaka Univ.)

「PAX6-positive microglia evolve locally in hiPSC-derived ocular organoids」

Discussant : Prof. Ishida (Hokkaido Univ.)

⑥ Erina Goda (Kagawa Univ.)

「A novel technique for subretinal hematoma migration: moving to artificial retinal detachment 」

Discussant : Prof. Akiyama (Gunma Univ.)

19:40～20:00

Scoring and awards
Presenter : Prof. Kimura (Yamaguchi Univ.)

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視聴方法のご案内

本講演はZoomを使用して配信を行います。
ブラウザからの視聴も可能ですが、スムーズな視聴が可能なアプリを推奨いたします。
Zoomアプリのインストール方法は下記「視聴方法」を御覧ください。

視聴用サイトは、**当日の18:25～**オープンになります。

事前登録URL

事前登録URLをブラウザのアドレスにコピー、または右の二次元バーコードをご認識ください。

▼事前登録URL：

https://us02web.zoom.us/webinar/register/WN_qM9VZxMaRB60YNeg4tJQNQ

※事前登録ページにて、『お名前』、『メールアドレス』、『ご所属』をご入力ください。

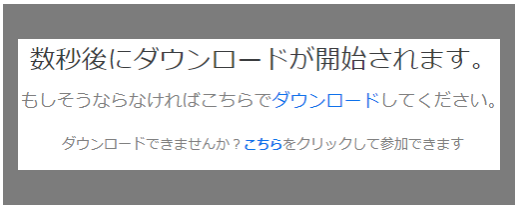
視聴方法

■ PCアプリ視聴

① 上記の事前登録URLにアクセスしてください
② 自動でアプリのダウンロードが始まります
③ 保存先のZoom…….exeをダブルクリック
④ インストールが始まります
⑤ インストール終了後に再度、視聴用リンクにアクセスしてください
⑥ “Zoom Meetingを開く”をクリック
⑦ 視聴画面へ切り替わります

■ PCブラウザ視聴

① 上記の事前登録URLにアクセスしてください
② “ダウンロードできませんか？こちらをクリックして参加できます”をクリック
③ 視聴画面へ切り替わります
※推奨ブラウザ:Google Chrome



■ iOS/Androidアプリ視聴

① 右記、QRコードからiOS端末をご利用の方はApp Store
Android端末をご利用の方はGoogle Play Storeにアクセスし
“Zoom Cloud Meetings”をインストールしてください
② 自動でアプリが起動した場合、一度終了してください
③ 視聴用リンクをタップすると、再度アプリが起動し視聴画面へ切り替わります

iOS

Android

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① Yuka Suimon (Hokkaido Univ.)

「The mechanism underlying low radiation sensitivity in some cases of MALT lymphoma」

【Purpose】 Low dose of external beam radiation therapy is the standard treatment for mucosa-associated lymphoid tissue (MALT) lymphoma restricted to the conjunctiva; however, some tumors don't disappear after radiation therapy, and others recur though they disappear once. The mechanism of poor response to radiation therapy in MALT lymphomas has not been disclosed. The aim of this study was to elucidate clinical and pathological features of localized conjunctival MALT lymphoma concerning radiosensitivity, focusing on Ki-67 and mismatch repair proteins.

【Methods】 We retrieved 24 patients who were diagnosed with localized conjunctival MALT lymphoma and were treated with radiotherapy in Hokkaido University Hospital from 2007 to 2020. Thirty-seven specimens of 24 patients were examined with immunohistochemistry using antibodies for Ki-67 and antibodies for representative mismatch repair proteins MLH1 and MSH2. Positive rates for each antibody in a high-power field at a hot spot were counted manually with image analyzing software FIJI, and were compared among groups.

【Results】 Nineteen cases showed disappearance of the tumor without recurrence (effective group). Three cases showed temporary disappearance of the tumor, which later recurred (relapse group). Two cases did not show disappearance of tumor (ineffective group). The median age at the onset of all cases was 53 years, while the onset of 2 cases in the ineffective group was at 29 and 37 years of age. There were not significant differences among groups in Ki-67, MLH1 and MSH2 positive rates.

【Conclusions】 The two ineffective patients were relatively young. Significant pathological features concerning radiosensitivity could not be elucidated in this study.

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② Naoki Kiyota (Tohoku Univ.)

「Constitutively active Ras promotes protection and axon regeneration in retinal ganglion cells after optic nerve injury」

[Abstract]

Axons in the optic nerve do not usually regenerate when they are injured, causing permanent loss of vision. However, recent studies indicate that stimulation of RAF/MEK/ERK signaling promotes axon regeneration and neuroprotection. In this study, we examined the effects of constitutively active Ras, K-RasV12, which powerfully activates the RAF/MEK/ERK signaling, on retinal ganglion cell (RGC) protection and axon regeneration using an optic nerve crush (ONC) model. We prepared AAV2-K-RasV12 and injected it intravitreally in C57BL/6J mice. One or two weeks after the injection, ONC was performed, and one or eight weeks later, survived RGCs in the retina or cholera toxin B subunit (CTB647)-labeled regenerating axons were analysed. AAV2-K-RasV12 treatment demonstrated increased number of RGCs compared with the control after ONC. Furthermore, AAV2-K-RasV12 treatment induced significant amounts of RGC axon regeneration even after 1 week, and some regenerating axons reached the optic chiasm after 8 weeks. These data indicated that AAV2-K-RasV12 treatment induces powerful RGC axon regeneration. Thus, AAV2-K-RasV12 may be useful for treatment of CNS axon injury in future, and it may be a good tool to study mechanisms for RGC axon regeneration and protection.

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③ Ai KIdo（Kyoto Univ.）

「Anti-inflammatory Treatment After Intravitreal Injection of Brolucizumab 2020-2021: A Nationwide Population-Based Cohort Study」

【Purpose】 The purpose of the current study was to evaluate anti-inflammatory treatment after vitreous injection of Brolucizumab (IVBr) in real-world practice in Japan.

【Methods】 This was a population-based longitudinal cohort study using The National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB). The database is a national claims database managed by Japan Ministry of Health, Labor, and Welfare (MHLW). As Japan employs universal health coverage, the NDB covers more than 95% of claims issued in Japan. We accessed all data stored in the NDB under the permission of the MHLW. We identified patients treated with IVBr between May 2020 and May 2021. We assessed the practice pattern of anti-inflammatory treatment given after IVBr. Anti-inflammatory treatment was defined as the use of any of Betamethasone eye drop, sub-Tenon's or intravitreal injection of Triamcinolone Acetonide or oral corticosteroids.

【Results】 During the 13-month period, 8,877 patients who underwent IVBr were identified. Of these, 674 (7.6%) received any anti-inflammatory treatment after IVBr. Among them, 540 (80.1%) received the treatment by their third IVBr; 257 (38.1%) after the first IVBr, 173 (25.7%) after the second IVBr, and 110 (16.3%) after the third IVBr. The mean duration between the first IVBr to the anti-inflammatory treatment was 92.0±77.2days.

【Conclusions】 This is a nationwide population-based cohort study to evaluate anti-inflammatory treatment given after IVBr in clinical practice.

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④ Kazuma Saito（Gunma Univ.）

「Maternal hypothyroidism causes M-opsin developmental delay in neonatal mice」

【Objective】 Thyroid hormones are critical for the development of opsin involved in color vision. Primary hypothyroid mice show delayed M-opsin development and expanded distribution of S-opsin on the retina. However, the effects of central hypothyroidism and maternal hypothyroidism on opsin development remain unknown. This study investigates the effects of central hypothyroidism and maternal hypothyroidism on opsin development in thyrotropin-releasing hormone knockout (TRH−/−) mice established in our laboratory that exhibits central hypothyroidism.

【Methods】 Retinal structure was evaluated by HE staining, and the function was evaluated by electroretinogram in wild-type (TRH+/+), TRH−/−. We examined mRNA expression and protein distribution of S/M-opsin in TRH+/+ mice, TRH−/− mice born to TRH+/−, or TRH−/− dams at postnatal days (P)12, 17, and 30. We conducted S/M-opsin analysis in TRH+/− mice born to TRH+/− or TRH−/− dams at P12.

【Results】 There were no abnormalities in retinal structure and function in TRH-/-. S/M-opsin expression did not significantly differ between TRH+/+ and TRH−/− mice born to TRH+/− dams at any postnatal day. M-opsin expression was significantly lower in TRH−/− born to TRH−/− dams than in TRH+/+ mice at P12, whereas S-opsin expression did not significantly differ. Notably, M-opsin expression was lower in TRH+/− mice born to TRH−/− dams than in those born to TRH+/− dams.

【Conclusions】 1) TRH deficiency does not affect retinal structure or function; 2) TRH−/− is mildly hypothyroid and does not cause opsin developmental delay; 3) Maternal hypothyroidism affects M-opsin development.

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⑤ Nobuhiko Shiraki (Osaka Univ.)
「PAX6-positive microglia evolve locally in hiPSC-derived ocular organoids」

【Purpose】 Microglia are the resident immune cells of the central nervous system (CNS). The immune cells from the general circulation cannot reach the CNS due to the blood-brain barrier. The microglia provide immune protection to the posterior eye, including the neural retina, and are involved in some sight-threatening conditions, uch as uveitis. However, it is not known how the microglia develop in the eye.

【Methods】 We studied human-induced pluripotent stem cells that had been expanded into a self-formed ectodermal autonomous multi-zone (SEAM) (Hayashi et al. Nature 2016) of cells that mimicked the human eye development. We searched and investigated the microglia-like cells.

【Results】 We discovered that they contained immune cells that were significantly similar to the microglia cells in SEAM. Moreover, the RNA-seq data and qPCR showed that the cells were more similar to primary microglia cells than to immortalized human microglia. Furthermore, single-cell RNA seq revealed that the cells resembled yolk sac-derived myeloid progenitors and not macrophages.

【Conclusions】 Our results showed that microglia-like cells showing characteristics of yolk sac-like linage cells naturally develop in SEAM, which lack vascular components. These cells are unique because they are paired box protein 6 (PAX6)-positive, yet possess some characteristics of the mesoderm. Our data support the possibility of the existence of an isolated and locally developing immune system in the eye, which is independent of the body's vasculature and general immune system.

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⑥ Erina Goda (Kagawa Univ.)

「A novel technique for subretinal hematoma migration: moving to artificial retinal detachment」

【Purpose】 In submacular hematoma migration using tissue plasminogen activator (tPA), the hematoma often migrates downward. If the lesion is above the macula, it can impair the normal macula during the hematoma migration process. We devised a method to control the direction of hematoma migration by selecting the site of tPA injection.

【Methods】 The subjects were 18 patients who required hematoma migration by vitreous surgery. Artificial retinal detachment was created by subretinal injection of tPA into the lower healthy retina from the temporal of the fovea. The posterior pole side of the retinal detachment was continuous with the submacular hematoma, and tPA was also infused with the lesion. The vitreous cavity was replaced with SF6, and the operation was completed. After the operation, he was instructed to face down and to lie down on the temporal.

【Results】 The average foveal subretinal hematoma was 610±489 μm preoperatively and 68±134 μm one month postoperatively. The submacular hematoma moved downward from the temporal of the fovea in all cases. The average difference in the angle between the positions of the tPA injection centered on the fovea centralis and the hematoma post-movement one month after surgery was 26±25°. Postoperative submacular hematomas tended to migrate to artificial retinal detachment sites.

【Conclusion】 Moving the hematoma to an artificial retinal detachment created by subretinal injection of tPA outside the lesion site by submacular hematoma migration and controlling the direction of hematoma migration are possible.