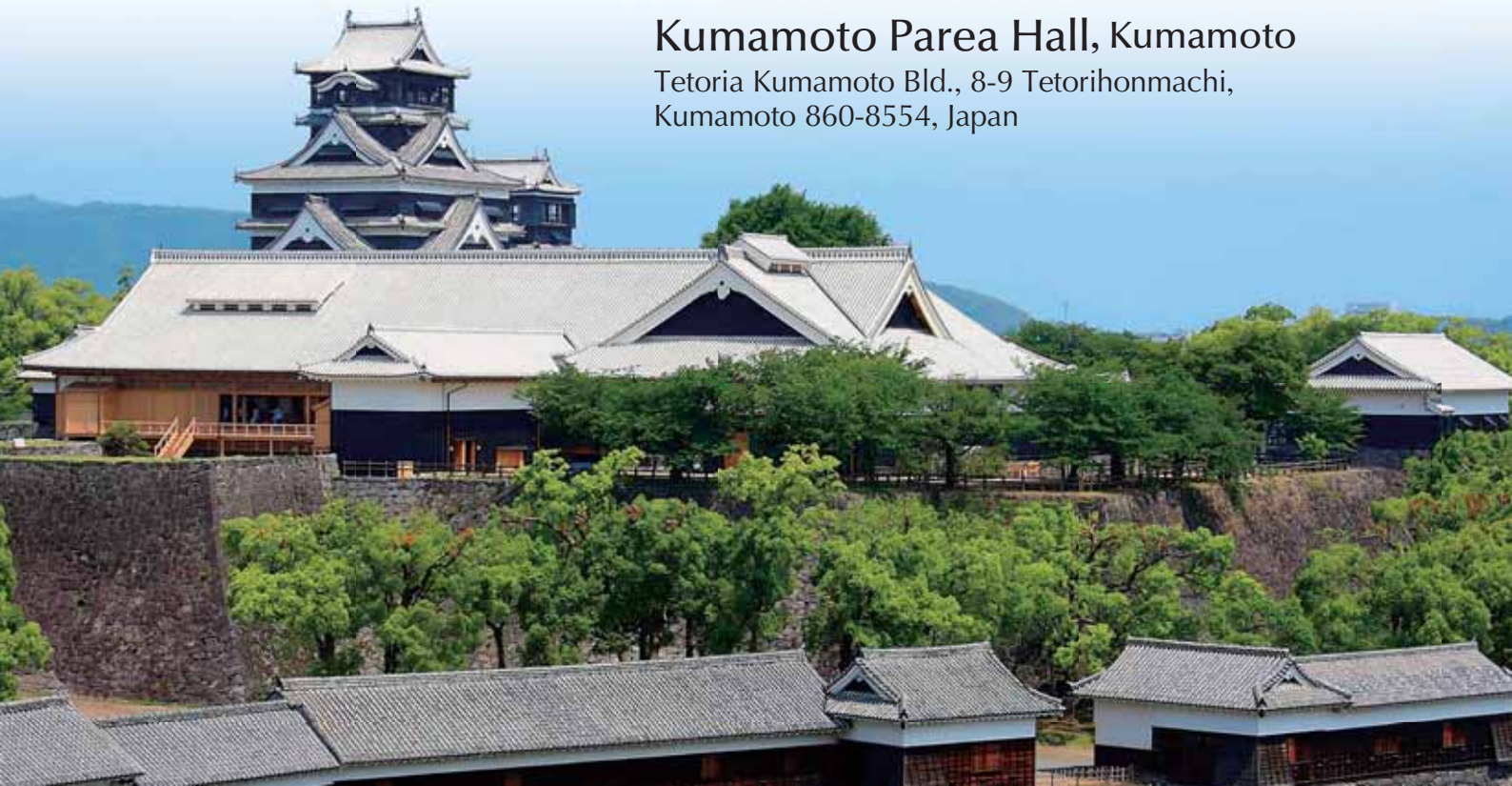
18th International Symposium on Molecular Cell Biology of MACROPHAGES 2010

Macrophage Activation and Disease Process

May 20–21, 2010

Kumamoto Parea Hall, Kumamoto

Tetoria Kumamoto Bld., 8-9 Tetorihonmachi,
Kumamoto 860-8554, Japan



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Sponsored by

The Japanese Society for Molecular Cell Biology of Macrophages

◆

Secretariate

Department of Cell Pathology,
Graduate School of Medical Sciences,
Kumamoto University

Welcome to Kumamoto

It is my great pleasure to invite you to join the 18th International Symposium on Molecular Cell Biology of Macrophages 2010. This Symposium is sponsored by The Japanese Society for Molecular Cell Biology of Macrophages which was founded in 1991 by Professor Kouji Matsushima with its aim to promote the basic science as well as the clinical research in the field of macrophage/dendritic cell research. The symposium has been held annually and made a large contribution to the world-wide advance of this research field.

This year's symposium will last two full days including lectures by 18 invited speakers from United States, The Netherlands, Italy, Korea and Japan, and poster presentations by society members. The main theme of the Symposium is "Macrophage Activation and Disease Process". Special emphasis will be given to the following four topics: "Regulation of Inflammation", "Innate Immune Recognition", "Macrophage-related molecules and Diseases", and "Tumor Microenvironment". It is our intention to enable all participants from abroad and Japan to create international and interdisciplinary interactions as well as friendship.

Kumamoto City is located in the center of Kyushu Island and is the prefectural capital of Kumamoto Prefecture. It has a long history and is known a "City of Forests" since it is blessed with an abundance of nature. When seeing the sights of Kumamoto, the historical 400-year old Kumamoto Castle and Kumamoto's classic Japanese style garden known as Suizenji Park will surely fascinate you. It is my hope and belief that you will enjoy the symposium and have a wonderful stay in Kumamoto !

May 20, 2010

Motohiro Takeya

Conference Chairperson

Conference Chairperson:

Motohiro Takeya
Department of Cell Pathology
Faculty of Life Sciences, Kumamoto University
1-1-1 Honjo, Kumamoto, 860-8556, Japan
TEL:+81-96-373-5095 FAX:+81-96-373-5096
E-mail: takeya@kumamoto-u.ac.jp

Organizing Committee:

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President, Japanese Society of Molecular Cell Biology of Macrophages
The University of Tokyo
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FAX: +81-3-5684-2297
E-mail: Koujim@m.u-tokyo.ac.jp

Osamu Yoshie (Kinki University)
Yasuyuki Imai (University of Shizuoka)
Yoshiro Kobayashi (Toho University)
Kensuke Miyake (The University of Tokyo)
Shigeo Koyasu (Keio University)
Makoto Naito (Niigata University)
Kenjiro Matsuno (Dokkyo Medical University)
Naofumi Mukaida (Kanazawa University)

General Information

Date: May 20（Thu）to May 21（Fri）, 2010

Venue: Kumamoto Parea 9F, 10F（テトリアくまもとビル9階・10階）

Official Language: English

Home Page: http://secand.co.jp/macrophages/index.html

Get-Together Party（Fee JPY 2,000）

Date and Time: May 20（Thu） 18:30－20:30

Place: Restaurant "SAI", City Hall 14F（See Access Map）
（カフェレストラン「彩」熊本市役所14階 地図参照）

Registration

Place: In front of Parea Hall（10F）

Opening Hour: May 20：9:00－17:00, May 21：9:00－16:40

Registration fee

Member（Before Apr 30）	JPY 5,000
Member（After May 1 or On site）	JPY 7,000
Non-member	JPY 10,000
Student	JPY 3,000

来年度の開催予告

第19回マクロファージ分子細胞生物学国際シンポジウム

（第76回日本インターフェロン・サイトカイン学会学術集会との合同開催）

日　時：2011年5月25日（水）、26日（木）、27日（金）

会　場：全日空ゲートタワーホテル大阪（大阪府泉佐野市）
〒598－8511 大阪府泉佐野市りんくう往来北1番地
TEL：072－460－1111　Fax:072－460－1177

当番幹事（学術集会長）：近畿大学医学部細菌学　義江　修

Instructions for Speakers

Oral Session (Invited speakers)

An LCD projector will be provided. Please bring your Power Point file on a Windows readable USB memory stick or CD-ROM. Macintosh users or speakers using movie files should bring your own computers. In order to avoid technical problems, we ask you to kindly bring your Power Point Presentation to the PC center (10F) at least 30 min prior to the session.

Short oral presentation for Young Investigator Award

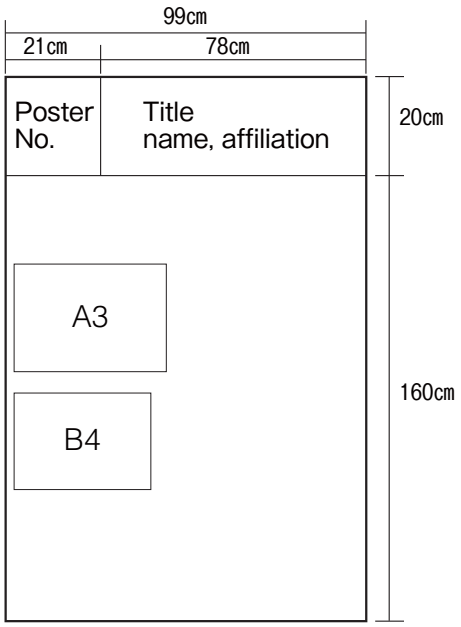
Young Investigator Award was established to encourage young investigators who have made significant contributions to this symposium. The committee will select two awardees from the first authors of the posters, who are graduated students or were awarded PhD degree within five years. The person eligible for this award will send the PDF (Power Point) file summarizing his/her paper in two pages to the Conference Chairperson by e-mail (cellpath@kumamoto-u.ac.jp) by May 14 and will present his/her paper with this slide in two minute in Session 3 in the evening of May 20. The awardees are kindly asked to make a short oral presentation of their accomplishment shown in their posters (10 min talk). The organizing committee asks the persons eligible for this award to bring a Power Point file (USB memory or CD-ROM) for oral presentation. Awardees of the first and the second place will receive a certificate and prize money (JPY 100,000 and JPY 50,000, respectively).

Poster Session

Poster session will be held in Room 1 (9F). (9階 第1会議室)

Poster Set Up	May 20 (Thu)	9:00-12:00
Poster Session	May 20 (Thu)	17:10-18:10
Poster Removal	May 21 (Fri)	16:40-17:00

The size of the poster board is 99-cm wide and 160-cm high. We will provide the poster numbers only. Please prepare the title (including names and affiliations of authors) of the poster by yourself. Mounting media will be available in the room.



Acknowledgments

This symposium is partly supprted by a Good Practice（GP）program “Advanced Medical Education Program” and a Kumamoto University Core Research Project B “Center for Frontier Research on Life Style and Stress Signal”.

The organizers sincerely appreciate the generous support and participation for 18th International Symposium on Molecular Cell Biology of Macrophages 2010 by the following foundations and groups.

第18回マクロファージ分子細胞生物学国際シンポジウムの開催に際して、日本学術振興会 組織的な大学院教育改革推進プログラム「臨床・基礎・社会医学一体型先端教育の実践」ならびに熊本大学拠点形成研究Ｂ「ライフスタイルとストレスシグナルの先端研究拠点」の補助を受けています。

また、本シンポジウムの開催に対し、以下の財団および団体からご援助、ご寄付を戴いております。ここに厚く御礼申し上げます。

SPONSORS AND CONTRIBUTORS

（2010年4月12日現在）

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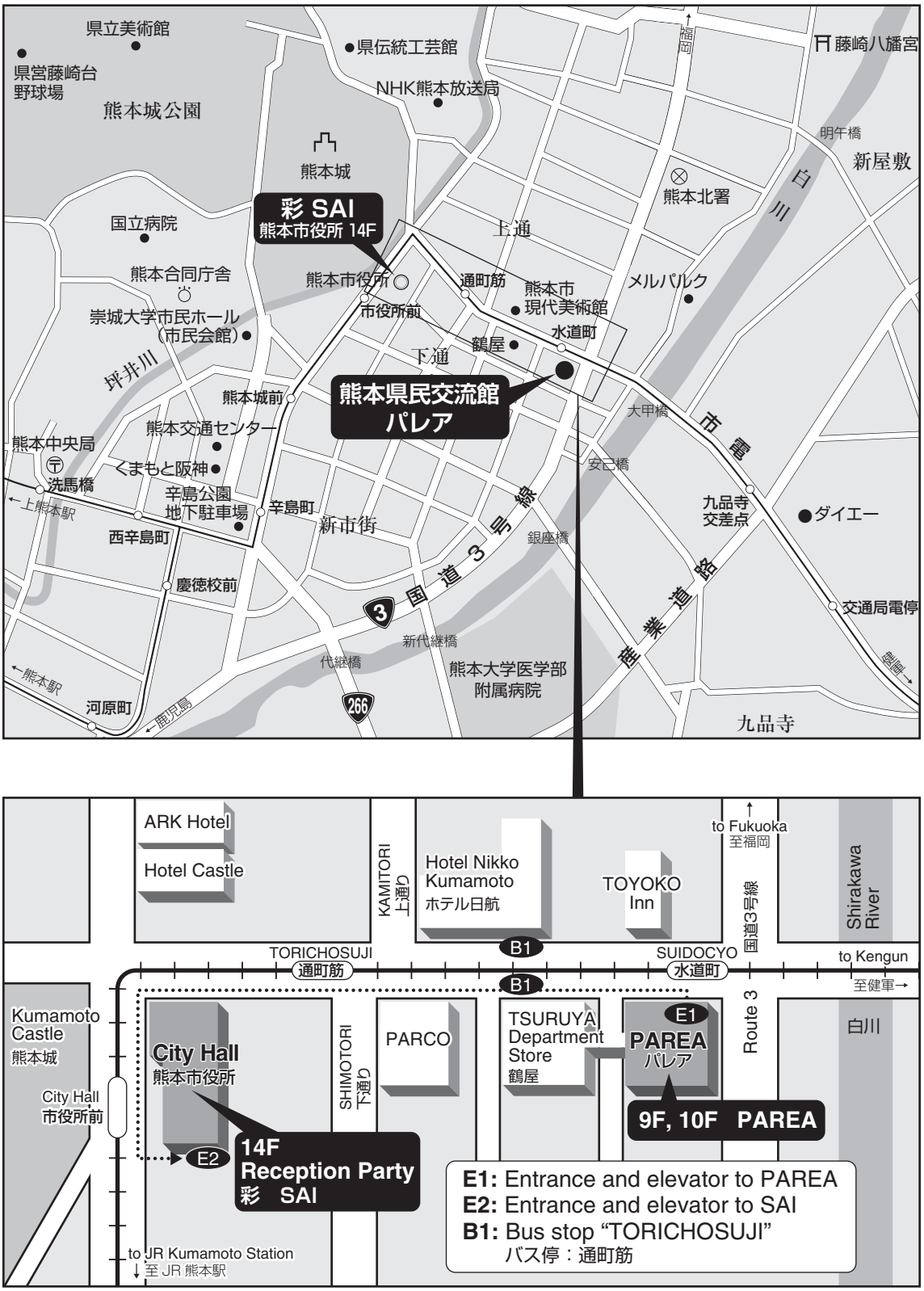
熊本大学細胞病理学分野同門会

Almuni Association of Department of Cell Pathology, Kumamoto University

Access Map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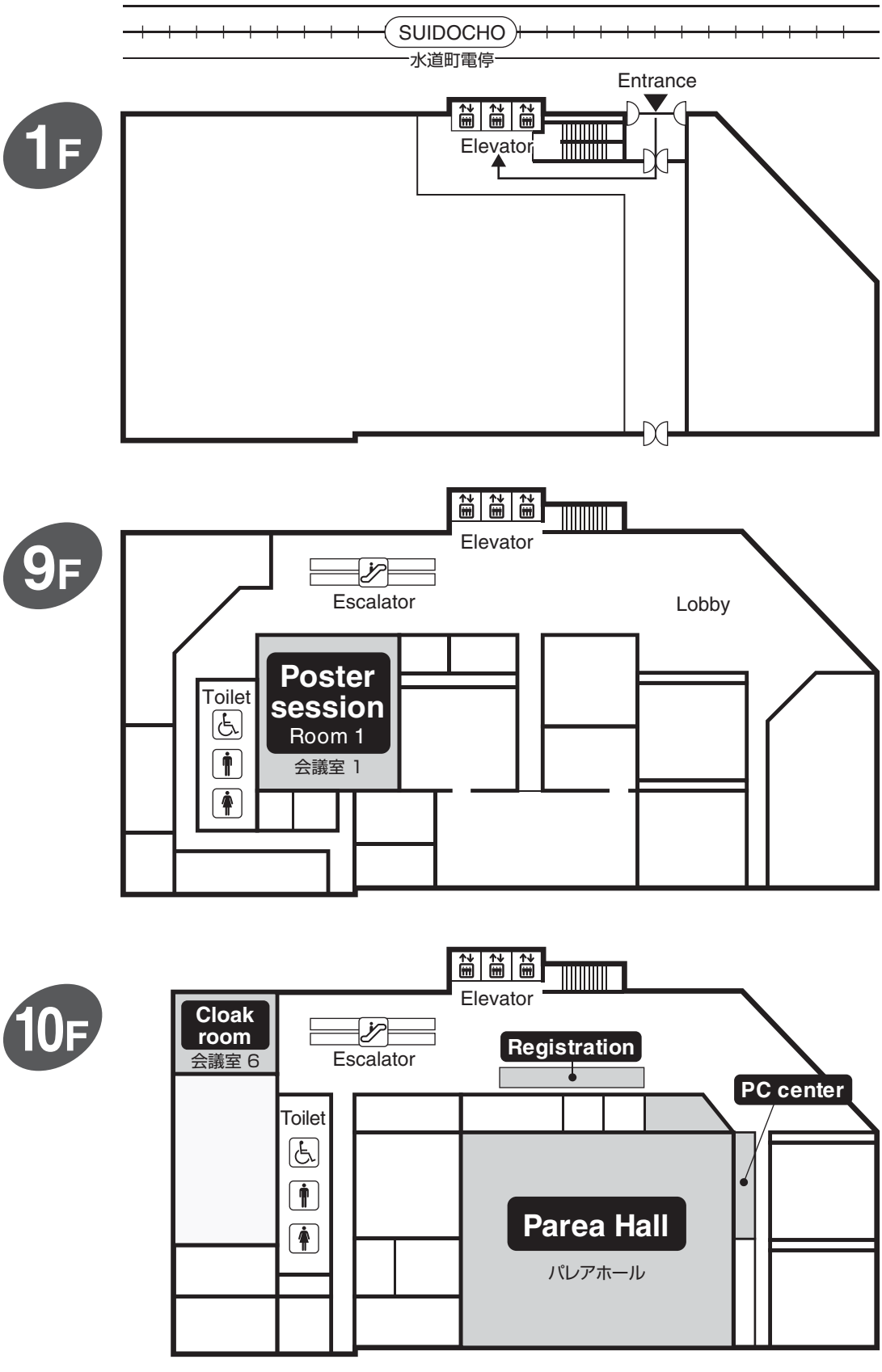
九品寺
ARK Hotel
Hotel Castle
KAMITORI 上通り
Hotel Nikko Kumamoto ホテル日航
TOYOKO Inn
to Fukuoka 至福岡
国道3号線
Shirakawa River
TORICHOSUJI 通町筋
B1
SUIDOCYO 水道町
to Kengun 至健軍
Kumamoto Castle 熊本城
City Hall 熊本市役所
City Hall 市役所前
SHIMOTORI 下通り
PARCO
TSURUYA Department Store 鶴屋
E1
PAREA パレア
Route 3
白川
9F, 10F PAREA
E2
14F Reception Party 彩 SAI
E1: Entrance and elevator to PAREA
E2: Entrance and elevator to SAI
B1: Bus stop “TORICHOSUJI”
バス停：通町筋
to JR Kumamoto Station 至 JR 熊本駅

Kumamoto Parea

（熊本県民交流館パレア）



Program

May 20 (Thursday)

9:00- Registration

9:25-9:30 Opening Address (**Motohiro Takeya**)

Session 1: Regulation of Inflammation

Chairpersons: Osamu Yoshie (Kinki University)
Yoshiro Kobayashi (Toho University)

9:30-10:00 Evaluating the role of macrophage as a source of the chemokine MCP-1/CCL2 during the inflammatory responses.
Teizo Yoshimura (National Cancer Institute Frederick, USA)

10:00-10:40 Regulation of M-CSF receptor expression by mononuclear phagocytes in inflammation.
Pieter JM Leenen (Erasmus Medical Center, Netherland)

10:40-10:55 Coffee Break

10:55-11:25 Spred-2, a negative regulator of MAP kinase cascade, controls inflammatory responses.
Akihiro Matsukawa (Okayama University, Japan)

11:25-12:05 Role of macrophages and T lymphocytes in inflammatory lymphangiogenesis.
Gou Young Koh (Advanced Institute of Science and Technology, KAIST, Korea)

12:05-13:20 Lunch and Poster Viewing

Session2: Innate Immune Recognition

Chairpersons: Tatsuro Irimura (The University of Tokyo)
Norimitsu Kadowaki (Kyoto University)

13:20-13:50 Innate inflammation by Th2 cytokines derived from "Natural Helper" cell.
Shigeo Koyasu (Keio University School of Medicine, Japan)

13:50-14:15 Distribution and immunological implications of MGL2.
Kaori Denda-Nagai (Graduate School of Pharmaceutical Sciences, The University of Tokyo, Japan)

14:15-14:40 Hierarchical nucleic acid sensing system for innate immune responses.
Hideyuki Yanai (Graduate School of Medicine, The University of Tokyo, Japan)

14:40-15:20 Redox remodeling controls innate immunity.
Anna Rubartelli (Istituto Nazionale per la Ricerca sul Cancro, Italy)

15:20-15:35 Coffee Break

15:35-16:15 Self and non-self recognition through C-type lectin receptors.
Sho Yamasaki (Research Center for Infection Network, Kyushu University)

16:20-16:50 **Session 3: Short poster presentation**

Chairperson: Naomi Sakashita (Kumamoto University)

16:50-17:10 Business Meeting

17:10-18:10 Poster Viewing and Discussion

18:30-20:30 Get-Together Party

May 21 (Friday)

9:00- Registration

Session 4: Macrophage-related molecules and Diseases

Chairpersons: Kenjiro Matsuno (Dokkyo University)
Akihiro Matsukawa (Okayama University)

9:20-9:50 Different activity and downstream signaling of IL-34 and M-CSF, which share the receptor Fms.
Shinya Suzu (Center for AIDS Research, Kumamoto University)

9:50-10:20 Galectin-9 beneficially modulates macrophage functions in inflammation and cancer.
Mitsuomi Hirashima (Faculty of Medicine, Kagawa University)

10:20-10:35 Coffee Break

10:35-11:15 The ACAT1 enzyme and its pathophysiological roles in atherosclerosis and Alzheimer disease.
Ta-Yuan Chang (Dartmouth Medical School, USA)

11:15-11:45 Roles of Angiopoietin-like protein2 in inflammation and its-related diseases.
Yuichi Oike (Graduate School of Medical Sciences, Kumamoto University)

11:45-12:15 **Session 5: Young Investigator Award Presentation**

Chairpersons: Kouji Matsushima (The University of Tokyo)
Motohiro Takeya (Kumamoto University)

12:15-13:30 Lunch and Poster Viewing

Session 6: Tumor Microenvironments

Chairpersons: Teizo Yoshimura (National Cancer Institute Frederick, USA)
Motohiro Takeya (Kumamoto University)

13:30-13:55 Significance of M2 macrophage infiltration in malignant tumors.
Yoshihiro Komohara (Kumamoto University)

13:55-14:20 Dynamics of $CCR7^{+}$ tumor-infiltrating dendritic cells that regulate anti-tumor immune responses.
Satoshi Ueha (Graduate School of Medicine, The University of Tokyo)

14:20-15:00 S100 proteins and the tumor microenvironment.
Geetha Srikrishna (The Burnham Institute for Medical Research, USA)

15:00-15:15 Coffee Break

15:15-15:55 Macrophage polarization in tumour development.
Antonio Sica (Istituto Clinico Humanitas, Italy)

15:55-16:35 Macrophage Diversity Promotes Tumor Progression and Metastasis.
Jeffrey W Pollard (Albert Einstein College of Medicine, USA)

16:35- Closing Remarks
Kouji Matsushima (The University of Tokyo)

Poster Session

(*Candidates for Young Investigator Award)

P1* Suppression of TLR4-mediated inflammatory response by macrophage class A scavenger receptor (CD204).

Koji Ohnishi[1,2], Yoshihiro Komohara[1], Yukio Fujiwara[1], Kenichi Takemura[1], XiaoFeng Lei[1,3], Naomi Sakashita[1], and Motohiro Takeya[1]

[1]Department of Cell Pathology, Graduate School of Medical Sciences, Faculty of Life Sciences, Kumamoto University; [2]Department of Surgical Pathology, Kumamoto University Hospital, Kumamoto; [3]Department of Biochemistry, Showa University School of Medicine, Tokyo, Japan

P2 Apoptosis of macrophages by N-Arachidonyl Glycine is mediated by GPR18.

Rina Takenouchi, Kazuhiko Inoue, Atsuro Miyata

Department of Pharmacology, Graduate School of Medical and Dental Sciences, Kagoshima University

P3 EP2 and EP4 receptors on muscularis resident macrophages mediate LPS-induced intestinal dysmotility via iNOS upregulation through cAMP/ERK signals.

Masatoshi Hori[1], Tsuyoshi Tajima[1,2], Takahisa Murata[1], Kosuke Aritake[3], Yoshihiro Urade[3], Toshiyuki Matsuoka[4], Syu Narumiya[4], and Hiroshi Ozaki[1]

[1]Department of Veterinary Pharmacology, Graduate School of Agriculture and Life Sciences, The University of Tokyo, Tokyo, Japan, [2]Laboratory of Veterinary Pharmacology, Nippon Veterinary and Life Science University, Tokyo, Japan, [3]Department of Molecular Behavioral Biology, Osaka Bioscience Institute, Osaka, Japan, [4]Department of Pharmacology, Graduate School of Medicine, Kyoto University, Kyoto, Japan

P4 Overexpression of Wiskott-Aldrich syndrome protein (WASP) N-terminal domain inhibits inflammatory responses in LPS-activated macrophages.

Chisato Sakuma[1,2], Mitsuru Sato[1], Joe Chiba[2], Hiroshi Kitani[1]

[1]Transgenic Animal Research Center, National Institute of Agrobiological Science, [2]Department of Biological Science and Technology, Graduate school of Faculty of Industrial Science and Technology, Tokyo University of Science

P5 Silica and alum induce type 2 immunity via inflammasome-independent mechanisms.

Etsushi Kuroda[1], Ken J Ishii[2,3] and Yasuo Morimoto[4]

[1]Department of Immunology and Parasitology and [4]Department of Occupational Pneumology, University of Occupational and Environmental Health, Japan, [2]Department of Molecular Protozoology, Research Institute for Microbial Diseases, Osaka University, Japan, [3]Laboratory of Host Defense, WPI Immunology Frontier Research Center, Osaka University, Japan

P6 Mint3 enhances the activity of HIF-1 in macrophages by suppressing the activity of FIH-1.

Takeharu Sakamoto and Motoharu Seiki

Department of Cancer Cell Research, Institute of Medical Science, The University of Tokyo

P7* Spermine involved methylation status on ITGAL promoter possibly regulates the expression of LFA-1.

Yoshihiko Kano, Kuniyasu Soda, and Fumio Konishi

Department of Surgery, Saitama Medical Center, Jichi Medical University

P8 Tim-3 mediates phagocytosis of apoptotic cells by inflammatory macrophage and $CD8^+$ dendritic cell subsets.

Kazuyoshi Takeda[1], Masafumi Nakayama[1,2], Hisaya Akiba[1], Yuko Kojima[3], Hideo Yagita[1], Koetsu Ogasawara[2], and Ko Okumura[1]

[1]Department of Immunology and [2]Division of Biomedical Imaging Research, Biomedical Research Center, Juntendo University School of Medicine, [3]Department of Immunobiology, Institute of Development, Aging and Cancer, Tohoku University

P9 M-CSF-dependent red pulp macrophages regulate CD4 T cell responses.

Daisuke Kurotaki[1,2], Kyeonghwa Bae[2], Toshimitsu Uede[1,2], and Junko Morimoto[2]

Division of [1]Matrix Medicine and [2]Molecular Immunology, Institute for Genetic Medicine, Hokkaido University

P10 Rheumatoid arthritis patient-derived synoviocytes are more sensitive to cigarette smoke condensate extracts-induced IL-1 beta expression through NF-kB activation than OA patient-derived synoviocytes, human lung fibroblasts and human lung epithelial cells.

K. Onozaki[1], S. Okamoto[1], M. Yokoyama[1], T. Arakawa[1], M. Adachi[1], K. Yamada[1], K. Akita[1], S. Itoh[1], T. Takii[1], Y. Waguri-Nagaya[2], T. Otsuka[2] and K. Hayakawa[3]

[1]Graduate School of Pharmaceutical Sciences, [2]Graduate School of Medical Sciences, Nagoya City University, [3]Kanazawa University

P11 Absence of IFN-γ accelerates thrombus resolution through enhanced MMP-9 and VEGF expression.

Mizuho Nosaka[1], Yuko Ishida[1], Akihiko Kimura[1], Yumi Kuninaka[1], Naofumi Mukaida[2], and Toshikazu Kondo[1]

[1]Department of Forensic Medicine, Wakayama Medical University, Wakayama, Japan, [2]Division of Molecular Bioregulation, Cancer Research Institute, Kanazawa University, Kanazawa, Japan

P12 CCR7-independent trafficking of skin antigens to regional lymph nodes by cells in the dermis.

Miya Yoshino, Kazuki Okuyama, Akihiko Murata, Yuki Egawa, Atsuko Sawada, Shin-Ichi Hayashi

Division of Immunology, Department of Molecular and Cellular Biology, School of Life Science, Faculty of Medicine, Tottori University

P13 A proteasome inhibitor bortezomib suppresses immunostimulatory activity of human plasmacytoid dendritic cells by targeting intracellular trafficking of nucleic acid-sensing Toll-like receptors and endoplasmic reticulum homeostasis.

Makiko Hirai[1], Norimitsu Kadowaki[2], Toshio Kitawaki[2], Haruyuki Fujita[2], Akifumi Takaori-Kondo[2], Ryutaro Fukui[3], Kensuke Miyake[3], Takahiro Maeda[4], Shimeru Kamihira[5], Yoshiki Miyachi[1], Takashi Uchiyama[2,6]

[1]Department of Dermatology and [2]Department of Hematology and Oncology, Graduate School of Medicine, Kyoto University, Kyoto, Japan; [3]Division of Infectious Genetics, The Institute of Medical Science, The University of Tokyo, Tokyo, Japan; [4]Department of Island and Community Medicine, and [5]Department of Laboratory Medicine, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan; [6]Kitano Hospital, The Tazuke Kofukai Medical Research Institute, Osaka, Japan

P14 Z39Ig is a novel cell surface marker of macrophages in murine large intestine.

Masashi Tanaka, Taku Nagai, Kazuhisa Hasui, Takami Matsuyama

Department of Immunology, Graduate School of Medical and Dental Sciences, Kagoshima University

P15* High-mobility Group Box-1 Protein Promotes Granulomatous Nephritis in Adenine-induced nephropathy.

Yoko Oyama[1], Teruto Hashiguchi[1], Noboru Taniguchi[2], Salunya Tancharoen[3], Tomonori Uchimura[1], Kamal K. Biswas[1], Ko-ichi Kawahara[1], Takao Nitanda[4], Yoshihisa Umekita[5], Martin Lotz[2] and Ikuro Maruyama[1]

[1]Department of Laboratory and Vascular Medicine, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan, [2]Department of Molecular and Experimental Medicine, The Scripps Research Institute, La Jolla, California, [3]Pharmacology Department, Faculty of Dentistry, Mahidol University, Bangkok, Thailand. [4]Division of Surgical Pathology, Kagoshima University Hospital, Kagoshima, Japan. [5]Department of Tumor Pathology, Field of Oncology, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan.

P16 Class A scavenger receptor promotes osteoclast differentiation via the enhanced expression of receptor activator of NF-κB (RANK).

Kenichi Takemura, Naomi Sakashita, Yukio Fujiwara, Yoshihiro Komohara, XiaoFeng Lei, Koji Ohnishi, Motohiro Takeya

Department of Cell Pathology, Graduate School of Medical Sciences, Kumamoto University

P17 The defensive role of interferon-γ produced by myeloid cells in invasive group A *Streptococcus* infection.

Takayuki Matsumura[1], Tadayoshi Ikebe[2], Haruo Watanabe[2], Kazuo Kobayashi[1], and Manabu Ato[1]

[1]Department of Immunology and [2]Department of Bacteriology I, National Institute of Infectious Diseases, Tokyo, Japan

P18 Targeting of folate receptor β-expressing macrophages in bleomycin induced pulmonary fibrosis.

Taku Nagai, Masashi Tanaka, Kazuhisa Hasui, Takami Matsuyama

Department of Immunology, Graduate School of Medical and Dental Sciences, Kagoshima University, Kagoshima, Japan

P19 What are effector cells in the liver transplant rejection ?

Hisashi Ueta, Xue-dong Xue, Bin Yu, Yasushi Sawanobori, Yusuke Kitazawa, Kenjiro Matsuno

Department of Anatomy, Dokkyo Medical University

P20* Translocation of ACAT1 from ER to Late Endosomal Associated Membranes in Cholesterol-rich Human Macrophage.

XiaoFeng Lei[1,2], Naomi Sakashita[2], Yukio Fujiwara[2], Catherine CY Chang[3], Ta-Yuan Chang[3], Motohiro Takey[2], Akira Miyazaki[1]

[1] Department of Biochemistry, Showa University School of Medicine, Tokyo, Japan
[2] Department of Cell Pathology, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan, [3] Department of Biochemistry, Dartmouth Medical School, Hanover, NH, USA

P21* Macrophage and neutrophils have different response to hypoxia in expression of long pentraxin 3 (PTX3) in human atherosclerosis.

Alexander S. Savchenko[1], Riuko Ohashi[1], Kenji Inoue[2], Shuying Jiang[1,3], Go Hasegawa[1], Makoto Naito[1]

[1]Department of Cellular Function, Division of Cellular and Molecular Pathology, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan; [2]Department of Cardiology, Juntendo University Nerima Hospital, Tokyo, Japan, [3]Perseus Proteomics Inc., Tokyo, Japan

P22 A symbiotic growth of nasal NK/T-cell lymphoma cells with CD204-positive macrophages would defense themselves from endogenous reactive oxygen spices-induced cell necrosis.

Kazuhisa Hasui[1], Xinshan Jia[2], Motohiro Takeya[3], Takuro Kanekura[1], Yoshifumi Kawano[1], Shuji Izumo[1], Yoshito Eizuru[1], Takami Matsuyama[1]

[1]Kagoshima University Graduate School of Medical and Dental Sciences,[2]China Medical University, and [3]Kumamoto University Graduate School of Medical Sciences

P23* Involvement of M2 macrophages in the ascites of advanced epithelial ovarian cancer in tumor progression via Stat3 activation.

Kiyomi Takaishi[1,2], Yoshihiro Komohara[1], Hironori Tashiro[2], Hidetaka Katabuchi[2], and Motohiro Takeya[1]

[1]Department of Cell Pathology and [2]Department of Gynecology, Graduate School of Medical Sciences, Kumamoto University

P24* Infiltration of macrophages plays a key role in tumor angiogenesis and progression.

Kosuke Watari, Yuji Basaki, Michihiko Kuwano, Mayumi Ono

Department of Pharmaceutical Oncology, Graduate School of Pharmaceutical Sciences, Kyushu University, Fukuoka, Japan

Session 1: Regulation of Inflammation

Chairpersons: Osamu Yoshie (Kinki University)
Yoshiro Kobayashi (Toho University)

Speakers: Teizo Yoshimura
Pieter JM Leenen
Akihiro Matsukawa
Gou Young Koh

Evaluating the role of macrophages as a source of the chemokine MCP-1/CCL2 during the inflammatory responses

Teizo Yoshimura

Laboratory of Molecular Immunoregulation, Cancer and Inflammation Program,
Center for Cancer Research, National Cancer Institute at Frederick, Frederick, MD 21702

MCP-1 is a chemokine regulating the recruitment of monocytes into sites of inflammation and cancer. MCP-1 can be produced by a variety of cell types, including macrophages, neutrophils, fibroblasts, endothelial cells and epithelial cells. Among them, macrophages have been shown to produce a high level of MCP-1 in vitro in response to proinflammatory stimuli, leading us to hypothesize that this cell type is a major source of MCP-1 produced in vivo during the inflammatory responses. To test the hypothesis, we constructed myeloid cell (neutrophil and macrophage)-specific conditional MCP-1-deficient mice using the Cre/loxP system and evaluated the role of these cells in MCP-1 production in a TG-induced peritonitis model. Contrary to the hypothesis, we did not detect a significant reduction in MCP-1 concentration in the peritoneal fluids of the conditional MCP-1-deficient mice. Furthermore, adoptive transfer of resident peritoneal cells of wild-type mice into the peritoneal cavities of systemic MCP-1-deficient mice did not alter MCP-1 concentration in the peritoneal fluids after TG injection. Similar results were obtained in a zymosan-induced peritonitis model. Taken together, our results indicated that non-myeloid cells, such as mesothelial cells, in the peritoneal cavity are the major source of MCP-1 in this model and that non-myeloid cells play a larger role in the development of inflammatory responses than we originally expected. We are currently using other disease models to further evaluate the role of macrophages as a source of MCP-1.

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Education

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Research and Professional Experience

1983-1984 Researcher at the Department of Pathology, Kumamoto University Medical School, Kumamoto, Japan.

1984-1985 Assistant Professor at the Department of Pathology, Kumamoto University Medical School, Kumamoto, Japan.

1985-1987 Guest Researcher at Immunopathology Section, Laboratory of Immunobiology, NCI-FCRF, Frederick, MD.

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Honors and Awards

1985-1987: Oversea Research Fellowship (Foundation for Promotion of Cancer Research, Tokyo, Japan)

Selected Publication:

1. Yoshimura, T., Matsushima, K., Oppenheim, J. J., and Leonard, E. J.: Neutrophil chemotactic factor produced by lipopolysaccharide (LPS) stimulated human blood mononuclear leukocytes. Partial characterization and separation from interleukin 1 (IL 1). J. Immunol. 139:788-793, 1987.
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Poster Abstracts

P1 Suppression of TLR4-mediated inflammatory response by macrophage class A scavenger receptor (CD204)

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The class A scavenger receptor (SR-A; CD204), one of the principal receptors expressed on macrophages, has been found to regulate inflammatory response and attenuate septic endotoxemia. However, the detailed mechanism of this process has not yet been well characterized. To clarify the regulative mechanisms of lipopolysaccharide (LPS)-induced macrophage activation by SR-A, we evaluated the activation of Toll-like receptor 4 (TLR4)-mediated signaling molecules in SR-A-deficient ($SR\text{-}A^{-/-}$) macrophages. In a septic shock model, the blood levels of tumor necrosis factor (TNF)- α , interleukin (IL)- 6 and interferon (IFN) - β were significantly increased in $SR\text{-}A^{-/-}$ mice compared to wild-type mice, and elevated nuclear factor kappa B (NF κ B) activation was detected in $SR\text{-}A^{-/-}$ macrophages. SR-A deletion increased the production of pro-inflammatory cytokines, and the phosphorylation of mitogen-activated protein kinase (MAPK) and NF κ B *in vitro*. SR-A deletion also promoted the nuclear translocation of NF κ B and IFN regulatory factor (IRF)-3. These data indicated that SR-A suppresses both TLR4-mediated myeloid differentiation factor 88-dependent and -independent pathways. In addition, a competitive binding assay with acetylated low-density lipoprotein, an SR-A-specific ligand, and anti-SR-A antibody induced significant activation of TLR4-mediated signaling molecules in wild-type macrophages but not in $SR\text{-}A^{-/-}$ macrophages. These results indicate that SR-A suppresses the macrophage activation by inhibiting the binding of LPS to TLR4 in a competitive manner and it plays a pivotal role in the regulation of the LPS-induced inflammatory response.

P2 Apoptosis of macrophages by N-Arachidonyl Glycine is mediated by GPR18

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N-arachidonyl glycine (NAGly) is one of lipoamino acids which are fatty acid-amino acid conjugates. NAGly was first identified from the bovine and rat brain. Following study found that NAGly is present in a variety of tissues including spinal cord, small intestine, kidney, skin and blood. NAGly has close relationships with the anandamide (N-arachidonyl ethanol amide; AEA) not only structurally but also in terms of biological actions including analgesia, calcium ion mobilization and anti-inflammatory effects. At the same time, NAGly has a weak affinity for anandamide transporter, cannabinoid receptor CB1and vanilloid receptor VR1. It was also indicated that NAGly regulated AEA in macrophage. In addition, NAGly has been identified as a ligand of G-protein coupled receptor (GPCR) GPR18 and GPR92. So NAGly is an anticipated substance as pharmacological targets, but it has not demonstrated whether GPR18 and GPR92 were involved in these NAGly-induced physiological effects. Here, we focused physiological effects of NAGly in macrophage and the relations of GPCRs to the effects.

In this study, mouse macrophage derived cell line RAW264.7 were used. Cell apoptosis was determined by Cell counting kit-8 (CCK-8) and Annexin V stain. NAGly and AEA suppressed RAW264.7 cell survival rate and induced apoptosis but arachidonyl acid didnt. Westernblotting analysis revealed that NAGly activated MAP kinases (ERK1/2, JNK, p38 MAPK) and caspase-3 pathway. In particular, pretreatment with p38 MAPK inhibitor prevented NAGly-induced apoptosis. Pretreatment Gi protein inhibitor also prevented the action of NAGly, but it didn't affect the action of AEA. Both GPR18 and GPR92 are expressed in RAW264.7 and GPR18 is coupled with Gi protein. GPR18 knocked-down RAW264.7 failed to induce apoptosis by NAGly. Our findings indicate that NAGly induced apoptosis in macrophage mediated by p38 MAPK activation and caspase-3 pathway.

Most recently it has been reported that macrophage apoptosis caused by lipids was mediated by the increase of fatty acid-binding protein-4(aP2), regulator of macrophage ER stress. Alteration of aP2 expression by NAGly in RAW264.7 is currently under investigation.

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