

京都大学若手人材海外派遣事業 スーパージョン万プログラム
研究者派遣プログラム

英文報告書

提出日：平成 26 年 12 月 25 日

1. 渡航者 (日本語)			
氏名	原田 浩	採択年度	平成 25 年度
部局	医学部附属病院	電話	
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研究課題名	がん細胞におけるエネルギー代謝系と放射線治療抵抗性のクロストーク		
海外渡航期間	平成 26 年 3 月 26 日～ 平成 26 年 10 月 31 日		
渡航先 (英語表記)	国名： イギリス 大学等研究機関名： オックスフォード大学 研究室名等： Hammond Lab. (Hypoxia Group) 受入研究者名： Prof. W. Gillies McKenna; Dr. Ester M. Hammond		
2. 渡航の報告 (英文)			
渡航先の研究環境、研究者との交流、研究発表の状況等、渡航中の滞在経験について英語 (500～1000 語) で記述して下さい。受入研究者と撮影した写真や研究発表で用いた図等について、可能な範囲で別添として提出して下さい。ページ数については増加してもかまいません。			
1. 渡航先の研究環境			
<p>I visited CRUK/MRC Oxford Institute for Radiation Oncology, Department of Oncology, University of Oxford from 26th March to 31st October, 2014. The institute was designated as Gray Institute for Radiation Oncology and Biology before its reorganization. There are approximately 25 research groups/laboratories in the institute each of which focuses on radiation chemistry, systems biology, molecular imaging, DNA damage response, DNA repair, tumor microenvironment, translational research, radiation biophysics, genome instability, radioresistance of cancer, radiation oncology, or chemoradiotherapy. Principal Investigators (PI)/Group Leaders of these laboratories are world-leading scientists, who have published scientific papers in prestigious journals; therefore, I could get latest knowledge from internal meetings of the institute. The institute adopts the so-called open laboratory (Picture 1), in which there is principally no partition compartmenting laboratories; and therefore, scientists can freely and frequently have discussions regardless of laboratories they belong. Most laboratory instruments are shared in the institute, which encourages junior group leaders to establish their own laboratories.</p>			
2. 研究者との交流			
<p>CRUK/MRC Oxford Institute for Radiation Oncology is a well-known institute especially in the research fields of radiation oncology, radiation biology, and hypoxia biology. The institute regularly holds two kinds of seminars every week; external seminar and internal seminar. The institute officially invites one world-leading scientist per week for the external seminar. The seminar enables institute members not only</p>			

to gain latest knowledge, but also to have a chance to directly contact the world-class scientists to visit their laboratories for study and research. In the internal seminar, on the other hand, one young member, such as a postdoc or graduate student, in the institute is assigned a chance to give a talk about his/her own research. This seminar facilitates exchanging knowledge among different research groups and gives young members a chance to present their data in English. In addition to these two regular seminars, each of the 25 research groups has their own group meeting to discuss the progress of research approximately once per week. Furthermore, there is a research community focusing on cellular adaptive responses to hypoxic stimuli in University of Oxford and the community weekly hold a conference. This community annually has a big meeting with colleagues belonging Cambridge University; the annual meeting is designated as HypOxiBridge, it is a newly coined word by combining Hypoxia, Oxford, and Cambridge. The scientific level of HypOxiBridge is quite high and almost same as Keystone Symposia and Gordon Research Conference.

In addition to these official meetings, institute members frequently go out to a pub for discussion with some drinks, such as beer, wine and cider (Picture 2). This custom was good occasion for me to deepen a relationship with colleagues from all over the world, and to get familiar with various kinds of English pronunciation.

3. 研究発表の状況等

The most important mission of my visit to UK was to collaborate with Prof. WG McKenna, Prof. RJ Muschel and Prof. EM Hammond on molecular mechanisms underlying the crosstalk between energy metabolism and radioresistance of cancer cells. Following two papers were accepted for publication in *Oncogene* and *Nature Communications* due to the fruitful collaboration.

1. Zeng L, Morinibu A, Kobayashi M, Zhu Y, Wang X, Goto Y, Yeom CJ, Zhao T, Hirota K, Shinomiya K, Itasaka S, Yoshimura M, Guo G, Hammond EM, Hiraoka M, Harada H. Aberrant IDH3 α expression promotes malignant tumor growth by inducing HIF-1-mediated metabolic reprogramming and angiogenesis. *Oncogene*. in press.
2. Goto Y, Zeng L, Yeom CJ, Zhu Y, Morinibu A, Shinomiya K, Kobayashi M, Hirota K, Itasaka S, Yoshimura M, Tanimoto K, Torii M, Sowa T, Menju T, Sonobe M, Kakeya H, Toi M, Date H, Hammond EM, Hiraoka M, Harada H. UCHL1 provides novel diagnostic and antimetastatic strategies due to its deubiquitinating effect on HIF-1 α . *Nature Communications*. in press.

Following two papers were submitted to *Oncogene* and *Cancer Discovery* and are now under peer review (as of 12th Nov. 2014).

3. Olcina M, Senra J, Leszczynska K, Isa N, Harada H, Hammond EM. H3K9me3 facilitates hypoxia-induced p53-dependent apoptosis through repression of APAK. *Oncogene*. under review.
4. Yeom CJ, Zeng L, Goto Y, Morinibu A, Zhu Y, Shinomiya K, Kobayashi M, Itasaka S, Yoshimura M, Hur CG, Kakeya H, Hammond EM, Hiraoka M, Harada H. LY6E; a conductor of malignant tumor growth through modulation of the PTEN/PI3K/Akt/HIF-1 axis. *Cancer Discovery*. under review.

In addition to these publications, I gave following three talks in the Internal Seminar, Hammond's Lab Meeting, and Hypoxia Meeting during my visit in Oxford.

1. Hypoxia: importance in tumor biology & radiation oncology -What I have analyzed and what I plan

to analyze-. Hammond's Lab Meeting. 7th Apr. 2014.

2. HIF-1 as a Rational Target for Cancer Therapy. Internal Seminar Series 2014. 29th May 2014.
3. UCHL1 provides novel diagnostic and antimetastatic strategies due to its deubiquitinating effect on HIF-1alpha. Hypoxia Meeting 2014. 4th Jul 2014.

4. 渡航中の滞在経験

Oxford city is located approximately 100 km from London. It takes 50 min from Paddington station, London to Oxford Rail Station by train, and 100 min from Victoria Coach Station, London to Oxford City Centre (Gloicester Green Oxford Bus Station) by coach. Because of these convenient public transportation networks, Oxford city is recognized as one of the most popular city; and therefore, house rent is very expensive. Most young scientists share a house or flat with their friends to save money. Such a situation helps to foster sociability as well as skills for English conversation.

University of Oxford was established in the 11th centuries, and many historical buildings are still in use (Picture 3). The university does not have a main campus; instead, all the buildings and facilities are scattered throughout the center of Oxford city. When we visit the center of Oxford city, we can easily feel long history of UK. The population of Oxford city is about 140,000 and approximately 20% of them are students belonging to University of Oxford or Oxford Brookes University. That is why Oxford is called a university town.

Oxford was the best choice for me not only for research but also for expanding my view of the world. I would choose University of Oxford again if I got a chance to go abroad for my research in future (Picture 4).

At the end of this report, I would like to express my appreciation to the John Mung Advanced Program, Kyoto University and Professor Masahiro Hiraoka, Department of Radiation Oncology and Image applied Therapy, Kyoto University Graduate School of Medicine for giving me this great opportunity to visit University of Oxford.

※ご提出いただいた報告書は、電話番号、メールアドレスを除いて、「京都大学若手人材海外派遣事業 ジョン万プログラム」公式ホームページ（<http://www.john-man.rp.kyoto-u.ac.jp/researcher/index.html>）に掲載させていただきますので、あらかじめご了承ください。