MMCB 2014

The 22nd International Symposium on
Molecular Cell Biology of Macrophages

Macrophage in Maintenance of Tissue Homeostasis and Disease

Date June 2 (Mon) – 3 (Tue), 2014

Venue The Kobe Chamber of Commerce and Industry (Kobe CCI), Kobe, Japan

MMCB 2014

The 22nd International Symposium on
Molecular Cell Biology of Macrophages

Macrophage in Maintenance of Tissue Homeostasis and Disease

SECRETARIAT

MMCB2014 Office

Toshiyuki Tanaka, Ph.D.
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Welcome to MMCB2014 in Kobe

Dear Colleagues and Friends,

Welcome to 22nd International Symposium on Molecular Cell Biology of Macrophages (MMCB2014). This symposium is sponsored by The Japanese Society for Molecular Cell Biology of Macrophages, which was founded in 1991 by Professor Kouji Matsushima to promote basic and clinical research in the field of macrophage and dendritic cell biology. Since then, this symposium has been held each year, and made a significant contribution in creating attractive and interactive platform for both young and experienced scientists in this research field.

This year's symposium provides a 2-day scientific program with 22 invited lectures, including those by speakers from abroad, and poster presentations by the members of our society. The theme of the symposium is "Macrophages in Maintenance of Tissue Homeostasis and Disease", and the program puts a strong emphasis on the topics of "Development and Functions", "Innate Recognition and Metabolism", "Inflammation, Immunity and Disease" as well as "Tumor Microenvironment". I sincerely hope that all the participants from both abroad and Japan actively participate in the discussion, leading to develop international and interdisciplinary interactions as well as friendship.

Please enjoy MMCB2014 and have a wonderful time during your stay in Kobe.

June 2, 2014

Toshiyuki Tanaka
Conference Chairperson

Conference Chairperson:

Toshiyuki Tanaka
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Organizing Committee:

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The University of Tokyo
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Toshiaki Ohteki (Tokyo Medical and Dental University)
Norimitsu Kadowaki (Kyoto University)
Akihiro Matsukawa (Okayama University)
Kensuke Miyake (The University of Tokyo)
Shigeo Koyasu (RIKEN Center for Integrative Medical Sciences)
Motohiro Takeya (Kumamoto University)
Kenjiro Matsuno (Dokkyo Medical University)

General Information

Date: June 2 (Mon) - 3 (Tue), 2014

Venue: The Kobe Chamber of Commerce and Industry (Kobe CCI)
（神戸商工会議所・神商ホール）

Official Language: English

Home Page: http://www.huhs.ac.jp/studygroup/mmcb2014/

General Meeting: June 2 (Mon) 16:30 - 17:00（神戸商工会議所・神商ホール）

Poster Viewing: June 2 (Mon) 16:30 - 18:30（神戸商工会議所・第二会議室）

Get-together Party: June 2 (Mon) 18:30 - 20:30（クオリティホテル神戸･2階バレンシア）
Fee ¥3,000 (Student Fee ¥2,000)

Registration: June 2 (Mon): 8:30 - 18:30, June 3 (Tue): 8:30 - 16:30

Registration fee:

Member (before May 2)	¥5,000
Non-Member (before May 2)	¥7,000
Member (on-site)	¥7,000
Non-Member (on-site)	¥10,000
Student	¥3,000

来年度の開催予告

International Conference of Cancer Immunotherapy and Macrophages 2015

第23回マクロファージ分子細胞生物学国際シンポジウム
（MMCB2015）

（第19回日本がん免疫学会（JACI）学術集会との合同開催）

日　時：2015年7月9日（木）～11日（土）

会　場：伊藤国際学術研究センター 伊藤謝恩ホール
〒113-0033 東京都文京区本郷7-3-1
TEL：03-5841-0779　FAX：03-5841-0932
http://www.u-tokyo.ac.jp/ext01/iirc/index.html

当番幹事：順天堂大学　竹田 和由

Instructions for the Presentation

Oral Session (Invited Speakers)

An LCD projector will be provided. Please bring your own PC to make your presentation. The secretariat will prepare a Mini D-sub 15 pin PC cable connector. If your PC is not compatible with this cable connector, please bring an adaptor to connect your PC to the Mini D-sub 15 pin PC cable connector. In order to avoid technical problems, we ask you to kindly bring your PC to PC center at least 30 min prior to the session.

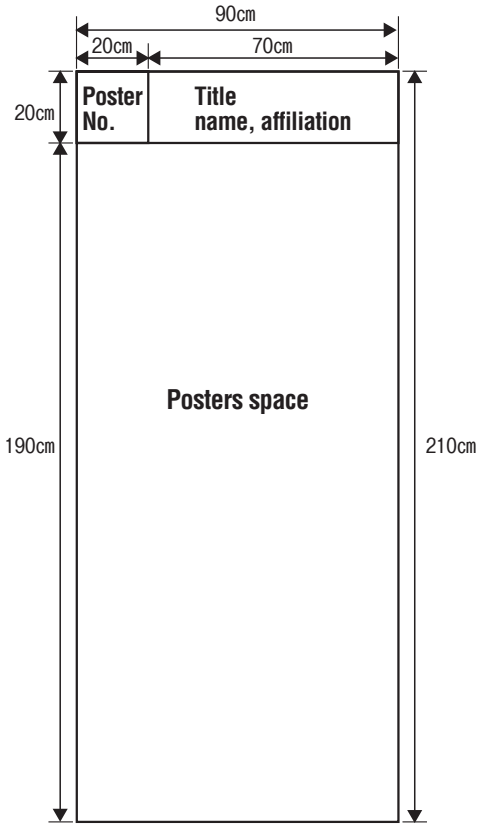
Poster Presentation

Poster will be presented in the poster room throughout the conference. The size of poster board is 90-cm in width and 210-cm in height. We will provide the poster numbers only. Please prepare the title of your poster yourself.

Poster set up: June 2, 2014 8:40 - 11:45

Poster removal: June 3, 2014 16:40 - 17:00

Each presenter should mount the poster on the designated board. Please use pushpin to affix your poster presentation on the board firmly. The secretariat will provide equipment and items required for affixing the posters. Any poster left after the scheduled removal time will be discarded by the secretariat.



Young Investigator Award

Young Investigator Award was established to encourage young investigators who have made significant contributions to this symposium. Candidates of this award are marked as "*" after each poster number. The committee will select three awardees from the first authors of the posters, who are graduate and undergraduate students or were awarded Ph.D. degree within five years. There will be voting by the invited speakers and members of the organizing committee, and posters getting the top three places will be selected.

Acknowledgement for Sponsorship（平成26年5月22日現在）

The organizing committee of MMCB2014 gratefully acknowledges the generous financial support of the following organizations.

GRANTS（助成金）

The Nakatomi Foundation（公益財団法人 中冨健康科学振興財団）

The Novartis Foundation (Japan) for Promotion of Science
（公益財団法人 ノバルティス科学振興財団）

The Tokyo Biochemical Research Foundation（公益財団法人 東京生化学研究会）

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Kobe Convention & Visitors Association（一般財団法人 神戸国際観光コンベンション協会）

Tsutomu Nakauchi Foundation（公益財団法人 中内力コンベンション振興財団）

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YOUNG INVESTIGATOR AWARDS（若手研究奨励賞）

BioLegend, Inc.（BioLegend Japan 株式会社）

Access Map

神戸商工会議所 〒650-8543 神戸市中央区港島中町6-1

The Kobe Chamber of Commerce and Industry (KOBE CCI)

6-1 Minatojima-nakamachi, Chuo-ku Kobe 650-8543, Japan

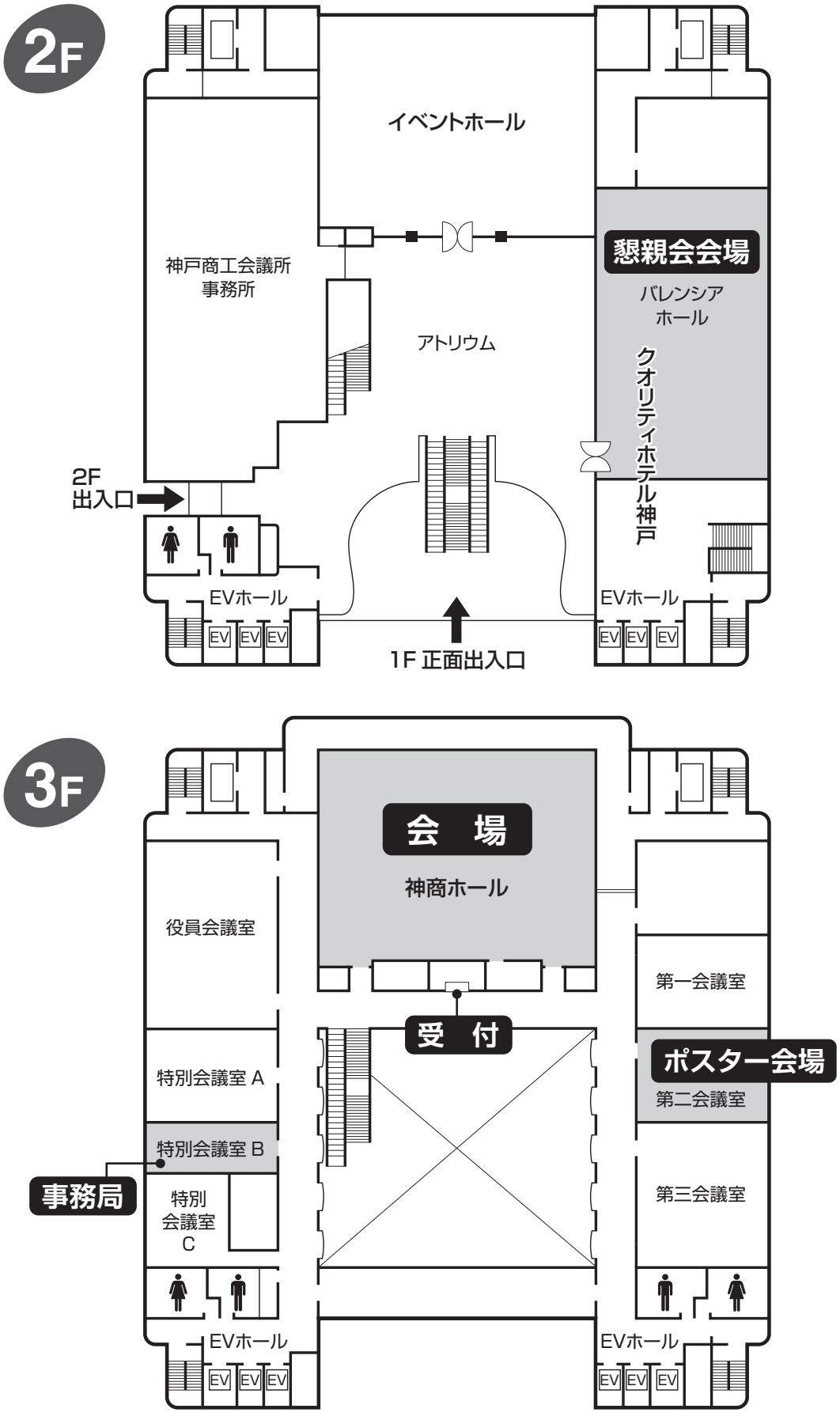
会場への交通

■ 三宮駅からポートライナーで
「みなとじま・キャンパス前駅」下車（約11分）、徒歩約5分

■ 新神戸駅から車で約15分

■ 神戸空港からポートライナーで
「みなとじま・キャンパス前駅」下車（約13分）、徒歩約5分

Venue Map


2F
イベントホール
神戸商工会議所
事務所
アトリウム
懇親会場
バレンシア
ホール
クオリティホテル神戸
2F
出入口
EVホール
EV EV EV
EVホール
EV EV EV
1F 正面出入口
3F
会　場
神商ホール
役員会議室
第一会議室
受　付
特別会議室 A
ポスター会場
第二会議室
特別会議室 B
事務局
特別
会議室
C
第三会議室
EVホール
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Program

June 2（Monday）

8:30- **Registration**

8:55-9:00 **Opening: Toshiyuki Tanaka** (Hyogo University of Health Sciences, Japan)

Session 1: Development and Functions (9:00-11:45)

Chairpersons: **Kenjiro Matsuno** (Dokkyo Medical University, Japan)
Katsuaki Sato (Miyazaki University, Japan)

9:00-9:30 **Tissue resident macrophages self-maintain locally throughout adult life with minimal contribution from circulating monocytes**
Daigo Hashimoto (Hokkaido University, Japan)

9:30-10:00 **Ontogeny of tissue-resident macrophages**
Florent Ginhoux (Singapore Immunology Network, Singapore)

10:00-10:30 **Plasmacytoid dendritic cell development**
Nobuyuki Onai (Tokyo Medical and Dental University, Japan)

10:30-10:45 **Coffee Break**

10:45-11:15 **Two sides of a coin: Intestinal macrophages and brain microglia**
Alexander Mildner (Weizmann Institute of Science, Israel)

11:15-11:45 **Macrophage self-renewal and lineage identity**
Michael Sieweke (Centre d'Immunologie de Marseille-Luminy, France)

Lunch Time Special Lecture 1 (12:00-13:00)

Chairperson: **Toshiyuki Tanaka** (Hyogo University of Health Sciences, Japan)

12:00-13:00 **Adjuvant recognition through C-type lectin receptors**
Sho Yamasaki (Kyushu University, Japan)

Session 2: Innate Recognition and Metabolism (13:30-16:15)

Chairpersons: **Osamu Takeuchi** (Kyoto University, Japan)
Satoshi Uematsu (Chiba University/ The University of Tokyo, Japan)

13:30-14:00 **Immunological functions of semaphorins and pathological implications of mitochondrial DNA**

Atsushi Kumanogoh (Osaka University, Japan)

14:00-14:30 **Understanding and manipulation of NLRP3-inflammasome**

Tatsuya Saitoh (Osaka University, Japan)

14:30-15:00 **Interplay between innate and adaptive immune system controls age-related inflammation**

Vishwa Deep Dixit (Yale School of Medicine, USA)

15:00-15:15 **Coffee Break**

15:15-15:45 **A novel scavenging system for biological garbage promoted by circulating AIM protein and its therapeutic application**

Toru Miyazaki (The University of Tokyo, Japan)

15:45-16:15 **Immune regulation of adipose tissue**

Anthony W. Ferrante Jr. (Columbia University, USA)

16:30- **General Meeting (MMCB)**
Poster Presentation & Poster Viewing

18:30- **Get-together Party (Quality Hotel Kobe, Room: Valencia/2F)**

8:30- **Registration**

Session 3: Inflammation, Immunity and Disease (9:00-11:45)

Chairpersons: **Toshiaki Ohteki** (Tokyo Medical and Dental University, Japan)
Akihiro Matsukawa (Okayama University, Japan)

9:00-9:30 **Activation of spinal microglia causing neuropathic pain**
Kazuhide Inoue (Kyushu University, Japan)

9:30-10:00 **Hematopoiesis and programmed cell removal**
- Self-Recognition system mediated through CD47-SIRPA interaction -
Katsuto Takenaka (Kyushu University, Japan)

10:00-10:30 **Perivascular leukocyte cluster formation via perivascular macrophages is required for optimal elicitation of contact hypersensitivity**
Kenji Kabashima (Kyoto University, Japan)

10:30-10:45 **Coffee Break**

10:45-11:15 **Intravital imaging analysis of different macrophages, bone-destroying osteoclasts and inflammatory macrophages in obese adipose tissues**
Masaru Ishii (Osaka University, Japan)

11:15-11:45 **Studying monocytes and Kupffer cells in infection and sterile injury**
Paul Kubes (University of Calgary, Canada)

Lunch Time Special Lecture 2 (12:00-13:00)

Chairperson: Kazuyoshi Takeda (Juntendo University, Japan)

12:00-13:00 **Immune modulation by the gut microbiota**
Kenya Honda (RIKEN IMS, Japan)

Session 4: Tumor Microenvironment (13:30-16:15)

Chairpersons: **Naofumi Mukaida** (Kanazawa University, Japan)
Norimitsu Kadowaki (Kyoto University, Japan)

13:30-14:00 **Chronic inflammatory responses in gastrointestinal cancer development**
Masanobu Oshima (Kanazawa University, Japan)

14:00-14:30 **Distinct macrophage subsets in the tumor microenvironment and in non-cancerous tissues**
Jo A. Van Ginderachter (VIB-Vrije Universiteit Brussels, Belgium)

14:30-15:00 **Significance of macrophage infiltration in human malignancies**
Motohiro Takeya (Kumamoto University, Japan)

15:00-15:15 **Coffee Break**

15:15-15:45 **Gut microbiota control responses of innate immune cells to anti-cancer therapies**
Noriho Iida (Kanazawa University, Japan)

15:45-16:15 **Development of a novel type of cancer vaccine linking innate and adaptive immunity**
Shin-ichiro Fujii (RIKEN IMS, Japan)

16:15- **Award Ceremony**

Closing: Kouji Matsushima (The University of Tokyo, Japan)

Session 1: Development and Functions

Chairpersons: **Kenjiro Matsuno** (Dokkyo Medical University, Japan)
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Alexander Mildner (Weizmann Institute of Science, Israel)
Michael Sieweke (Centre d'Immunologie de Marseille-Luminy, France)

S1-1 Tissue resident macrophages self-maintain locally throughout adult life with minimal contribution from circulating monocytes

Daigo Hashimoto
Department of Hematology, Hokkaido University Graduate School of Medicine, Sapporo, Japan

Recently, accumulating evidences suggest local self-maintenance of tissue macrophages in the steady state. Using hematopoietic stem cell fate mapping system, we found that tissue resident macrophages in the lung, spleen, peritoneal lavage, brain, and bone marrow differentiated, at least, partially independently of bone marrow hematopoietic stem cells. Next we examined if these tissue resident macrophages self-maintain locally independently of circulating monocytes. In parabiosis experiments, B6-*Ccr2*$^{-/-}$ mouse and B6-CD45.1^{+} mouse were sutured side by side to form a shared circulatory system. Although 75~90% of circulating monocytes in the *Ccr2*$^{-/-}$ parabiont derived from the WT parabiont, tissue resident macrophages remained of host origin for more than a year. Similarly, we found that after depletion of macrophages, the majority of repopulation occurs by enhanced local proliferation. This repopulation from a non-circulating population was observed after cytoablation and infection-induced cell death of local macrophages. We also found that after bone marrow transplantation, host tissue macrophages retain the capacity to expand without any contribution from donor circulating cells. The rate of host macrophage-expansion was slow, but these cells were functional and prevented the development of alveolar proteinosis in mice transplanted with Csf-2 receptor-deficient bone marrow cells. Collectively, these results indicate that tissue resident macrophages and circulating monocytes should be classified as independent mononuclear phagocyte lineages.

Next, we focused on macrophages in the gut. Unlike other tissue resident macrophages, gut macrophages are quickly replaced by circulating precursors in parabiotic mice. Interestingly, these macrophages produce IL-1β in the response to MyD88-dependent sensing of gut microflora. IL-1β from macrophages stimulates CSF-2 production from innate lymphoid cells. CSF-2 from innate lymphoid cells, in turn, stimulates gut dendritic cells and macrophages to produce IL-10 and retinoic acid, maintaining the regulatory T cells in the gut.

In conclusion, tissue resident macrophages self maintained locally independently of circulating precursors with the exception of gut macrophages. Tissue resident macrophages play critical roles in the maintenance of tissue homeostasis. In particular, the reciprocal interaction between gut macrophages and innate lymphoid cells is critical to maintain regulatory T cells in the gut and induce oral tolerance.

P-30 MafB promotes atherosclerosis by inhibiting foam-cell apoptosis

Michito Hamada[1)], Megumi Nakamura[1)], Mai Thi Nhu Tran[1)], Satoko Arai[2)], Takashi Kudo[1)], Hitoshi Shimano[3)], Toru Miyazaki[2)], Peter Tontonoz[4)] and Satoru Takahashi[1)]

1) Anatomy and Embryology, Faculty of Medicine, University of Tsukuba
2) Division of Molecular Biomedicine for Pathogenesis, Faculty of Medicine, University of Tokyo
3) Department of Internal Medicine (Endocrinology and Metabolism), University of Tsukuba
4) Department of Pathology and Laboratory Medicine, Howard Hughes Medical Institute, University of California

MafB is a transcription factor that induces myelomonocytic differentiation. However, the precise role of MafB in the pathogenic function of macrophages has never been clarified. Here we demonstrate that MafB promotes hyperlipidemic atherosclerosis by suppressing foam-cell apoptosis. Our data show that MafB is predominantly expressed in foam cells found within atherosclerotic lesions, where MafB mediates the oxidized LDL-activated LXR/RXR-induced expression of apoptosis inhibitor of macrophages (AIM). In the absence of MafB, activated LXR/RXR fails to induce the expression of AIM, a protein that is normally responsible for protecting macrophages from apoptosis; thus, Mafb-deficient macrophages are prone to apoptosis. Haematopoietic reconstitution with Mafb-deficient fetal liver cells in recipient LDL receptor-deficient hyperlipidemic mice revealed accelerated foam-cell apoptosis, which subsequently led to the attenuation of the early atherogenic lesion. These findings represent the first evidence that the macrophage-affiliated MafB transcription factor participates in the acceleration of atherogenesis.

P-31 Lysosomal oligopeptide transporter SLC15A4 is critical for TLR7/9-mediated inflammatory responses

Toshihiko Kobayashi[1)], Tadashi Okamura[2)] and
Noriko Toyama-Sorimachi[1)]

1) Department of Molecular Immunology and Inflammation, Research Institute, National Center for Global Health and Medicine
2) Department of Infectious Diseases, Research Institute, National Center for Global Health and Medicine

The endolysosome plays pivotal roles as signaling platforms in ligand recognition and the subsequent signaling of TLR7, or TLR9. However, the precise molecular mechanism by which signaling events at the endosomal/lysosomal compartments are regulated in the course of inflammatory responses is not fully understood.

Solute Carrier family (SLC) 15A4 is a lysosomal resident proton-coupled oligopeptide transporter highly expressed in plamacytoid dendritic cells, macrophages and B cells, and carries histidine and oligopeptides from inside the lysosome to the cytosol. We have previously reported that SLC15A4 is necessary for TLR7- and TLR9-dependent cytokine productions and responsible for Tri-DAP transfer to the cytosolic NOD1. Importantly, SLC15A4 is involved in the pathogenesis of diseases of colitis, viral infection, and lupus-like autoimmunity. How SLC15A4 contributes to diseases or molecular bases of SLC15A4-dependent TLR7/9 signaling is however largely unknown.

We investigated SLC15A4's function at the lysosomes using SLC15A4 deficient mice. SLC15A4 deficiency cased a change of amino acid components in the lysosome-rich vesicular fraction. In addition, SLC15A4-/- dendritic cells showed disturbance of lysosomal pH regulation upon TLR7 stimulation. These results suggest that SLC15A4-dependent movement of amino acids/protons is crucial for regulating lysosomal functions. To investigate whether the transporter activity of SLC15A4 is actually required for TLR7/9 functions, we established a SLC15A4 mutant lacking the transporter activity, and showed that the transporter activity is required for TLR7/9-dependent cytokine productions including IFNβ, IL-12, IL-6 and TNFα. Furthermore, we found that SLC15A4's function is also important for signaling downstream of IFNAR which is essential for the establishment of the IFN-I-IRF7 circuit.

Our finding suggested that SLC15A4 plays a crucial role for conditioning the endolysosomal environments to efficiently transmit TLRs- or IFNAR-triggered signals at the lysosomes.

P-32 A crucial role for chemokine receptor-interacting molecule, FROUNT, in macrophage migration and tumor metastasis

Yuya Terashima, Etsuko Toda and Kouji Matsushima

Department of Molecular Preventive Medicine, Graduate School of Medicine, the University of Tokyo, Tokyo, Japan.

Japan Science and Technology Agency, Project for Development of Innovative Research on Cancer Therapeutics (P-Direct), Tokyo, Japan.

Chemokine receptors CCR2 and CCR5-mediated migration of monocytes/macrophages into the tumor site enhances tumor growth and metastasis. However, the intracellular signaling mechanisms of monocytes/macrophages migration remain largely unexplored. We identified an intracellular modulator, named FROUNT, which interacts with chemokine receptor CCR2 (Nature Immunology 2005). FROUNT functions as a protein hub which regulates cell migration signals via CCR2 and another chemokine receptor CCR5 (Journal of Immunology 2009 & Biochemical Journal 2014).

To assess the role of FROUNT in the tumor microenvironment, we generated FROUNT conditional knockout mouse (FROUNT-cKO). FROUNT deficient monocytes/macrophages poorly migrated in vitro. FROUNT deficiency impaired the formation of metastatic foci in experimental metastasis models. Although the number of major leukocyte subsets was not altered in control and FROUNT-cKO, the number of macrophages accumulated in the metastatic foci was decreased in FROUNT-cKO.

These results indicate the potent role of FROUNT in macrophage migration and tumor metastasis.

MMCB2014

Secretariat: **MMCB2014 Office**
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Macrophages 2014

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