CMX Annual Report 2023

CMX令和５年度年次報告書

Kobe University Graduate School of Medicine

神戸大学大学院医学研究科

Center
for
Medical
Transformation

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TAKUMI Toru, Professor, Division of Physiology, Department of Physiology and Cell Biology

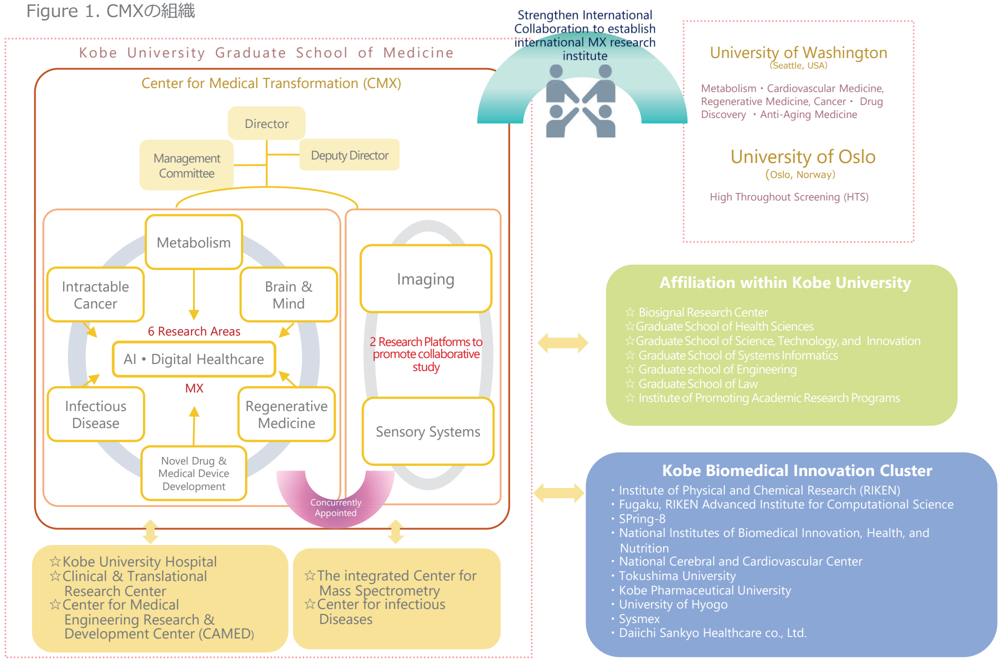
メディカルトランスフォーメーション研究センター（CMX: Center for Medical Transformation）は神戸大学の強みであるシグナル伝達研究を深化させデジタルトランスフォーメーション時代にふさわしい国際メディカルイノベーション創出拠点を形成するために令和４年４月に設置されました。

6つの研究分野と2つのプラットフォーム(Figure 1.参照)を設置し、生理・病理の概念的進歩につながる基礎研究、難治性がん、精神神経疾患、感染症等の諸疾患の病因・病態の解明や創薬候補、予防・診断バイオマーカー候補の探索を推進し、その成果(シーズ)を医学研究科・学内他研究科や国内外の研究機関、企業との共同研究により、組織的に創薬研究や臨床診断法、医療機器開発などのメディカルイノベーションの創出へつなげ、安心・安全でQOLの高い社会の実現に貢献することを目標としています。

令和5年度は４月に「脳こころ研究分野」に篠山隆司教授(外科系講座脳神経外科学分野)、菱本明豊教授(内科系講座精神医学分野)をお迎えし、12月にはイメージング研究プラットフォームに菊田順一教授(未来医学講座免疫学分野)に新たにメンバーとして参画いただくことになりました。また、アドバイザリーボードをご担当いただいた後藤由季子教授(東京大学)と濱田博司先生(理研BDR)が離任され、後任として大隅典子先生(東北大学)、熊ノ郷敦教授(大阪大学)にご着任いただきました。(Table 1. 参照)。

令和5年度は、5月に新型コロナウイルスが5類感染症に引き下げられ、3年余り続いた感染対策が平時の体制に切り替わった節目の年でした。また、個人的には38年ぶりに阪神タイガースが日本一に輝いた記念すべき年でもありました。CMXも新たに迎えたメンバーとともに国際的な医療革新のための努力を続け、輝かしい未来に貢献してまいります。

Figure 1. CMXの組織



CMX was founded in April 2022 to advance signal transduction, an area of Kobe University's expertise, in response to the digital transformation era. The mission of CMX is to form a center for international medical innovations.

The organization is composed of six research units and two platforms (refer to Figure 1) dedicated to conducting primary research to advance our understanding of physiology and pathology, investigating the causes and mechanisms of various diseases, such as intractable cancer, neuropsychiatric disorders, and infectious diseases aiming to identify potential candidates for drug discovery, as well as biomarkers for prevention and diagnosis, and to apply its scientific findings to develop innovative medical solutions, including new drugs, clinical diagnostic methods, and medical devices for a range of illnesses. To achieve these goals, CMX plans to collaborate on research with other university departments, domestic and international research institutes, and companies. Ultimately, CMX aims to contribute to the creation of a safer and more prosperous society with an improved quality of life.

In 2023, Professor Takashi Sasayama (Department of Neurosurgery, Division of Surgery Related) and Professor Akitoyo Hishimoto (Department of Psychiatry, Division of Internal Related) joined the Brain and Mind Research Unit in April. Additionally, Professor Junichi Kikuta (Department of Immunology, Division of Future Medical Sciences) joined the Imaging Research Platform in December as a new member. There were changes in the Advisory Board: Professor Yukiko Gotoh (the University of Tokyo) and Dr Hiroshi Hamada (RIKEN BDR) left their posts and were replaced by Professor Noriko Osumi (Tohoku University) and Professor Atsushi Kumanogo (Osaka University). (see Table 1).

The year 2023 was a milestone year for everyone, as there were significant developments in the fight against the new coronavirus; the virus was downgraded to a category-five infectious disease, leading to a shift from infection control measures to a peacetime system that had been in place for over three years. On a personal note, it was a memorable year to remember for me as the Hanshin Tigers clinched the Japanese championship for the first time in 38 years. CMX, along with its new members, will continue to strive for international medical innovation and contribute to a bright future.

Table 1. CMXの構成員

Intractable Cancer	Metabolism	Brain & Mind	Infectious Disease	Regenerative Medicine	Novel Drug & Medical Device Development	Imaging Platform	Sensory Systems Platform
Suzuki (Med) DepDir	Nitta (Med) DepDir	Takumi (Med) Director	Y. Mori (Med)	Aoi (Med)	Fukumoto (Med)	Nitta (Med)	Nibu (Med)
Kakeji (Med)	Ogawa (Med)	Sakisaka (Med)	Kubo (Med)	Enomoto (Med)	Sasaki (Med)	Furuyashiki (Med)	Nakamura (Med)
Murata (Med)	Shinohara (Med)	Sasayama (Med)	Kodama (Med)	Kuroda (Med)	Fujisawa (Med)	Kikuta (Med)	Ueyama (Biosignal)
Y. Minami (Med)	Hirata (Med)	Hishimoto (Med)	Shoji (Med)		Yano (Med)		
Yokozaki (Med)	Takahashi (Visiting)	Furuyashiki (Med)	Nibu (Med)		H. Minami (Med)		
Ito (Biosignal)		Matsumoto (Med)	Nozu (Med)		Shima (Innovation)		
		Ueyama (Biosignal)	Kameoka (Health Sci.)				
		Kowa (Health Sci)	Morinobu (Visiting)				
		Shirafuji (CMX)					

Advisory Board

OSUMI Noriko (Tohoku Univ.)
KASUGA Masato (Asahi Life Foundation)
KUMANOGO Atsushi (Osaka Univ.)
NAKAGAMA Hitoshi (National Cancer Center Japan)
NISHIDA Eisuke (RIKEN BDR)
YONEDA Yoshihiro (BIKEN)

Full-time Faculty | Concurrently-Appointed Faculty | Unit Head

Steering Committee Members *blue underlined
a director and two deputy directors

Ⅱ.新規参加メンバーの紹介 *New members*

菊田　順一　未来医学講座　免疫学分野　教授

この度、2023年12月より未来医学講座 免疫学分野 教授を拝命し、イメージング研究プラットフォームに参画させていただきました。CMXでは、基礎・臨床医学の連携、異分野融合による連携、国際連携など様々な形での連携を積極的に行い、これまで培ってきた独自の生体イメージング技術を活かしたトランスレーショナル研究を推進したいと考えています。特に、自己免疫疾患や線維化疾患、がんなど様々な難治性疾患の発症初期における病態を解析し、「病気がなぜ引き起こされるのか」を明らかにすることで、副作用の少ない理想的な治療法の開発に役立てたいと考えおります。また、次世代の医学研究を担う若手医学研究者・Physician Scientistの育成にも尽力してまいります。今後とも御指導御鞭撻の程どうぞ宜しくお願い申し上げます。

篠山 隆司　外科系講座　脳神経外科学分野　教授

2020年9月より脳神経外科学分野教授を拝命しております。当教室のテーマは、悪性脳腫瘍に対する診断の向上と新規治療の開発です。これまで、脳腫瘍でのマイクロRNA発現・機能解析、腫瘍特異的なシグナル経路、転移や播種の促進物質の同定、腫瘍特異的代謝経路と糖・アミノ酸リモデリング機構などの研究を行ってきました。最近は、腫瘍の不均一性、腫瘍免疫微小環境の解明を目標としています。また、てんかんを中心とした機能的疾患に対する電気生理的研究より、脳内の神経ネットワーク研究なども行っています。脳腫瘍に対する分子生物学的研究と神経に対する電気生理的研究を融合させて、更にコンピュータサイエンスを用いた統合解析で脳を包括的に研究することを目指しています。基礎・臨床の研究室との連携やCMXの他のセクションとも密に連携して、脳研究を発展させたいと思います。今後ともご指導ご鞭撻をよろしくお願い致します。

菱本　明豊　内科系講座　精神医学分野　教授

私は令和5年1月より現職を拝命しております。研究室では様々な精神疾患の分子生物学的機序の解明を目指しています。特に当教室では長年、法医学分野や兵庫県監察室と共同で自死された方の血液や死後脳試料を収集してきました。現在、自殺既遂者DNA試料は1500検体を超え、世界的に有数の自殺研究のメッカとなっています。令和5年度からはJSTが推進するムーンショット型研究開発事業に採択されて、今後ますます重要となるメンタルヘルス研究の社会実装を目指した未来型研究に取り組んでいます。

Ⅲ.1年間の活動紹介 *Activities*

1．CMX若手共同研究プロジェクト Young Scientists Collaborative research Project

1）令和４年度採択課題 研究進捗発表会　令和5年６月22日(木)　神緑会館記念ホール
Progress Review Meeting for Selected Project of FY 2022

研究分野を横断した若手研究者の共同研究を支援する競争的共同研究費助成事業「若手共同研究プロジェクト」の令和4年度採択課題の進捗発表会を開催した。令和5年度は4件の課題について発表があった。この発表会は、採択課題の中間審査も兼ねており、センターのアドバイザリーボードにより、優れた点、推進すべき点、疑問点等について後日、書面によるコメントをいただき、発表者へフィードバックしている。

発表会後はセンターのアドバイザリーボードである大隅典子先生(東北大学副学長）に「放射状グリア：哺乳類神経新生を支えるしくみ」と題した特別講演をいただいき、放射状グリア内のmRNA輸送のしくみについて、ご自身の研究の最新成果をご紹介いただくとともに、仮説を検証する研究という営みの面白さをお話しくださった。当日はWeb参加を含め109人が聴講した。

KIKUTA Junichi, Professor, Div. of Immunology, Dept. of Future Medical Sciences

In December 2023, I was appointed as Professor in the Department of Immunology. And I am pleased to join the CMX Imaging Research Platform. Through collaboration with other departments within Kobe University, interdisciplinary collaborations, and international collaborations, we hope to promote translational research utilizing our unique intravital imaging technology. In particular, we hope to analyze the pathogenesis of various intractable diseases such as autoimmune diseases, fibrotic diseases, and cancer in their early stages of development, and to clarify "why diseases occur" in order to develop ideal treatments with fewer side effects. We would also like to make efforts to nurture young medical researchers and physician-scientists who will lead the next generation of medical research. We look forward to your continued guidance and encouragement.。

SASAYAMA Takashi, Professor, Div. of Neurosurgery, Dept. of Surgery Related

Brain research is progressing rapidly. The theme of our department is developing new diagnosis and treatments for malignant brain tumors. To date, we have researched on microRNA expression and function in brain tumors, tumor-specific signal pathways, identification of molecules that promote metastasis and dissemination, tumor-specific metabolic pathways. Recently, we are focusing tumor heterogeneity and tumor immune microenvironment. In addition, we are researching on neural networks in the brain through electrophysiological, radiological and anatomical approach. We would like to develop brain research in collaboration with basic and clinical laboratories and in close collaboration with other sections of CMX. We appreciate your continued guidance and cooperation.

HISHIMOTO Akitoyo, Professor, Div. of Psychiatry, Dept. of Internal Related

I have been in my current position since January 2023. In my laboratory, we aim to elucidate the molecular biological mechanisms of various psychiatric disorders. In particular, we have been collecting blood and postmortem brain samples from suicide victims in collaboration with the Department of Forensic Medicine and the Hyogo Prefectural Coroner's Office for many years. Currently, we have more than 1,500 DNA samples from individuals who have attempted suicide, making our department one of the world's leading meccas for suicide research. Since 2023, we have been selected for the Moonshot R&D Program promoted by JST, and is engaged in future-oriented research aimed at social implementation of mental health research, which will become increasingly important in the future.

On June 25th, the progress review meeting for projects selected in the Young Scientists' Joint Research Project for the FY 2022, a competitive joint research funding program, took place. This project aims to support collaborative research among young researchers across various fields within the graduate school of medicine. The presentations provided a unique opportunity for the winners and served as an interim review of the proposals. Following the presentations, the CMX Advisory Board provided written comments on outstanding points, areas for improvement, and questions for the presenters.

Subsequently, Dr. Noriko Osumi, Vice President of Tohoku Univ. and a member of the CMX Advisory Board delivered a special lecture entitled "Radial glia: the basis for mammalian neurogenesis." During the lecture, she presented the latest results of her research on the mechanism of mRNA transport in radial glia. She also shared insights into the enjoyment of research through hypothesis testing. The lecture was attended by 109 people, including those who participated via the web.

大隅先生(右)と和やかに交流する仁田副センター長(左)と参加者

若手共同研究プロジェクト令和4年度採択課題	
新規	「腸内分泌細胞—神経コネクトミクス解析による過敏性腸症候群の病態解明～ストレスとともに蘇る腸管の記憶～」 “Enteroendocrine cells – elucidation of irritable bowel syndrome through neuroconnectoomics analysis ～ Intestinal memory revived with stress ～” (研究代表者)井上 潤 INOUE Jun　(共同研究者)木下 雅登 KINOSHITA Masato
新規	「マクロファージをターゲットした、大動脈解離の発症、進展予防法の解明」 “Targeting macrophages for prevention of the development and progression of aortic dissection.” (研究代表者)江本 拓央 EMOTO Takuo (共同研究者)山中 勝弘 YAMANAKA Katsuhiro　谷口 将之 TANIGUCHI Masayuki
新規	「患者由来がんオルガノイド評価系を用いた新規Rasシグナル伝達阻害剤の開発研究」 “Development of novel RAS signaling inhibitors using patient-derived organoids assay.” (研究代表者)槙野 義輝 MAKINO Yoshiteru　(共同研究者)青井(小柳)三千代 AOI-KOYANAGI Michiyo
新規	「腸管ブドウ糖排泄機構の生理的意義の解明」 “Elucidation of physiological significance of the mechanism of intestinal glucose excretion.” (研究代表者)森田 靖子 MORITA Yasuko　(共同研究者)曽 菲比 ZENG Feibi


研究進捗発表会で発表する採択者

特別講演

2）令和５年度CMX若手共同研究プロジェクト

令和5年度「若手共同研究プロジェクト」を募集し、8件の応募があった。アドバイザリーボードとセンターの運営委員から選出された審査員の厳正な審査の結果、6件の共同研究が採択された。

The FY 2023 call for “Young Scientists’ Collaborative Research Projects” received eight applications. After a rigorous review by the Advisory Board and a panel of judges selected from the CMX Steering Committee members, six joint research projects were selected.

若手共同研究プロジェクト令和５年度採択課題	
新規	「SAMD4Bによる癌進展機構の全貌解明と治療薬開発」 “Molecular mechanism of cancer progression by SAMD4B and development of therapeutic agents” (研究代表者)大谷 淳二 OTANI Junji　(共同研究者)西森 誠 NISHIMORI Makoto
新規	「膵癌におけるWnt5a-Ror1シグナルの機能解析」 “Functional analysis of Wnt5a-Ror1 signaling in pancreatic cancer” (研究代表者)紙崎 孝基 KAMIZAKI Koki　(共同研究者)辻前 正弘 TSUJIMAE Masahiro
新規	「母体免疫活性化が引き起こす概日リズム破綻メカニズムの解明」 “Investigation of circadian rhythm of maternal immune activation model mice” (研究代表者)玉田 紘太 TAMADA Kota　(共同研究者)益子 尚久　MASUKO Naohisa
新規	「麻酔と覚醒の変遷過程における生体マルチセンシング」 “In vivo multi-sensing during the transition between anesthesia and awareness.” (研究代表者)中井 信裕 NAKAI Nobuhiro　(共同研究者)西村 太一 NISHIMURA Taichi
新規	「患者由来がんオルガノイド評価系を用いた新規Rasシグナル伝達阻害剤の開発研究」 “Development of novel RAS signaling inhibitors using patient-derived organoids assay.” (研究代表者)槙野 義輝 MAKINO Yoshiteru　(共同研究者)青井(小柳)三千代 AOI-KOYANAGI Michiyo
新規	「腸管ブドウ糖排泄機構の生理的意義の解明」 “Elucidation of physiological significance of the mechanism of intestinal glucose excretion.” (研究代表者)森田 靖子 MORITA Yasuko　(共同研究者)曽 菲比 ZENG Feibi

2．CMXリトリート「若手道場」 CMX Retreat “Wakate Dojo”

令和5年10月10日(金)～10月11日(土)　淡路夢舞台国際会議場

メディカルトランスフォーメーション研究センター（CMX）・リトリート「若手道場」は、令和5年10月6日と7日の2日間にわたり、古屋敷智之オーガナイザーのもと、若手教員中心の実行委員会の運営により実施された。「若手道場」は平成30年度に前身の「シグナル伝達医学研究展開センター（CSMI）・リトリート」として始まり、今回で6回目の開催となった。このリトリートは、当センターに所属する若手研究者を中心に、発表、交流、相互理解を深める場を提供することで、研究者間の連携を強化し、新たな共同研究の創出や組織の活性化を目的としている。

The Center for Medial Transformation (CMX) Retreat “Wakate Dojo” was held over two days, October 6 and 7, 2023, organized by Prof. Tomoyuki Furuyashiki and managed by a committee mainly composed of young faculty members. The “Wakate Dojo” began as the “Center for Cell Signaling and Medical Innovation (CSMI) Retreat” in 2018, and this year marked its sixth time. The retreat aims to strengthen collaboration among researchers and revitalize the organization by providing a platform for presentations, exchanges, and mutual understanding, particularly among young researchers affiliated with the center.

昨年度に引き続き、今年度も対面で開催され、総勢68名と過去最大の参加者数を記録した。今年度は「ゆとり」をテーマに掲げ、その一環として1日目にエクスカーションの時間を設けた。夢舞台ガイドツアーや植物園ツアーに参加したりテニスをするなど自由な時間を過ごすことで、研究室の垣根を超えた自然な交流が育まれた。

As in previous years, this year’s retreat was held face-to-face, with a total of 68 participants, the largest number ever recorded. This year’s theme was “Yutori (leeway),” and as part of this, excursion time was set aside on the first day of the retreat. Spending free time on activities such as the Yumebutai guided tour, botanical garden tour, or playing tennis fostered natural interactions beyond laboratory boundaries.

特別講演には、名古屋大学大学院医学系研究科神経情報薬理学講座の深田正紀教授と、大阪大学大学院医学系研究科・生命機能研究科免疫細胞生物学教室の石井優教授をお招きした。深田正紀先生には「シナプスの制御機構とシナプス疾患の病態機構」という演題で、シナプス伝達や可塑性を担うシナプス蛋白質PSD-95の調節機構から、その破綻により生じる脳病態機構まで幅広くお話しいただいた。石井優先生には「生体イメージングによる免疫炎症動態の解明：新たな病原性細胞の発見」という演題で、生体イメージングを駆使した関節リウマチや肝臓の炎症における新たな免疫細胞動態の発見についてお話しいただいた。特別講演は大学院講義とすることで、現地参加ができない大学院生も参加できるように配慮した。

The special lectures featured Prof. Masaki Fukata from the Division of Neuropharmacology at Nagoya University Graduate School of Medicine and Prof. Masaru Ishii from the Department of Immunology and Cell Biology at Osaka University Graduate School of Medicine and Graduate School of Frontier Biosciences. Dr. Fukata delivered a lecture on “Mechanisms of synaptic function and synaptic disorders,” covering a wide range of topics from regulatory mechanisms of synaptic protein PSD-95, which is responsible for synaptic transmission and plasticity, to the pathological mechanisms of brain disorders caused by their disruption. Dr. Ishii gave a lecture on “Intravital imaging dissecting immune cellular dynamics and identifying novel pathogenic cell types in vivo,” discussing the discovery of new immune cell dynamics in rheumatoid arthritis and liver inflammation using in vivo imaging techniques. The special lectures were designed to be graduate lectures so that graduate students who could not attend on-site could also participate.

質の高い発表に耳を傾ける参加者たち。
レセプションホールB @淡路夢舞台国際会議場

Participants listening attentively to the high quality presentations. @Reception Hall B, Awaji Yumebutai International Conference Center

古屋敷オーガナイザー(左)と深田先生(右)

参加者(左)と交流する石井先生(右)

ポスターセッションの様子

参加した大学院生全員が口頭発表、ポスター発表、フラッシュトークいずれかの形式で発表を行うことで、大学院生が主体的に関与し議論できる機会が持てるよう心がけた。ポスター発表は夕食と同じ会場で行い、その後もフランクな話ができる場として同会場で情報交換会を設けた。本会では9演題の口頭発表と18演題のポスター発表が行われた。すべての発表のクオリティが非常に高く、各演者が十分に準備してきたことが伺えた。優秀プレゼンテーション賞を設け、口頭発表から1名、ポスター発表から3名を選出した。加えて本会では、共同研究への発展を目指し、「ラボ紹介」として各研究室から6名の教員が研究テーマや実験機器・技術の紹介を行った。

最後にセンター長の内匠透教授より、多分野の若手研究者が一同に会し、交流を深めることができたことは有意義であったとの総評を頂き、好評のうちに閉幕した。

All participating graduate students presented their work in either oral, poster, or flash talk format, so that they could actively engage and have opportunities for discussion. Poster presentations were held at the same venue as dinner, followed by an information exchange session in the same venue, providing an opportunity for informal discussion. Nine oral presentations and eighteen poster presentations were given at the retreat. The quality of all presentations was very high, indicating that each presenter had prepared thoroughly. Awards for excellent presentations were given, selecting one winner from the oral presentations and three winners from the poster presentations. In addition, six faculty members from each laboratory introduced their research topics, experimental equipment, and techniques as "Lab introductions," with the aim of developing into collaborative research.

The retreat concluded with Prof. Toru Takumi, Director of the Center, providing an overall evaluation, emphasizing the significance of young researchers from diverse fields gathering together face-to-face and deepening their interactions, and thus, the retreat ended on a high note.

優秀発表賞受賞者による参加感想文

Participation reflection from the best presentation awardees.

KOMORI Satomi, Academic Researcher, Biosignal Regulation

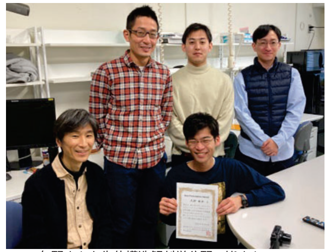
First of all, I would like to express my gratitude for receiving the Best Presentation Award at "Wakate-dojo." "Wakate-dojo" provided me with a valuable lecture and research presentation venue. I had the great opportunity to interact with people from other fields in the retreat. It's been a long time since I attended "Wakate-dojo" last time, but the event was so lively, and I was able to spend two fulfilling days. During the flash talk on the first day, we could touch on various research topics even though we had limited time. I was also very inspired by the lively discussion that took place during the poster presentations. For oral presentations, I reaffirm the importance of preparing with an emphasis on how to explain my research in an easy-to-understand manner. Also, during the Q&A session of the oral presentation, I received very insightful comments, which can be helpful for my study. At the keynote lectures given by Professor Fukata and Professor Ishii, I learned a lot about their latest research and very interesting experimental methods. The lectures were very easy to understand and very exciting for me. Moreover, I refreshed myself by going on an excursion to Awaji Island and having a wonderful time at a hotel. I charged my energy for future research.
Once again, I would like to thank my mentor, Professor Matozaki, all participants, as well as organizers of the retreat.

表彰式の様子

小森さんと生体シグナル制御部門の皆さん

KUNO Syuhei, Doctoral Student ※申込時

Thank you very much for this prestigious award. I would like to take this opportunity to express my gratitude to the members of the organizing committee, everyone in the division of structural medicine and anatomy, and all those involved in the presentation of this work. The sixth meeting of Wakate Dojo provides an excellent platform for exchange and discussions among scientists from different departments within the Kobe University School of Medicine.
At this meeting, I had the opportunity to engage in discussions with individuals from other laboratories, which was very insightful. The poster session was particularly rewarding as some participants approached deficits of research and expressed their interests in listening to my presentation.
Recently, I have come to feel the value of interacting with associates of the same generation through them. Engaging in conversations with people who hold different perspectives or share similar ones allows me to lose track of time. I am happy to share this kind of fun with associates. Due to the impact of the COVID-19 pandemic, I have not had much opportunity with onsite meetings. Therefore, I feel that this meeting serves the role of a "Dojo" in the sense of gaining invaluable experience.
Once again, thank you for this opportunity and recognition.

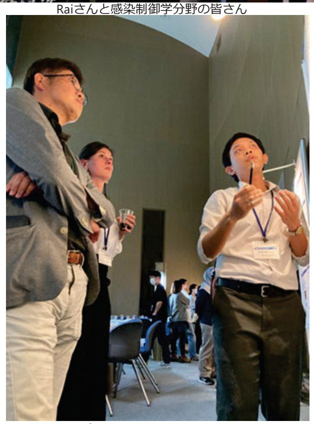


久野さんと生体構造解剖学分野の皆さん

Raiさんと感染制御学分野の皆さん

GN Rsi Suwardana, Doctoral Student, Dept. of Infectious Disease Control

CMX Retreat "Wakate Dojo" held on October 6th-7th this year was a valuable scientific experience for an inexperienced student like me. The atmosphere of this meeting is very positive with lots of lessons, questions, and insight from the keynote speakers, oral and poster presenters, including feedback from the participants. The schedule and flow during the meeting were also convenient. Allow me to sincerely express my gratitude to all of the teachers, staff, and students who organized this meeting. I am looking forward to attending this meeting again next time.
I feel honored to receive the Best Presenter Award in the poster session at this meeting. It encourages me to work harder. I would also express my sincere gratitude to Prof. Ikuo Shoji, M.D., Ph.D., and all my mentors in the Division of Infectious Disease Control for always supporting my research activity.



ポスターセッションの様子

ポスターセッションの様子

沼さん(右)と古屋敷先生(左)薬理学分野にて

優秀発表賞受賞者による参加感想文

NUMA Chisato, Undergraduate Student, Dept. of Pharmacology

I am Chisato Numa, an MD-PhD student at the Division of Pharmacology and in the 5th year of the MD program. I would like to show my gratitude to Ms. Haneda, Ms. Amo, Dr. Furuyashiki, and members of the executive committee for organizing the CMX retreat "Wakate Dojo", held at Awaji Yumebutai International Conference Center from October 6th to 7th. I am very honored to receive the poster presentation award. "Wakate Dojo" is a unique opportunity for me to socialize with graduate students and researchers from different fields in the Center for Medical Transformation at Kobe University. This was my 1st time joining the retreat. I enjoyed delicious dinner and cozy drinking, catching up with familiar colleagues, getting acquainted with researchers in other divisions, and even seeing acquainted researchers who had moved to Kobe University recently, which was a pleasant surprise. At the poster session, I found it advantageous for my research to take questions and get advice from various scopes of researchers from multiple research fields, and I enjoyed listening to their presentations and asking questions casually, too. Also, the lectures were inspiring. I was amazed, in Dr. Fukata's talk, by the molecular machinery forming nanoclusters in synapse and its contribution to epilepsy, and in Dr. Ishii's talk, by convincing in-vivo images visualizing osteoclasts and their acid emission as well as the cancerous nature of causal osteoclast in Rheumatoid Arthritis. These occasions to socialize with researchers from different fields truly help me think outside of the box, and I hope I will be able to join this retreat again!

10/6（金）

10:30-10:42　開会挨拶 (古屋敷 智之 教授)
注意事項説明 (実行委員：篠原 亮太 実行委員長)

10:42～11:30 【セッション１】フラッシュトーク
（進行：伊藤 圭祐　実行委員）

1．田　博文　（薬理学分野）
2．大田　康平　（薬理学分野）
3．久末　敏博　（薬理学分野）
4．Wenran Qiu　（薬理学分野）
5．李　東芮　（薬理学分野）
6．張　李爽　（薬理学分野）
7．Yunhui Zhu　（薬理学分野）
8．Guowei Chen　（薬理学分野）
9．高　榕蔚　（薬理学分野）
10．山本　真理奈　（生理学分野）
11．Peishuan Ho　（生理学分野）
12．任　修志　（生理学分野）
13．揚　鎮亞　（生理学分野）
14．上田　隆　（生体シグナル部門）
15．青木　亮麿　（細胞生理学分野）
16．山本　佳奈　（生理学分野）

12:30～14:00　【セッション２】ラボ紹介（座長：今崎　剛　実行委員）
1．伊藤　圭祐（神経分化・再生分野）「神経分化・再生分野のご紹介・変異マウス作製へのお誘い」
2．加藤　尭彬（生体構造解剖学分野）「トランススケール構造生物学」
3．中井　信裕（生理学分野）「いろいろあるよ生理学分野」
4．篠原　亮太（薬理学分野）「ストレスとレジリエンスの生物学的基盤の解明」
5．有井　潤　(臨床ウイルス学分野）「臨床ウイルス学分野」

14:00～17:00　エクスカーション

17:30～19:00 【セッション３】　基調講演１　(座長：古屋敷 教授)
「シナプスの制御機構とシナプス疾患の病態機構」
"Mechanisms for synaptic function and synaptic disorders"
深田　正紀　先生
（名古屋大学大学院医学系研究科附属神経疾患・腫瘍分子医学センター 神経情報薬理学講座教授)

19:00～21:30　夕食/ポスターセッション　(挨拶：榎本 秀樹 教授)

10/7（土）

9：30～11:00【セッション４】基調講演２　（座長：古屋敷 教授）
「生体イメージングによる免疫炎症動態の解明：新たな病原性細胞の発見」
"Intravital imaging dissecting immune cellular dynamics and identifying novel pathogenic cell types in vivo"
石井　優　先生
(大阪大学大学院医学系研究科・感染症免疫学講座生命機能研究科・個体機能学講座免疫細胞生物学教授)

11:20～12:20【セッション５】口頭発表（座長：有井 潤 実行委員）
1．藤間　秀平 (生理学分野)　「島皮質抑制性ニューロンを介した社会行動の調節機構」
2．小牧　遼平 (脳神経内科学分野)　「細胞間接着分子による神経細胞の変性と死の制御機構」
3．堀川　伊和 (薬理学分野)　「脂質代謝―血液―脳軸に着目した双極性障害の病態解明」
4．Mukhanmad Sunardi (神経分化・再生分野)
"Exploring the therapeutic potential of endogenous stem cells in congenital organ deficits."

13:20～14:53　【セッション６】口頭発表　（座長：内藤 元彦 実行委員）
5．長谷川 夏美 (臨床ウイルス学分野)
「SARS-CoV-2の変異株に対して広く中和活性を持つ抗体の獲得とエピトープ解析」
6．鈴木 暖佳 (生体構造解剖学分野)
「クロマチンリモデリング因子BRMによる骨髄微小環境を介した造血幹細胞の老化制御機構の解明」
7．Aulia Fitri Rhamadianti (感染制御学分野)
"SARS-CoV-2 Papain-Like Protease Inhibits ISGylation of the Viral Nucleocapsid Protein to Evade Host Antiviral Immunity."
8．小森　里美 (生体シグナル部門)
「CD47は樹状細胞によるT細胞のネクロプトーシスを抑制することによって末梢T細胞の生存を促進する」
9．江本　拓央 (循環器内科学分野)「シングルセル解析で挑む血管病病態メカニズム解明」
ラボ紹介７　村田　陽二 (シグナル統合学部門)「細胞間シグナルCD47-SIRPα系の生理機能の理解と疾患治療への応用」

15:10　優秀プレゼンテーション賞表彰式　（贈呈者・古屋敷 教授　補佐・篠原実行委員長）
閉会挨拶（内匠教授）/写真撮影

3．CMXワークショップ　Emergence conference

令和６年１月１８日(木)　神緑会館記念ホール

「第4回Emergence Conference」を令和6年1月18日，神戸大学神緑会館記念ホールにて開催致しました．本カンファレンスの狙いは，「国内を代表する研究者をお招きし，その独創性の高い研究成果をご発表頂くことで最先端の研究動向を学び，臨床応用を含む新たな研究の着眼点を得ることで新たな共同研究が生まれる契機となる」ことを企図しています．今年度は発展が目覚ましく，再生医学における最もホットなトピックとなっている「オルガノイド医学」をテーマに企画致しました．
「オルガノイド」は，「in vivo器官の複雑な構造・機能の両側面を，細胞ベースで三次元に展開したin vitroモデルであり，ヒト組織における発生，疾患モデリング，そして創薬，診断，個別化医療への研究に資するもの」と定義され，現在も，新規プロトコールの開発，改変・最適化が全世界レベルで凌ぎを削っています．カンファレンスでは，本会のオーガナイザーを務めた医学部生理学分野の野村淳による「オルガノイドの研究トレンド・研究動向に関するレクチャー」の後，同大医学部消化器内科の児玉裕三先生による「患者由来オルガノイドを用いた早期膵がんの病態解明」，大阪大学医学部幹細胞応用医学の林竜平先生より「多能性幹細胞由来オルガノイドを用いた眼の再生治療法の開発」，同大学医学部幹細胞医学の小柳（青井）三千代先生より「オルガノイドを用いたヒト発生・病態メカニズムの解明と治療への応用」についてご講演頂きました．続いて，理研BDR-大塚製薬連携センターの坂口秀哉先生より「神経オルガノイドによって可能となる回路レベルのヒト神経活動評価およびオルガノイド医学としての展望」，大阪大学医学部幹細胞医学の林克彦先生より「生殖細胞と性分化課程の再構築と操作」をご講演頂いた後，特別講演として慶応義塾大学医学部の佐藤俊朗先生より「オルガノイドによる消化器がんの理解」についてご講演頂きました．特に大阪大学の林克彦先生におかれましては，Natureによる「2023年, 科学に貢献した10人」に選出されたタイミングであり，本会が企図した目的を具現化した好例と考えています．本カンファレンスを通し，講演者，参加者間で活発な質疑，意見交換が行われた事で本年度もカンファレンスの目的を無事果たすことが出来ました．関係者の皆様に改めて心より感謝申し上げます。

野村 淳 生理学分野 助教

13:00 Opening Remarks　SUZUKI Akira
Deputy Director of Center for Medical Transformation

13:05 Mini-Lecture “Challenges of Organoid Research-Basics and Trends in Organoid Research”
NOMURA Jun
Division of Physiology, Department of Physiology and Cell biology, Graduate School of Medicine, Kobe-U

13:15 Lecture 1 “Establishment of patient-derived organoids from early pancreatic cancer”
KADAMA Yuzo
Division of Gastroenterology, Department of Internal Medicine, Graduate School of Medicine, Kobe-U

13:45 Lecture 2　“Development of regenerative therapy for the eye using pluripotent stem cell-derived organoids”
HAYASHI Ryuhei
Department of Stem Cells and Applied Medicine, Osaka University Graduate School of Medicine

14:25 Lecture 3 “Using organoids to elucidate the mechanisms of human development and diseases and apply them to treatment”
KOYANAZI-AOI Michiyo
Division of Sem Cell Medicine, Department of Future Medical Science, Graduate School of Medicine, Kobe-U

The 4th Emergence Conference was held on January 18, 2024 at Kobe University Shinryokaikan Memorial Hall. The aim of this conference is to "invite leading Japanese researchers to present their highly original research, to learn about cutting-edge research trends, to gain new perspectives including clinical applications, and to provide an opportunity for new collaboration". This year's theme is "Organoid Medicine", which is the hottest topic in the field of regenerative medicine.

“Organoids” are defined as "cell-based, three-dimensional in vitro models of complex structural and functional aspects of organs in vivo, which contribute to research on development, disease modeling, drug discovery, diagnosis, and personalized medicine.

The development, modification, and optimization of new protocols are still being fought over on a global level.


坂口先生


林 克彦 先生

In the conference, Dr. Jun Nomura, Department of Physiology, Faculty of Medicine, who served as the organizer of this conference, gave a lecture on research trends on organoids. Dr. Ryuhei Hayashi, Osaka University School of Medicine, gave a lecture on "Development of regenerative eye treatment using pluripotent stem cell-derived organoids", and Dr. Michiyo Koyanagi-Aoi, Kobe University School of Medicine, gave a lecture on "Elucidation of human development and pathological mechanisms using organoids and their therapeutic applications". Next, Dr. Hideya Sakaguchi of the RIKEN BDR-OTSUKA Collaboration Center gave a lecture on "Evaluation of human neural activity at the circuit level enabled by neural organoids and its prospects for organoid medicine," and Dr. Katsuhiko Hayashi of Osaka University School of Medicine gave a lecture on "Reconstruction and manipulation of germline and sex differentiation processes. Dr. Toshiro Sato of Keio University School of Medicine gave a special lecture on "Understanding digestive cancers by organoids". Especially, Dr. Katsuhiko Hayashi of Osaka University was selected as one of the "10 people who contributed to science in 2023" by the "Nature". The conference successfully fulfilled its objectives this year as well, thanks to the active exchange of questions and opinions among the speakers and participants. I would like to express my sincere gratitude to all the people involved.
Jun Nomura, Kobe University Graduate School of Medicine


佐藤先生

15:20　Lecture 4 “Network-level analysis of human neural function using neural organoids and the future perspective of neural organoid technology as organoid medicine”
SAKAGUCHI Hideya
Neural Organogenesis Laboratory, BDR-Otsuka Pharmaceutical Collaboration Center, RIKEN Center for Biosystems Dynamics Research

16:00　Lecture 5 “Reconstitution and control of germ cell development and sex determination.”
HAYASHI Katsuhiko
Department of Genome Biology, Osaka University Graduate School of Medicine

17:00　Keynote Lecture “Understanding Gastrointestinal Cancers using Organoid Technology”
SATO Toshiro
Department of Organoid Medicine, Keio University School of Medicine

18:00　Closing Remarks　TAKUMI Toru
Director of Center for Medical Transofrmation

4．KU-UW Alliance Project

令和6年3月13日(水)〜3月15日(金)　神緑会館記念ホール 他

令和６年３月13日〜15日、ワシントン大学(米国 シアトル)との交流事業Kobe U – UW Alliance Projectを実施した。ワシントン大学からは、招へい研究者9名と4名の大学院生が参加した。13日には国際共同研究の促進のため個別または少人数によるラボビジットを実施。当研究科の14研究室が参加し45分×27コマの研究室見学・ディスカッションを行った。14日には国際合同シンポジウム、15日には理研計算科学研究センター等へのエクスカーションを実施した。

Session 1 *session chair：Ayaka Bota*

9:20　Signatures of lateral hypothalamic neurons and striatum-wide dopamine dynamics during consumption
Adam Gardon-Fennell　**(UW)**

9:40　The neural mechanism of social behavior via inhibitory parvalbumin neurons in the insular cortex
Shuhei Fujima　**(KU)**

10:00　Characterizing the Effects of Cannabidiol and Terpenes for Pain Relief
Ben　Land　**(UW)**

Session 2 *session chair：Mitsuharu Endo*

10:40　Transcriptomic analysis of circuit-specific neuronal activation
Marta Soden　**(UW)**

11:10　Structural basis of minus-end directed motility of kinesin-14 along microtubule
Tsuyoshi Imasaki　**(KU)**

11:30　Sympathetic Motor Neuron Dysfunction is a Missing Link in the Age-Associated Loss of Organ Control
Oscar Vivas　**(UW)**

12:00　Greetings from the Dean
Takamichi Murakami　**(KU)**

Session 3 *session chair：Ling Deng*

13:30　Oxidative stress sensor Keap1 recognizes HBx protein to activate the Nrf2/ARE signaling pathway, thereby inhibiting hepatitis B virus replication
Ikuo Shoji　**(KU)**

13:50　Innate immune and functional genomics analyses of Zika virus infection at the maternal-fetal interface
Michael Gale. Jr　**(UW)**

14:20　Metabolic Mechanisms of Social Stress in Mice
Hirotaka Nagai　**(KU)**

14:40　Mitochondrial Calcium Overload in Fibrolamellar Cancer
Yasemin Sancak　**(UW)**

15:10　Mechanisms of cardiac pacemaker rate adaptability
Claudia Moreno　**(UW)**

Session 4 *session chair：Tomohiko Maehama*

16:10　A brain-penetrant microtubule-targeting agent that disrupts hallmarks of glioblastoma tumorigenesis
Nephi Stella　**(UW)**

16:40　Therapeutic potential of targeting of SIRPα and SIRPβ1 in cancer immunotherapy
Yoji Murata　**(KU)**

17:00　Anchored protein kinase pathologies
John D. Scott　**(UW)**

18:00　Closing Remarks　**John D. Scott**

ラボビジットの様子

理科学研究所計算科学研究センターにて富岳見学

The Kobe U-UW Alliance Project, an exchange program with the University of Washington (Seattle, USA), took place from March 13 to 15, 2024. The event involved nine invited researchers and four graduate students from the University of Washington. On March 13, there were individual or small-group laboratory visits aimed at fostering international joint research collaborations, which provided an opportunity for in-depth discussions and knowledge sharing among the participants. An international joint symposium was held on the 14th, serving as a platform for presenting and exchanging research ideas and facilitating discussions on potential collaborative projects. On the 15th, an excursion to the RIKEN Computational Science Centre and other facilities was organized, offering the participants insight into cutting-edge research developments and fostering networking opportunities.

Posters

No.	Name	Affiliation	Job Position	Poster　Title
1	Anthony English	UW	Graduate Student	THC-dependent Increases in mPFC Neuronal and Corresponding 2-AG Activity at Locomotion Initiation
2	Keiko Yamaguchi	KU	Graduate Student	Obesity resistance by MOB1 depletion in mouse adipocytes
3	Akihiro Tamura	KU	Associate Professor	Synergistic antitumor effects of anti-SIRPα and anti-GD2 antibodies against neuroblastoma
4	Io Horikawa	KU	Graduate Student	Chronic Stress Alters Lipid Mediator Profiles Associated with Immune-Related Gene Expressions and Cell Compositions in Mouse Bone Marrow and Spleen
5	Jun NOMURA	KU	Assistant Professor	Autism in a Dish: ES cell Models of Autism with Copy Number Variations Reveal Cell-Type-Specific Vulnerability
6	Jerome Falcone	UW	graduate student	Preferential interactions of A-kinase anchoring proteins with different protein kinase A subtypes
7	QIU　WENRAN	KU	Graduate Student	Analysis of peripheral metabolic changes and their significance in chronic social stress in mice
8	Shuhei FUJIMA	KU	Graduate Student	The neural mechanism of social behavior via inhibitory parvalbumin neurons in the insular cortex
9	Aulia Fitri Rhamadianti	KU	Graduate Student	SARS-CoV-2 papain-like protease inhibits ISGylation of the viral nucleocapsid protein to evade host anti-viral immunity
10	Kacey Rosenthal	UW	Graduate Student	AKAP2 as a breast cancer signaling scaffold
11	Kohei Ota	KU	Graduate Student	Metabolic alterations in selective brain regions induced by chronic stress in mice and their involvement in emotional disturbance
12	Hiroto Kuno	KU	Graduate Student	Insular cortical neurons are responsible for the expression of motor tics in mice
13	Takashi Ueda	KU	Graduate student	SIRPα, a potential therapeutic target for the head and neck cancer
14	Maryanne Kihiu	UW	Graduate Student	Targeting Adrenal Cushing's Mutant, PKAc-L205R
15	Mao SUZUKI	KU	Graduate Student	Development of a multimodal VR system for cortical functional network analysis during mouse social behavior
16	Hidehisa Okamoto	KU	Graduate Student	Calcimimetics improve left ventricular hypertrophy by suppressing the renin-angiotensin-aldosterone system and cardiac fibroblast growth factor 23
17	LU TENGCHONG	KU	Graduate Student	Regulation of plasma membrane tension by BAR proteins
18	Jiang Guanhua	KU	Project assistant professor	Critical role of Pla2g2a in promoting glioblastoma stemness.

5．国際共同研究短期派遣招へい事業

CMXではセンターのミッションである国際共同研究の推進を図るため、将来を担い発展的研究を行うことのできる優秀な若手研究者を海外へ派遣、または海外から招へいするための渡航費用の一部を助成する事業を実施しており、令和6年度は派遣3件、招へい2件、計5件を支援した。

To promote international joint research, which is the center's mission, CMX has been implementing a program to subsidize part of the travel expenses for dispatching or inviting outstanding young researchers who are capable of leading the future and conducting advanced research abroad.

手術室見学の一コマ

木村 正夢嶺　脳神経内科学分野, 大学院生

KIMURA Masamune, MD Div. of Neurology, Doctoral Student

この度、メディカルトランスフォーメーション研究センター「国際共同研究短期派遣・招へい事業」により、フランスパリシテ大学に派遣されました（派遣期間：2023年8月26日～31日）。フランス滞在期間中、パリシテ大学脳神経外科よりワークショップを開催いただき、当研究室(松本教授、木村)、神戸大学脳神経外科学教室（藤本助教）、パリシテ大学脳神経外科(Emmanuel Mandonnet教授、研修医1名)、フランス国立情報学自動制御研究所(Inria)（François Bonnetblanc主任研究員、博士研究員1名、院生2名）が参加しました。

日本からは電気生理学的脳活動の指標である皮質皮質間誘発電位に関して、検査手法(刺激パラメータが電位に及ぼす影響)や解析結果（高周波数解析など）を、フランスからは脳外科手術に用いる脳内ネットワーク評価法や、白質刺激のシミュレーションモデルと誘発脳電位の解析方法を提示し、時間をかけてディスカッションを行いました。また、実際に手術室で脳腫瘍切除術を見学し、手術で用いる白質刺激の手法と解析方法を学びました。

今回フランス現地で対面での討議を行うことで、皮質・白質の刺激方法と計測すべきパラメータについて、詳細かつ円滑な議論を進めることができました。このような機会を与えてくださりましたメディカルトランスフォーメーション研究センター、ならびにサポートいただいた研究支援課には厚く御礼申し上げます。

パリシテ大学のみなさんと

With the support of the CMX "International Collaborative Research Short-Term Dispatch and Invitation Program," I was dispatched to Université Paris Cité, France (Dispatch period: August 26-31, 2023). During my stay in France, a workshop was held by the Department of Neurosurgery at Université Paris Cité. Participants included members from our research lab (Professor Matsumoto and myself, Kimura), the Department of Neurosurgery at Kobe University (Assistant Professor Fujimoto), the Department of Neurosurgery at Université Paris Cité (Professor Emmanuel Mandonnet and one resident), and the French National Institute for Research in Computer Science and Automation (Inria) (Chief Researcher François Bonnetblanc, one postdoctoral researcher, and two graduate students).

From Japan, we presented on cortico-cortical evoked potentials as electrophysiological indicators of brain activity, covering examination methods (effects of stimulation parameters on potentials) and analysis results (including high-frequency analysis). The French team presented on the evaluation methods for brain networks used in neurosurgery, as well as simulation models of white matter stimulation and evoked brain potential analysis methods. We engaged in thorough discussions over an extended period. Additionally, we observed a brain tumor resection surgery in the operating room, learning the methods of white matter stimulation and analysis techniques used during surgery.

By holding face-to-face discussions on-site in France, we were able to advance detailed and smooth discussions on stimulation methods for the cortex and white matter and the parameters to be measured.

I would like to extend my sincere gratitude to the CMX for providing this opportunity, as well as to the Research Support Division for their assistance.

橘吉寿 生理学分野 准教授

TACHIBANA Yoshihisa, Associate Professor
Dept. of Physiology & Cell Biology

この度、CMX国際共同研究短期派遣・招へい事業により、ボルドー大学に派遣いただきました（2024年3月18日～24日）。滞在期間中の主目的として、大脳基底核研究で著名なThomas Boraud博士を訪れ、依存症の病態メカニズム解明に関する共同研究をどのように進めていくかについて議論しました。Boraud博士は、パーキンソン病患者における脳深部刺激術の臨床応用、またその作用機序の解明を最初に行った大脳基底核研究の第一人者です。私は、Boraud博士と10年以上前から交流があり、これまで学会のシンポジウム共催や大脳基底核研究に関する意見交換を行ってきました。

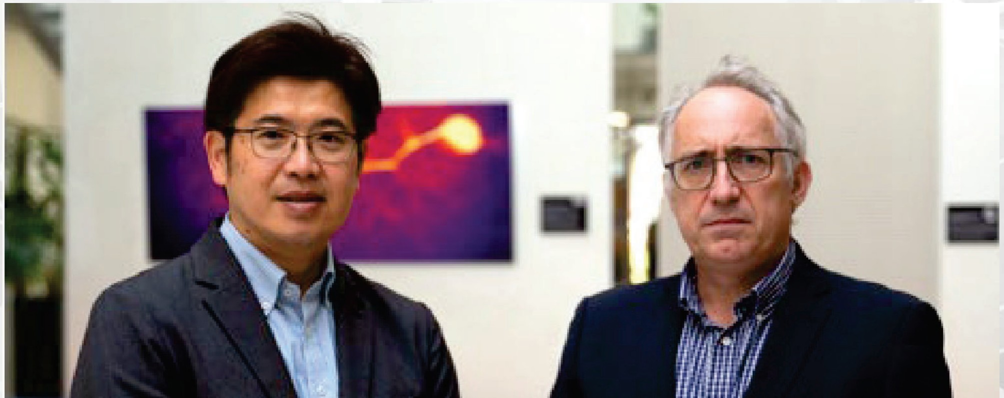
今回、初めてボルドー大学を訪れ、これから申請する国際グラントに関する具体的な研究立案を行ってきました。また、ボルドー大学には、Boraud博士の他、Nicolas Mallet博士やJérôme Baufreton博士など、国際的な大脳基底核研究者が多数おり、それぞれと非常に長時間のディスカッションを行うことが出来ました。私の研究もセミナーという形で時間を与えていただき、討論できたことは非常に有意義でした。

今回の渡航により、国際グラントの採択が実現されれば、さらに嬉しく思います。このような機会を与えてくださりましたCMX、ならびにサポートいただいた研究支援課には厚く御礼申し上げます。

Thanks to the CMX International Collaborative Research Short-term Dispatch and Invitation Program, I visited the University of Bordeaux from March 18th to 24th, 2024. The main purpose of my stay was to visit Prof. Thomas Boraud, renowned for his research on the basal ganglia, and discuss how to advance our collaborative research on elucidating the pathological mechanisms of addiction. Prof. Boraud is a leading researcher in basal ganglia research, having first conducted clinical applications and elucidations of the mechanisms of deep brain stimulation in patients with Parkinson's disease. I have had an exchange with Prof. Boraud for over ten years, during which we have co-organized symposiums at academic conferences and exchanged opinions on basal ganglia research. This was my first visit to the University of Bordeaux, where we concretely planned the research to be proposed for an international grant.

In addition to Prof. Boraud, the University of Bordeaux is home to many internationally renowned basal ganglia researchers, including Dr. Nicolas Mallet and Dr. Jérôme Baufreton. I had very extensive discussions with each of them. It was also very meaningful to have the opportunity to present my research in a seminar format and engage in discussions. I would be even more pleased if this visit leads to the successful adoption of our international grant proposal.

I would like to express my deep gratitude to CMX for providing such an opportunity, as well as to the research support division for their assistance.



橘准教授(左)とBoraud博士(右)

CMX International Collaborative Research Short-term Dispatch and Invitation Program

category	name	affiliation	to / from	duration
dispatch	KIMURA Masayume	Neurology	to Université Paris Cité, France	August 26-31, 2023
dispatch	TACHIBANA Yoshihisa	Physiology & Cell Biology	to University of Bordeaux, France	March 18 -24, 2024
dispatch	MATSUO Hidetoshi	Radiology	to the University of Zurich, Switzerland	March 2 – 5, 2024
invitation	Rini Rossanti	Pediatrics	from Padjadjaran University, Indonesia	February 3 – 19, 2024
invitation	KIRA Shinichiro	Physiology & Cell Biology	from Harvard University, the United States	March 21 – 31, 2024

チューリッヒの街並み

松尾 秀俊　放射線医学分野　助教

2024年4月から始まる国際共同研究に先立ち、神戸大学・京都大学とスイスのチューリッヒ大学の共同研究準備のため3月にチューリッヒ大学を訪問しました。この研究の目的は、チューリッヒ大学の多言語対応LLM技術と日本の高品質な医療情報を融合し、日本語に対応した高精度なLLMを開発することです。

今回の訪問では、1.データ収集、2.データ前処理、3.LLMの基礎構築、4.LLMの学習、5.オンプレミス環境構築、6.LLMの改善、7.LLMの性能評価という7つの研究段階に基づく密な技術交流と意見交換が行われました。特に、日本語医療情報対応LLMの構築やオンプレミス環境でのLLM稼働、多タスク対応性能の検討が中心的な課題として議論されました。

訪問中にはチューリッヒ大学側の研究室がスイスの国家プロジェクト「AI initiative」に参加しており、月2万時間の計算資源が確保されていることが確認されました。また、両者の協力により、医用画像を用いたLLMの研究が大いに進展することが期待されています。ただし、個人情報保護の観点からデータ共有のハードルが高いことも認識され、今後の課題として検討される予定です。
今回の訪問により、信頼関係が構築され、今後の共同研究に向けた基盤が整ったことに感謝しております。このような貴重な機会を与えて下さったメディカルトランスフォーメーション研究センターの関連の皆様に心より御礼申し上げます。

MATSUO Hidetoshi, Assistant Professor, Dept. of Radiology

In March 2024, as a precursor to the commencement of an international collaborative research project set to begin in April, we visited the University of Zurich. This visit was orchestrated to lay the groundwork for joint research between Kobe University, Kyoto University, and the University of Zurich, focusing on the integration of Zurich's multilingual LLM technology with Japan's high-quality medical information to develop an LLM capable of handling Japanese with high accuracy.

During our visit, we engaged in intensive technical exchanges and discussions based on seven research stages: data collection, data preprocessing, foundational LLM construction, LLM training, on-premises environment setup, LLM improvement, and LLM performance evaluation. Key issues discussed included the construction of a Japanese medical information-compatible LLM, the operation of LLM in an on-premises environment, and the evaluation of its multitasking capabilities.

It was noteworthy that the Zurich team's laboratory is part of the Swiss national project 'AI Initiative,' securing 20,000 hours of computational resources per month. Furthermore, through collaborative efforts, significant advancements in LLM research using medical imaging are anticipated. However, challenges in data sharing due to privacy protection were recognized, and these will be addressed as future challenges.
This visit not only established a strong foundation of trust but also prepared us for the upcoming joint research. We are deeply grateful for this invaluable opportunity provided by the Medical Transformation Research Center and all associated personnel.

チューリッヒの街並み

榊原 菜々 小児科学分野 学術研究員

この度、CMX 国際共同研究短期派遣・招へい事業のご支援により、2024年2月3日～19日の間、インドネシアのPadjadjaran大学からRini Rossanti先生を招へいさせていただきました。Rini Rossanti先生は以前、神戸大学大学院博士課程(小児科学)においてネフローゼ症候群を中心とした小児遺伝性腎疾患に関する研究に従事され、2022年に学位取得後、インドネシアで小児腎臓医として勤務されながら、研究を続けてこられました。
Rini Rossanti先生は、日本における研究経験を活かし、インドネシア内で小児ステロイド抵抗性ネフローゼ症候群の遺伝学的診断体系を確立することを目指しており、まずは共同研究という形で、当科のバックアップのもとインドネシアの小児ステロイド抵抗性ネフローゼ症候群に対する、次世代シークエンサーを用いた網羅的遺伝子解析を行うこととしました。滞在期間中24例分の解析を実施し、5例で遺伝子異常を同定することができました。今後さらに症例を増やし、インドネシアで解析を実施できるよう準備をすすめている段階です。
今回の招へい事業により、共同研究を進めることができました。このような機会を与えて下さったメディカルトランスフォーメーション研究センター、ならびに研究支援課の皆様に心より御礼申し上げます

中井 信裕　生理学分野　特命助教

2024年3月に米国ハーバード大学から吉良信一郎博士を招聘するにあたり、本事業より支援を受けました。当分野では以前より、VR技術を活用したマウスの社会行動実験と脳神経イメージングに取り組んでいます。そこで、VR行動課題を用いた神経科学研究に長けている吉良博士との共同研究を進めることで、さらに研究を発展させることを目指しました。
神戸大学滞在中、CMXセミナーを通じて、マウス用VRによる空間ナビゲーション課題や二光子カルシウムイメージング、光遺伝学操作実験の知見を深めることができました。また、当分野とハーバード大学のVR実験システムを比較検証しました。吉良博士からは、実験プラットフォームにおけるトレッドミルの動きの効率的なセンシング技術の導入など、VRシステムの改善について貴重なアドバイスをいただきました。今回の取り組みは、VRシステムによる社会ナビゲーションにおける脳機能の理解を深めるための基盤となるものであり、今後の研究として光遺伝学操作を組み合わせた実験系構築につながりました。
また、吉良博士には当分野の若手教員や大学院生と1対1で時間をかけた議論を行っていただきました。そこでは研究内容そのもののアドバイスだけでなく、海外での研究の取り組みやキャリアパスの重要性などを若手スタッフは学ぶことができたようで、非常に実り多き機会となりました。
最後になりましたが、このような貴重な機会を提供してくださったCMX関係者の皆様に心より感謝申し上げます。

小児科学分野での一コマ

中井先生(左)と吉良先生(右)

SAKAKIBARA Nana, Academic Researcher, Dept. of Pediatrics

Dr. Rini Rossanti was invited from Padjadjaran University in Indonesia from February 3, 2024 to 19th with the support of Center for Medical Transformation (CMX) short-term dispatch/invitation program. She was previously engaged in research on pediatric genetic kidney disease, focusing on nephrotic syndrome, at Kobe University Graduate School of Medicine (Pediatrics), and after receiving her PhD in 2022, she has continued her research while working as a pediatric nephrologist in Indonesia.
She aims to establish a genetic diagnostic system for steroid-resistant nephrotic syndrome in Indonesia by utilizing her research experience in Japan. As a first step, she has decided to conduct a comprehensive genetic analysis of steroid-resistant nephrotic syndrome in Indonesia using a next-generation sequencing system with the support of our department. In total, 24 patients were analyzed during her stay, and gene abnormalities were identified in 5 patients. She is currently preparing to increase the number of cases and conduct the analysis in Indonesia.
Through this invitation project, we were able to advance the collaboration research. We would like to express our sincere gratitude to the Medical Transformation Research Center and the Research Support Division for giving us this opportunity.

NAKAI Nobuhiro, Project Assistant Professor, Dept. of Physiology & Cell Biology

We received support from this program for inviting Dr. Shinichiro Kira from Harvard University in the United States in March 2024. Our department has been working on social behavior experiments with mice using VR technology and brain imaging. We aimed to further develop our research by collaborating with Dr. Kira, who excels in neuroscience research using VR behavioral tasks.
During his stay at Kobe University, we were able to deepen our knowledge of spatial navigation tasks using mouse VR, two-photon calcium imaging, and optogenetic manipulation experiments through the CMX seminar. We also compared the VR experimental systems of our department and Harvard University. Dr. Kira provided valuable advice on improving the VR system, such as introducing efficient sensing technology for treadmill movement in the experimental platform. This effort has become the foundation for understanding brain functions in social navigation using VR systems and has led to the development of experimental systems combining optogenetic manipulation for future research.
Additionally, Dr. Kira engaged in one-on-one discussions with young faculty members and graduate students in our department. These sessions provided not only advice on research content but also opportunities for young staff to learn about approaches to research abroad and the importance of career paths, making it an extremely fruitful experience.
Lastly, we would like to express our heartfelt gratitude to all CMX staff members who provided us with this valuable opportunity.

1．共同研究・受託研究・イノベーションの創出に資する成果
Collaborative and Contract researches, and results that contribute to innovation creations

区　分 / Category	件　数 / Number of Projects	金 額（千円）※直接経費 Amount (1000yen) ※direct cost
AMED	41件	393,657
JST	33件	214,966
共同 / Collaborative Research	53件	167,220
受託 / Contract Research	45件	68,010
計 / Total	**172件**	**843,853**

2．主要論文一覧
Major Papers

難治性がん　Intractable Cancers

Michiko Itoh, Atsushi Tamura, Sayaka Kanai, Miyako Tanaka, Yohei Kanamori, Ibuki Shirakawa, Ayaka Ito, Yasuyoshi Oka, Isao Hidaka, Taro Takami, Yasushi Honda, Mitsuyo Maeda, Yasuyuki Saito, Yoji Murata, Takashi Matozaki, Atsushi Nakajima, Yosky Kataoka, Tomoo Ogi, Yoshihiro Ogawa, Takayoshi Suganami **Lysosomal cholesterol overload in macrophages promotes liver fibrosis in a mouse model of NASH.** *The Journal of experimental medicine 2023 Nov 220(11):e20220681. DOI: 10.1084/jem.20220681 PMID: 37725372*

Mitsuharu Endo, Yuki Tanaka, Mayo Fukuoka, Hayata Suzuki, Yasuhiro Minami **Wnt5a/Ror2 promotes Nrf2-mediated tissue protective function of astrocytes after brain injury.** *Glia 2023 Oct 72(2) 411-432 DOI: 10.1002/glia.24483 PMID: 37904612*

Michiru Nishita, Koki Kamizaki, Kyoka Hoshi, Kana Aruga, Ikumi Nishikaku, Hiroshi Shibuya, Kunio Matsumoto, Yasuhiro Minami **Rho family small GTPase Rif regulates Wnt5a-Ror1-Dvl2 signaling and promotes lung adenocarcinoma progression.** *Journal of Biological Chemistry 2023 Sep 299(10):105248-105248. DOI: 10.1016/j.jbc.2023.105248 PMID: 37703992*

Ryosuke Takahashi, Koki Kamizaki, Keitaro Yamanaka, Yoshito Terai, Yasuhiro Minami **Expression of Ferredoxin1 in cisplatin-resistant ovarian cancer cells confers their resistance against ferroptosis induced by cisplatin.** *Oncology reports 2023 Jun 49(6):124. DOI: 10.3892/or.2023.8561 PMID: 37144519*

Jing Pu , Satoshi Kofuji , Yoshimi Okamoto-Uchida , Keiko Danzaki , Ruoxing Yu , Akira Suzuki , Satoshi Kitajima , Hiroshi Nishina **Lethal Phenotype-Based Database Screening Identifies Ceramide as a Negative Regulator of Primitive Streak Formation** *Stem Cells. 2023 Dec 41(12):1142-1156. DOI:10.1093/stmcls/sxad071. PMID: 37819786.*

Kotaro Sato , Ming Yang , Kae Nakamura , Hiromasa Tanaka , Masaru Hori , Miki Nishio , Akira Suzuki , Hideharu Hibi , Shinya Toyokuni **Ferroptosis induced by plasma-activated Ringer's lactate solution prevents oral cancer progression** *Oral Diseases 2023 Dec -:- .DOI: 10.1111/odi.14827 PMID: 38047766*

Yuki Yamamoto , Tomonori Kamiya , Megumu Yano , Vu Thuong Huyen , Masahiro Oishi , Miki Nishio , Akira Suzuki , Kishiko Sunami , Naoko Ohtani **Oral Microbial Profile Analysis in Patients with Oral and Pharyngeal Cancer Reveals That Tumoral Fusobacterium nucleatum Promotes Oral Cancer Progression by Activating YAP.** *Microorganisms 2023 Dec 11(12):2957. DOI: 10.3390/microorganisms11122957 PMID: 38138101*

Yuki Azumi, Yu-ichiro Koma, Shuichi Tsukamoto, Yu Kitamura, Nobuaki Ishihara, Keitaro Yamanaka, Takashi Nakanishi, Shoji Miyako, Satoshi Urakami, Kohei Tanigawa, Takayuki Kodama, Mari Nishio, Manabu Shigeoka, Yoshihiro Kakeji, Hiroshi Yokozaki **IFI16 Induced by Direct Interaction between Esophageal Squamous Cell Carcinomas and Macrophages Promotes Tumor Progression via Secretion of IL-1α** *Cells 2023 Nov 12(22):2603-2603. DOI: 10.3390/cells12222603 PMID: 37998338*

Yasuhiro Kodera, Kazuhiro Yoshida, Mitsugu Kochi, Takeshi Sano, Wataru Ichikawa, Yoshihiro Kakeji, Yu Sunakawa, Masahiro Takeuchi, Masashi Fujii **Addition of docetaxel to S－1 results in significantly superior 5-year survival outcomes in Stage III gastric cancer: a final report of the JACCRO GC-07 study.** *Gastric cancer : official journal of the International Gastric Cancer Association and the Japanese Gastric Cancer Association 2023 Aug :1063-1068. DOI:10.1007/s10120-023-01419-9 PMID: 37548812*

Satoru Matsuda, Yuko Kitagawa, Ryo Takemura, Jun Okui, Akihiko Okamura, Hirofumi Kawakubo, Manabu Muto, Yoshihiro Kakeji, Hiroya Takeuchi, Masayuki Watanabe, Yuichiro Doki, **Real-world Evaluation of the Efficacy of Neoadjuvant DCF Over CF in Esophageal Squamous Cell Carcinoma: Propensity Score-matched Analysis From 85 Authorized Institutes for Esophageal Cancer in Japan.** *Annals of surgery 2023 Jul 278(1):e35-e42-.DOI: 10.1097/SLA.0000000000005533 PMID: 35837977*

代謝　Metabolism

Hiromichi Okuma, Yumiko Saijo-Hamano, Hiroshi Yamada, Aalaa Alrahman Sherif, Emi Hashizaki, Naoki Sakai, Takaaki Kato, Tsuyoshi Imasaki, Satoshi Kikkawa, Eriko Nitta, Miwa Sasai, Tadashi Abe, Fuminori Sugihara, Yoshimasa Maniwa, Hidetaka Kosako, Kohji Takei, Daron M. Standley, Masahiro Yamamoto, Ryo Nitta **Structural basis of Irgb6 inactivation by Toxoplasma gondii through the phosphorylation of switch I** *Genes Cells 2023 Nov :29(1): 17-38 .DOI: 10.1111/gtc.13080*

Shintaro Yamada, Toshiyuki Ko, Masamichi Ito, Tatsuro Sassa, Seitaro Nomura, Hiromichi Okuma, Mayuko Sato, Tsuyoshi Imasaki, Satoshi Kikkawa, Bo Zhang, Takanobu Yamada, Yuka Seki, Kanna Fujita, Manami Katoh, Masayuki Kubota, Satoshi Hatsuse, Mikako Katagiri, Hiromu Hayashi, Momoko Hamano, Norifumi Takeda, Hiroyuki Morita, Shuji Takada, Masashi Toyoda, Masanobu Uchiyama, Masashi Ikeuchi, Kiminori Toyooka, Akihiro Umezawa, Yoshihiro Yamanishi, Ryo Nitta, Hiroyuki Aburatani, Issei Komuro **TEAD1 trapping by the Q353R–Lamin A/C causes dilated cardiomyopathy** *Sci. Adv. 2023 Apr: 9(15):eade7047. DOI: 10.1126/sciadv.ade7047 PMID: 37058558*

Toru Tanaka, Naoto Sasaki, Aga Krisnanda, Masakazu Shinohara, Hilman Zulkifli Amin, Sayo Horibe, Ken Ito, Motoaki Iwaya, Atsushi Fukunaga, Ken-Ichi Hirata, Yoshiyuki Rikitake **Novel UV-B Phototherapy With a Light-Emitting Diode Device Prevents Atherosclerosis by Augmenting Regulatory T-Cell Responses in Mice.** *J of Am Heart Assoc. 2024 Jan; 13(2):e031639.DOI: 10.1161/JAHA.123.031639 PMID: 38214259*

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Daichi Fujimoto, Masakazu Shinohara, Hiroyuki Kawamori, Takayoshi Toba, Shunsuke Kakizaki, Koichi Nakamura, Satoru Sasaki, Tomoyo Hamana, Hiroyuki Fujii, Yuto Osumi, Naomi Hayasaka, Shigenobu Kishino, Jun Ogawa, Ken-ichi Hirata, Hiromasa Otake **The relationship between unique gut microbiome-derived lipid metabolites and subsequent revascularization in patients who underwent percutaneous coronary intervention** *Atherosclerosis. 2023 Jun: 375:1-8. DOI: 10.1016/j.atherosclerosis.2023.05.001 PMID : 37216727*

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難治性がん Intractable Cancers × 創薬・医療機器　New Drug & Medical Device Development

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3．報道　Press

タイトル/内容	媒　体	報 道 月 日	対象者
「膵臓がん、AIで早期発見　画期的な技術、難治を克服へ 神戸大と富士フイルムが開発、初期でも精度高く」	神戸新聞	令和5年4月5日	児玉　裕三 KODAMA Yuzo
「活性酸素と難聴に関する研究内容」が日本科学未来館に常設展示（未来の選択肢_聴覚）	日本科学未来館	令和5年11月22日	上山　健彦 UEYAMA Takehiko

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