149th IDAC Biannual Meeting
Program

January 26, 2018, 13:00~ Center for Smart Aging Research 1F, IDAC

Institute of Development, Aging and Cancer, Tohoku University
Society of Institute of Development, Aging and Cancer, Tohoku University
Development of PET tracers for imaging neuropathological hallmarks
— From development to validation —

Ryuichi Harada

Alzheimer’s disease (AD), which is the most common cause of dementia, is an irreversible and progressive neurodegenerative diseases clinically characterized by memory loss and cognitive decline. Neuropathological hallmarks in AD are not only abundant neuronal loss and gliosis but also protein accumulation of amyloid-β and tau protein in the brain. Clinicopathological studies have established evidences that tau deposition is correlated with neuronal loss and the severity of cognitive impairment, but not amyloid deposition. Therefore, non-invasive imaging of tau pathology would provide new insights into the pathogenesis of AD. Through screening and the compound optimization, we developed several $^{18}$F-labeled quinoline derivatives as tau selective PET tracers. In clinical PET study, the latest derivative, $^{18}$F-THK5351 demonstrated elevated tracer retention in site susceptible to tau deposition in patients with AD. However, there are unexplained tracer retention in the basal ganglia and thalamus (i.e. off-target binding). Recent blocking studies identified monoamine oxidase-B (MAO-B) as an off-target substrate of $^{18}$F-THK5351. An imaging-autopsy
validation of a patient with AD who underwent $^{18}$F-THK5351 PET prior to death demonstrated that in vivo $^{18}$F-THK5351 retention significantly correlated with MAO-B levels in the whole brain and tau aggregates in the neocortex. MAO-B was dominantly expressed in astrocytes and its level increased in patients with AD, which is associated with neuroinflammatory changes characterized by reactive astrocytes. Astrogliosis is linked to neurodegeneration, although it is still debate regarding relationship between gliosis and AD pathophysiology and its time course. Now we are trying to develop selective tau and astrogliosis (MAO-B) through lead optimization to elucidate its relationship by longitudinal PET studies.

13:35 — 13:40 break

13:40 — 14:40 Sessions 1～4 Chair: Masanori Ikeda

1. **Metformin directly binds the alarmin HMGB1 and inhibits its proinflammatory activity**

Natsumi Sakata¹, Takahiro Horiuchi¹, Yoshihiro Narumi¹, Tomohiro Kimura¹, Takashi Hayashi², Keisuke Nagano³, Keyue Liu⁴, Masahiro Nishibori⁴, Sohei Tsukita⁵, Tetsuya Yamada⁵, Hideki Katagiri⁵, Ryutaro Shirakawa¹, and Hisanori Horiuchi¹

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³First Institute of New Drug Discovery, Tokushima Research Institute, Otsuka Pharmaceutical Co., Ltd.

⁴Department of Pharmacology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences

⁵Department of Metabolism and Diabetes, Tohoku University Graduate School of Medicine

2. **A mathematical model describing difference in chromosome dynamics between normal and cancer cells**

Manuel A Campos, Kenji Iemura, Kozo Tanaka

Department of Molecular Oncology, Institute of Development, Aging and Cancer, Tohoku University
3. New methodology to detect and quantitate extracellular vesicles in blood plasma
Masashi Takao¹, Tetsuhiko Ohba², and Yutaka Nagai³
¹Department of Project Program, IDAC, Tohoku University
²Department of Physics, Graduate School of Science and Faculty of Science, Tohoku University
³IVD Operations, Nihon Kohden Corporation

4. A novel and feasible antibody-based medicine for cancers targeting vasohibin-2
EunSeo LEE¹, Yasuhiro Suzuki¹, Hironori Nakagami², Hideki Tomioka³, Yasufumi Sato¹
¹Department of Vascular Biology, IDAC, Tohoku University
²Department of Health Development & Medicine, Osaka University. Graduate School of Medicine
³Department of Research & Development, FunPep Co.,Ltd

14:40 — 14:50 Coffee break

14:50 — 15:35 Sessions 5~7 Chair: Akihiro Yamada

5. Nrf2 plays a role in ischemia-reperfusion lung injury after lung transplantation
Takeo Togo¹, Yasushi Hoshikawa², Keiko Taguchi³, Hiroshi Yabuki ¹, Hideki Mitomo¹, Tatsuki Watanabe¹, Masafumi Noda¹, Junichi Funahashi¹, Masayuki Yamamoto³, Yoshinori Okada ¹
¹Department of Thoracic Surgery, Institute of Development, Aging and Cancer, Tohoku University
²Department of Thoracic Surgery, Fujita Health University School of Medicine
³Department of Medical Biochemistry, Tohoku University Graduate School of Medicine

6. Identification of molecular biological factors on effect of anti-EGFR treatment in colorectal cancer for a biomarker development
Akira Okita, Shin Takahashi, Kota Ouchi, Chikashi Ishioka
Department of Clinical Oncology, Institute of Development, Aging and Cancer, Tohoku University
7. Gene regulatory mechanisms by mechanical forces in cardiovascular system
Atsushi Kubo, Makoto Kanayama, Kakeru Watanabe, Takahiro Niida, Yusuke Watanabe, Ken Matsumoto, Toshihiko Ogura
Department of Developmental Neurobiology, Institute of Development, Aging and Cancer, Tohoku University

15:35 – 15:40 break

15:40 – 16:25 Sessions 8~10 Chair: Hiromitsu Ota

8. Involvement of IL-32 in the regulation of malignant mesothelioma cell growth and VEGF and IL-8 secretion
Muneo Numasaki, Jyuri Ueda, Aiko Ishiki, Naoki Tomita, Shoji Okinaga and Hiroyuki Arai
Department of Geriatrics and Gerontology, Institute of Development, Aging and Cancer, Tohoku University

9. Activation of NRF2 Alleviates Lethal Autoimmune Inflammation in Scurfy Mice
Takuma Suzuki¹,², Shohei Murakami¹, Shyam S. Biswal³, Shimon Sakaguchi⁴, Hideo Harigae⁵, Masayuki Yamamoto⁵ and Hozumi Motohashi¹
¹Department of Gene Expression Regulation, Institute of Development, Aging and Cancer, Tohoku University
²Department of Hematology and Rheumatology, Tohoku University Graduate School of Medicine
³Department of Environmental Health Sciences, Bloomberg School of Public Health, Johns Hopkins University
⁴Experimental Immunology, World Premier International Research Center, Immunology Frontier Research Center, Graduate School of Medicine, Osaka University
⁵Department of Medical Biochemistry, Tohoku University Graduate School of Medicine
Single cell RNA-Seq analysis defines distinct gene-expression profiles of tissue-specific plasma cells

Ari Itoh·Nakadai, Atsuko Kayaba, Toshiyuki Takai
Department of Experimental Immunology, Institute of Development, Aging and Cancer, Tohoku University

一般口演について
発表時間12分、討論3分とします。時間厳守にてお願いします。座長は
研究員会委員の集談会コンテスト係が行ないます。

16:25－16:30 Closing remarks Dr. Hozumi Motohashi

終了後
加齢研究実験研究棟7階セミナー室（1）におきまして18時から研究員会
主催新年会を開催いたします。皆様、多数ご参加くださいますようご案内
いたします。