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会告

未来材料創成工学専攻, セラミックス科学研究教育院および先進セラミックス研究センターの共催によりオーストラリア連邦科学産業研究機構のVictor STRELTSOV博士による特別講演会を次のように開催いたします。ⁱ

日時： 平成 24 年 6 月 6 日(水)14:40-16:10

場所： 名古屋工業大学（鶴舞キャンパス）2 号館 I2 教室(0231)

講演者： Victor STRELTSOV 博士

講演題目：

アルツハイマー病におけるアミロイドベータ重合体と金属付加
ー疾患の診断と治療に果たすナノマテリアルの役割ー

Abstract

Structural characterization of Amyloid- β oligomers and metal binding in Alzheimer's disease

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Alzheimer's disease (AD) is the most common cause of dementia and is characterized by the presence of misfolded protein depositions or plaques in the brain. Current evidence suggests that soluble non-fibrillar Amyloid- β (A β) oligomers are the major drivers of A β -mediated neuronal dysfunction and a significant source of the neurotoxicity is mediated by the interaction of A β with transition metals (Cu, Fe and Zn) which leads to altered neuronal metal homeostasis, oxidative injury and accumulation of toxic A β oligomers. Determining the structure of A β oligomers and the details of the A β metal binding site are vital steps towards understanding why neurotoxic aggregates and plaques occur – knowledge that is important in the development of new treatments.

Here, we describe the first atomic resolution x-ray crystallographic structure of an oligomeric A β (17-42) (p3) fragment [1] constrained within the CDR3 loop region of a shark IgNAR single variable domain antibody [2]. This discovery shows that the structure of oligomers is not like a piece of a fibril. The predominant oligomeric species is a tightly-associated A β dimer, with paired dimers forming a tetramer in the crystalline form. The general features of this oligomer match some recent predictions, thus potentially providing a model system for non-fibrillar oligomer formation in AD

Interfering with metal binding to A β is another emerging target for the development of AD therapeutics [3]. We have analyzed *in vitro* the structure of A β (1-16) (metal-binding region) complexed with transition metals [4] and Pt-based inhibitors by combined X-ray crystallography, absorption spectroscopy (EXAFS, XANES) and *ab initio* density functional calculations (DFT) [4,5].

[1] V.A. Streltsov, J. Vaghese, C. Masters, S. Nuttall, *J. Neurosci*, **2011**, 31(4), 1419-1426. [2] V.A. Streltsov, J. Vaghese, J.A. Carmichael, R.A. Irving, P.J. Hudson, S. Nuttall, *PNAS* **2004**, 101, 12444-12449.

[3] K.J. Barnham, V.B. Kenche, G.D. Ciccotosto, D.P. Smith, D.J. Tew, X. Liu, K. Perez, G.A. Cranston, T.J. Johanssen, I. Volitakis, A.I. Bush, C.L. Masters, A.R. White, J.P. Smith, R.A. Cherny, R. Cappai. *PNAS* **2008**, 105, 6813-6818. [4] V.A. Streltsov, S. Titmuss, V. Epa, K. Barnham, C. Masters & J. Varghese, *Biophysical Journal* **2008**, 95, 3447-3456. [5] V. Epa, V. A. Streltsov, J.N. Varghese, *Aust. J. Chem.* **2010**, 63(3), 345-349.

Keywords: Alzheimer's, Amyloid- β oligomer, Structure

講演者である STRELTISOV 博士はオーストラリア連邦科学産業研究機構・神経変性疾患プロジェクトリーダーです。同氏は構造生物学から鉱物科学まで広い範囲をカバーする結晶学者であり、現在はアルツハイマー疾患の原因を構造化学的に究明し、その診断と治療法を探っています。今回、JSPS 外国人招へい研究者としてセラ研に滞在される機会を利用して、最近の話題についてお話を伺うことにいたしました。講演は英語ですが、日本語演題のサブタイトルは演題をキャッチーにするため、招聘側の石澤が演者の了解を得たうえでつけたものです。多くの方々のご来聴と活発な討論をお願いできると幸いです。

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