第87回日本薬理学会年会サテライト国際シンポジウム

# アルツハイマー病における分子イメージングの新しい展開

## New Perspectives of Molecular Imaging on Alzheimer's Disease

**2014年**

**3月21日(金)** **15：45～17：15**

場 所▶東北大学百周年記念会館
川内萩ホール・会議室

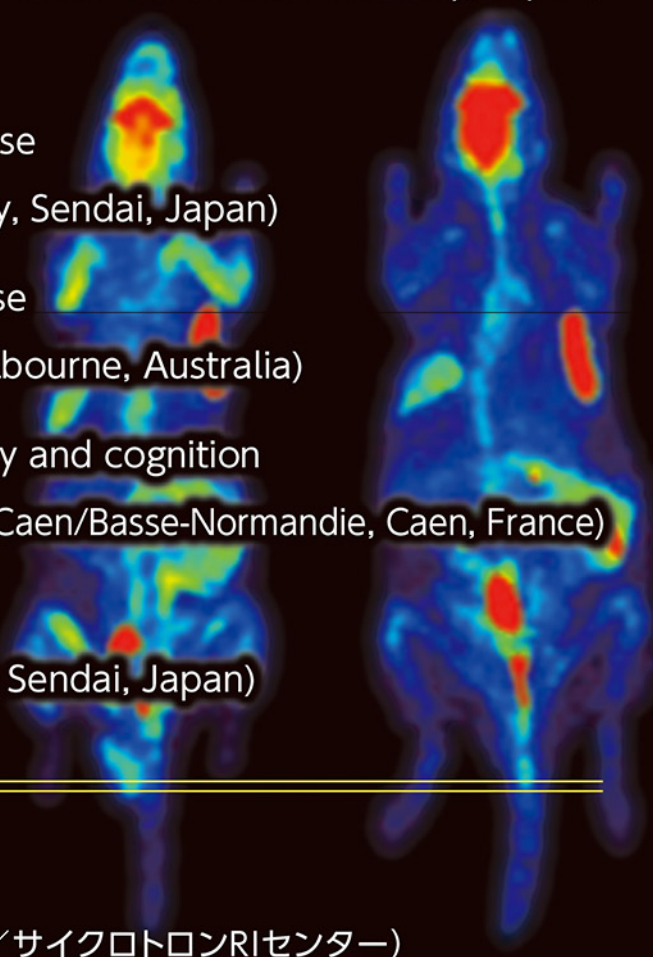
所在地▶〒980-8576 宮城県仙台市青葉区川内40

参加費 無 料

Chairpersons: Hiroyuki Arai and Nobuyuki Okamura (Tohoku University, Japan)

Tentative Titles and Speakers

1. Clinical biomarkers in Alzheimer's disease
   Katsutoshi Furukawa (Tohoku University, Sendai, Japan)
2. Amyloid-β imaging in Alzheimer's disease
   Victor L. Villemagne (Austin Health, Melbourne, Australia)
3. Relation between amyloid, brain atrophy and cognition
   Gael Chételat (Inserm-EPHE-Université de Caen/Basse-Normandie, Caen, France)
4. Tau imaging in Alzheimer's disease
   Nobuyuki Okamura (Tohoku University, Sendai, Japan)



主 催 東北大学分子イメージング研究推進室
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平成２６年１月２７日

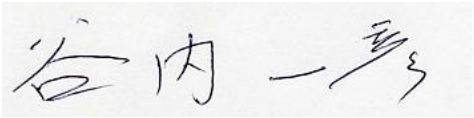
PET 関連施設関係者各位殿

厳寒の候、皆様ますますご清祥のこととお慶び申し上げます。日頃は分子イメージング教育に多大なるご協力を賜りまして厚く御礼申し上げます。

さて、この度東北大学分子イメージング教育コース国際シンポジウム「アルツハイマー病における分子イメージングの新しい展開：New Perspectives of Molecular Imaging on Alzheimer's Disease」を平成 26 年 3 月 21 日(金)・東北大学百周年記念会館　川内萩ホール会議室に於いて開催する運びとなりました。アルツハイマー病の分子イメージングに関する最新の発表がありますので、ご参加いただきたくでご案内申し上げます。本シンポジウムは第 87 回日本薬理学会年会サテライトとして行いますが、サテライト国際シンポジウムに関して参加費は無料ですので、お時間があればご参加ください。本国際シンポジウムは公益財団法人ノバルティス科学振興財団の平成 25 年度研究集会助成を得て行われます。詳細は東北大学分子イメージング教育コース HP（http://www.miec.umin.jp/index.html）にも掲載されていますので、ご参照ください。

また同時に開催される第 87 回日本薬理学会年会にもご参加をお願いしたく思います。テーマを「復興と創造」とし、分子イメージングを含む薬理学研究の更なる発展をめざしたいと考えております．今回のプログラムは、ノーベル賞受賞者を含むプレナリーレクチャー、江橋節郎賞受賞講演、特別講演、学術奨励賞受賞講演、公募シンポジウム、次世代の会シンポジウム、製薬企業企画シンポジウム、一般演題（口演，ポスター）、Meet the Distinguished Professor、日本毒性学会との合同シンポジウム、日本臨床薬理学会との共催シンポジウム、ランチョンセミナー、市民公開講座を予定しています。皆様のご参加を心よりお待ち申し上げております。詳細は年会 HP に掲載しておりますので合わせてご案内申し上げます。http://www.c-linkage.co.jp/jps2014/

お忙しい中お手数をおかけして申し訳ございませんが何卒よろしくお願い申し上げます。末筆ではございますが、皆様の益々のご盛栄を祈念申し上げます。



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第 87 回日本薬理学会年会サテライト国際シンポジウム
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所在地 〒980-8576 宮城県仙台市青葉区川内 40 （地図参照）
Tel./Fax. 022-795-3391 / 022-795-3390
日時：2014 年 3 月 21 日（金）15 時 45 分－17 時 15 分
参加費：無料



【主　催】東北大学分子イメージング研究推進室
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“New Perspectives of Molecular Imaging on Alzheimer’s Disease”
A Satellite Symposium of the 87th Annual Meeting of The Japanese Pharmacological Society
Chairpersons: Hiroyuki Arai and Nobuyuki Okamura (Tohoku University, Japan)
Title and Speakers

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**本国際シンポジウムは公益財団法人ノバルティス科学振興財団・平成 25 年度研究集会助成を得て行われます。**

# CLINICAL BIOMARKERS IN ALZHEIMER'S DISEASE

**Katsutoshi Furukawa**

Department of Geriatrics and Gerontology Division of Brain Sciences, Institute of Development, Aging and Cancer, Tohoku University, Sendai, Japan

Diagnosis of Alzheimer's disease (AD) was previously based on clinical manifestations and cognitive tests. However, biochemical techniques and neuroimaging methods have improved, and physicians and researchers have started focusing on biomarkers as diagnostic tools. There are several reasons why biomarkers are important. Biomarkers can detect pathological changes earlier and prior to observing disease-related symptoms. Biomarkers are also useful for identifying disease progression, assessing therapeutic effects, consolidating patient pathogenesis, especially in patients enrolled in drug trials, and screening large populations for risk assessment. According to "Consensus Report of the Working Group on Molecular and Biochemical Markers of Alzheimer's Disease" by the Ronald and Nancy Reagan Research Institute of the Alzheimer's Association and the National Institute on Aging Working Group, an ideal biomarker should detect a fundamental feature of neuropathology and should be confirmed by at least two independent studies conducted by qualified investigators with the results published in peer-reviewed journals. Further, an ideal biomarker should have a sensitivity of >80% for detecting AD and a specificity of >80% for differentiating Alzheimer's disease from other disorders. Finally an ideal biomarker should be reliable, reproducible, noninvasive, simple to perform, and inexpensive.

AD biomarkers are classified as either biofluid or imaging markers. Reliable biofluid markers, such as amyloid-β 1-42 (Aβ42), total tau (t-tau), and phosphorylated tau (p-tau) in cerebrospinal fluid (CSF), have been confirmed whereas volumetric magnetic resonance imaging (MRI), fluorodeoxyglucose PET (FDG-PET), and amyloid PET are recognized as reliable imaging markers. These biomarkers are divided into Aβ and neurodegenerative categories. The former includes CSF-Aβ42 and amyloid PET whereas the latter includes volumetric MRI, fluorodeoxyglucose PET, CSF t-tau, and CSF p-tau. Brain computed tomography (CT) and cerebral perfusion single-photon emission computed tomography (SPECT) are important for detecting biomarkers that are commonly used clinically; however, research projects such as the Alzheimer's Disease Neuroimaging Initiative (ADNI) do not investigate these biomarkers. Thus, I would like to present the recent progress of biofluid and imaging biomarkers for AD diagnosis.

# Aβ IMAGING IN ALZHEIMER'S DISEASE AND OTHER NEURODEGENERATIVE CONDITIONS

**Victor L Villemagne[1,2], Michelle T Fodero-Tavoletti[1,2], Vincent Doré[3], Colin L Masters[2], Christopher C Rowe[1]**

[1] Austin Health, Dept of Nuclear Medicine and Centre for PET, Melbourne, Australia
[2] The Florey Institute of Neuroscience and Mental Health, University of Melbourne, Australia
[3] The Australian eHealth Research Centre, CSIRO, Australia

β-amyloid (Aβ) is one of the neuropathological hallmarks of Alzheimer's disease (AD). Positron emission tomography (PET) radiotracers for the in vivo assessment of Aβ burden have transformed the evaluation of AD pathology, extending our insight into Aβ deposition in aging and AD by providing highly accurate, reliable, and reproducible quantitative statements of regional and global Aβ burden in the brain, essential for therapeutic trial recruitment and for the evaluation of anti-Aβ therapies. This progress has already resulted in the approval of two Aβ radiotracers for clinical use.

As new treatment strategies to prevent or slow disease progression through early-intervention are being developed and implemented, there is an urgent need for early disease recognition, which is reflected in the necessity of developing sensitive and specific biomarkers as adjuncts to clinical and neuropsychological tests. Because the molecular changes occur well before the phenotypical manifestation of the disease, a change in the diagnostic paradigm is needed, where diagnosis moves away from the identification of signs and symptoms of neuronal failure to the early and non-invasive detection of a particular trait underlying the pathological process, that will also allow evaluation of efficacy and monitoring of the molecular effects of disease-modifying therapies. Furthermore, given the complexity and sometimes overlapping characteristics of these disorders, it is unlikely that a single biomarker will be able to provide the diagnostic certainty required, especially for the identification of at-risk individuals before the development of the typical phenotype. Consequently, a multimodality approach is required for accurate diagnosis, monitoring disease progression and therapeutic efficacy.

# RELATION BETWEEN AMYLOID, BRAIN ATROPHY AND COGNITION

**Gaël Chetelat**

INSERM, Université de Caen, EPHE, CHU de Caen, U1077, Caen, France

Amyloid neuroimaging is one of the main hallmarks of Alzheimer's disease (AD) and is thought to play a central role in the physiopathology of the disease, although this role is not fully understood. The present talk will focus on the relationships between amyloid deposition as assessed in vivo with amyloid PET imaging, and memory deficits and atrophy, in different stages of AD, to improve our understanding of the physiopathological cascade of AD. Altogether, the link between global neocortical Aβ deposition and memory appears to be weak, early, and probably indirect though there may be a direct effect in specific brain regions. As for atrophy, studies suggest that PiB i) correlates to local atrophy only in the early stage and in regions of highest amyloid deposition; and ii) can be observed in the non expected direction (i.e. increased volume with increased PiB), especially in early stages. This suggests that atrophy in AD-typical brain regions is not directly caused by the degree of local amyloid deposition. As a whole, while Aβ disregulation and deposition is necessary for the development of AD, the relationship with neurodegeneration and dementia reveals to be complex, indirect, and not dose-dependent.

# PET TAU IMAGING IN ALZHEIMER'S DISEASE USING $^{18}$F-THK5105 AND $^{18}$F-THK5117

**Nobuyuki Okamura[1], Ryuichi Harada[1], Shozo Furumoto[2], Kazuhiko Yanai[1,2], Hiroyuki Arai[3], Yukitsuka Kudo[4]**

[1] Department of Pharmacology, Tohoku University School of Medicine, Sendai, Japan
[2] Cyclotron and Radioisotope Center, Tohoku University, Sendai, Japan
[3] Institute of Development, Aging and Cancer, Tohoku University, Sendai, Japan
[4] Clinical Research, Innovation and Education Center, Tohoku University Hospital

Noninvasive imaging of amyloid plaques and neurofibrillary tangles in the brain will contribute to the early and differential diagnosis of dementia, tracking disease progression and evaluating efficacy of disease-specific therapies. Several PET tracers have been developed for in vivo imaging of amyloid-β plaques and studied extensively in clinical trials. On the other hand, PET tracer for imaging tau deposits is still in the process of research and development. For the development of tau-selective PET tracer, we have screened β-sheet-binding small molecules and discovered novel quinoline derivatives with high binding selectivity to tau deposits in AD brain samples. Through the compound optimization process, we developed $^{18}$F-labeled 2-arylquinoline derivatives $^{18}$F-THK5105 and $^{18}$F-THK5117, which showed high binding affinity and selectivity to tau protein deposits in AD brain samples. Recent PET studies demonstrated $^{18}$F-THK5105 and $^{18}$F-THK5117 retention in sites with predilection for the deposition of tau pathology in AD patients and distinctly differentiated AD patients from aged normal individuals. Furthermore, these tracer retention was closely associated with dementia severity and brain atrophy. In this symposium, we will introduce the recent progress in the development of tau-selective PET tracer and the results of first-in-man PET studies using $^{18}$F-THK5105 and $^{18}$F-THK5117.