

## 二国間交流事業 共同研究報告書

令和5年4月27日

独立行政法人日本学術振興会理事長 殿

[日本側代表者所属機関・部局]  
公益財団法人川崎市産業振興財団  
ナノ医療イノベーションセンター  
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[課題番号]  
JPJSBP 120209938

1. 事業名 相手国: スペイン (振興会対応機関: OP) との共同研究

2. 研究課題名

(和文) 効果的な肥満及び膠芽腫治療の為の特異的脳細胞内 CPT1 ナノ医薬ターゲティング

(英文) Nanomedicine based Drug targeting CPT1 in specific brain cells for effective Obesity and Glioblastoma therapy

3. 共同研究実施期間 令和2年 4月 1日 ~ 令和5年 3月 31日 (3年 0ヶ月)【延長前】 令和2年 4月 1日 ~ 令和4年 3月 31日 (2年 0ヶ月)

4. 相手国側代表者(所属機関名・職名・氏名【全て英文】)

Universitat Internacional de Catalunya, Associate Professor,  
Rodriguez Rosalia Rodriguez

5. 委託費総額(返還額を除く)

本事業により執行した委託費総額		3,800,001 円
内訳	1年度目執行経費	1,900,000 円
	2年度目執行経費	1,900,001 円
	3年度目執行経費	- 円

6. 共同研究実施期間を通じた参加者数(代表者を含む)

日本側参加者等	13名
相手国側参加者等	8名

\* 参加者リスト(様式 B1(1))に表示される合計数を転記してください(途中で不参加となった方も含め、全ての期間で参加した通算の参加者数となります)。

7. 派遣・受入実績

	派遣		受入
	相手国	第三国	
1年度目			( )
2年度目			( )
3年度目	1		1( )

\* 派遣・受入実績(様式 B1(3))に表示される合計数を転記してください。

派遣:委託費を使用した日本側参加者等の相手国及び相手国以外への渡航実績(延べ人数)。

受入:相手国側参加者等の来日実績(延べ人数)。カッコ内は委託費で滞在費等を負担した内数。

## 8. 研究交流の概要・成果等

### (1)研究交流概要(全期間を通じた研究交流の目的・実施状況)

This joint collaboration study between iCONM (Japan) and UIC Barcelona (Spain) aims to: (i) develop nanomedicine-based drugs that can target and manipulate brain CPT1s that are crucially linked to obesity and brain tumors; (ii) validate the use of this nano-drug delivery approach targeting CPT1s in mice obesity model and mice brain-tumor model; and (iii) thus address unmet medical needs in terms of managing brain cancer and obesity.

Towards the above mentioned goal we developed a polymeric micelle (PM)-type nanomedicine that demonstrated excellent biological activity upon delivery of the CPT1A inhibitor in brain cells, particularly to neurons, after intracerebroventricular (ICV) administration making the crosslinked PM valuable for in vivo applications.

Throughout the entire research exchange period, we had numerous bilateral meetings (online), we conducted online lectures, seminars and symposiums. Notably, despite the challenges related to COVID19 crisis we could successfully conduct researcher exchange to and from the partner countries. Few most significant activities are presented below-

- As a part of our ongoing collaboration between UIC (Spain) and iCONM (Japan), a virtual Bilateral Meeting was successfully held on 3rd of February, 2021. Universitat de Barcelona (Spain) and the National Institute of Health Sciences (Japan) are also partners in this collaboration. In total, 20 participants from these four different research institutes and two different countries: iCONM (JP), NIHS (JP), UIC (ES), UB (ES) participated in the virtual bilateral meeting.
- Dr. Rosalia Rodriguez-Rodriguez from UIC-Barcelona, the CoPI of Japan-Spain bilateral project, was invited to an open seminar "COINS Seminar No 60" organized by iCONM on October 7th, 2021. Dr. Rosalia's presentation title was "Targeting Neurons: More Brain than Brawn to Solve Obesity."
- On November 10th, 2021, Dr. Sabina Quader gave a special online lecture at the International University of Catalunya (Barcelona, Spain), describing the research prospects for innovative nanomedicine being developed at iCONM.
- In May 2022, Dr. West Paraiso participated in a research visit to Spain- He attended a conference in Valencia, Spain, where he presented a poster highlighting the main academic results obtained through our Japan-Spain bilateral project and received valuable suggestions from the attendees. He also made some new connections, especially with those who prepare in vitro and ex vivo models for nasal epithelial tissue. Dr. West also managed to participate in the tour of the facilities of a polymer manufacturer (Curapath). After the conference attendance in Valencia, he visited the lab of our collaborator Dr. Rosalia Rodriguez in UIC, Barcelona. In UIC, he was welcomed by Dr. Rodriguez and the rest of the Neurolipid group at UIC. Dr. West had the chance to visit their lab facilities and classrooms. And then he also presented a seminar communicating the primary research findings from our Japan-Spain project.
- As part of the Japan-Spain collaboration, Mr. Jesús García, a final year PhD Student and a member of the research team from UIC Barcelona, participated in research at iCONM as an internship student from May to August 2022. This research visit was a significant attachment to his PhD training. He accomplished essential skills in nanotechnology experiments at iCONM and acquired maturity as an independent researcher in an international atmosphere.

### (2)学術的価値(本研究交流により得られた新たな知見や概念の展開等、学術的成果)

In this study, polymeric micelle type nanomedicines were designed that encapsulate drugs capable of inhibiting CPT1A involved in neuronal lipid metabolism, and it was proven both in cell models (2D and 3D cultures) and in animal testing (mice) that the polymeric micelles had a more remarkable ability to enter neurons compared to the free drug. Another benefit of these nanomedicines is the significant improvement in liver and brown adipose tissue metabolic indicators, showing that this is a new generation of therapies to deal with pathologies such as obesity. This research can potentially create and validate a new generation of nanomedicine-based strategies by focusing on brain lipid metabolism to control food and body weight. In addition, this work emphasizes the significance of nanotechnology beyond its current biological uses. It makes it easier to comprehend the early stages of energy balance (i.e., acute satiating actions), critical for the emergence of complex disorders like obesity and diabetes.

(3)相手国との交流(両国の研究者が協力して学術交流することによって得られた成果)

Through this bilateral research collaboration between iCONM-UIC, we have already jointly published one peer-reviewed review article, one peer-reviewed editorial piece and two peer-reviewed original articles.

In addition to peer-reviewed publication, Neuro Central published an interview “A peek behind the paper – Sabina Quader and Rosalia Rodríguez-Rodríguez on nanomedicines for neuron targeting”.

(4)社会的貢献(社会の基盤となる文化の継承と発展、社会生活の質の改善、現代的諸問題の克服と解決に資する等の社会的貢献はどのようにあったか)

During Mr. Jesús García's research stay at iCONM, Mr. Garcia participated in two significant cultural/social events. At iCONM, we organize an internal communication event where a presenter showcases their home country/town and cultural specialties. Mr. Garcia participated in this event as a presenter and offered a virtual tour of Barcelona, specifying the city's unique architectural styles and designs. This presentation by Mr. Garcia was endorsed by iCONM staff members very well and had a long-lasting impact.

In addition to this communication event, Mr Garcia volunteered in the King Skyfront Summer event held on 10th August 2022. This event is mainly intended for elementary school students to have fun while becoming more familiar with science. Mr. Garcia assisted iCONM staff members during the science exhibition and workshop sessions and actively interacted with many school children and their parents.

On November 10th, 2021, Dr. Sabina Quader gave a special online lecture at the International University of Catalunya (Barcelona, Spain), describing the research prospects for innovative nanomedicine being developed at iCONM. During this presentation, Dr Quader presented a detailed overview of the King Skyfront (KSF) area, the convenient location of KSF in the close vicinity of Haneda airport, unique features of iCONM, such as “Under the One Roof comprehensive nanomedicine research facility” of iCONM, core research concept of iCONM that is “in body hospitals” and ultimately specific research activities.

Overall, this JSPS-funded bilateral project between iCONM (Japan) and UIC (Spain) profoundly shaped the research culture of the two institutes, closely linked to the inheritance and development of a culture that forms the foundation of society. Most importantly, the main research focus of this Bilateral project itself is closely attached to a more significant social issue, which is obesity and other metabolic disorders. Accordingly, it can be expected that this bilateral project will continue to have a broader social impact, nationally and internationally.

(5)若手研究者養成への貢献(若手研究者養成への取組、成果)

One direct influence of this iCONM (Japan) and UIC (Spain) bilateral project is that one of the main participants Dr. West Paraiso from Japan side who did his Ph.D. at the Hokkaido University in 2017 under the supervision of a globally renowned academic/researcher in the field of lipid-based nanoparticles, Professor Hideyoshi Harashima, has been invited to join UIC, Barcelona, Spain as an Assistant Professor. From the beginning, Dr. Paraiso participated in this Japan-Spain bilateral project and was involved in day-to-day experiments. Accordingly, Dr Paraiso is expected to connect these two institutes, UIC and iCONM, more closely through his new position at UIC as an Assistant Professor.

Additionally, this bilateral project profoundly impacted building a stable platform for the other young researchers of iCONM to get close exposure to international collaboration, research exchange, and scientific communication between partner countries. Many of these young researchers have become PIs of new international collaborative projects.

From UIC (Spain) side many young researchers actively participated in the project and co-authored scientific publications with authors from Japan side. Mr. Jesús García's research stay at iCONM during the summer of 2022 has already been highlighted earlier. Followed by Mr Jesus Garcia, Mr Carlos Palacin, a current master's student from UIC, Barcelona is now in the process of visiting Japan during this autumn as a research trainee at iCONM. Mr. Jordi Gene, a final year undergraduate student of UIC is also in the process of visiting Japan, early next year as a research trainee at iCONM.

(6)将来発展可能性(本事業を実施したことにより、今後どのような発展の可能性が認められるか)

In our newly adopted 10-year project, Center of Healthy Longevity and Nursing Innovation with Global Ecosystem (CHANGE), funded by JST/MEXT, the iCONM (Japan)-UIC (Spain) bilateral project-derived research theme has already been included. This implies that the potential for future development goals through recognizing results derived from the already existing iCONM-UIC bilateral project has been realized. In addition, both PIs, Dr Quader and Dr Rosalia, are actively looking for future co-funding opportunities to reinforce and expand the current bilateral research collaboration platform.

(7)その他(上記(2)~(6)以外に得られた成果があれば記載してください)

例:大学間協定の締結、他事業への展開、受賞など

We have signed a memorandum of understanding (MOU) between iCONM, Japan and UIC, Spain to strengthening our relationship by serving as a host institution for the Master's Degree in Experimental Biomedical Research (MEBR)

program at UIC's Faculty of Medicine and Health Sciences. We believe that collaboration between our institute, iCONM, and MEBR, UIC can advance the internationalization of these two organizations and allow students to complete some of their coursework abroad and come into contact with various scientific, social, and cultural realities. We are thinking about accepting on 1-2 visiting students a year from UIC. Similar plans have also been explored, in which Dr. Rodriguez would work with UIC to host Japanese researchers and research trainees who would come to the university for brief research trips.

In addition to signing a MOU for student exchange we have committed to continue our bilateral research project through securing additional national and international grants. One particular example is that we recently submitted a Sakura Science Fellowship, offered by JST to invite a Masters student from UIC in our institute.