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In vivo analysis of amyloid β aggregates in the brain of a transgenic mouse model of Alzheimer's disease using ^{19}F-MRI

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Abstract

Amyloid β (Aβ) deposition in the brain is generally considered to be the initial phase in Alzheimer's disease (AD). Amyloid imaging is widely studied in diagnosing AD and evaluating disease stage, with considerable advances achieved in recent years. Several types of probes have been developed in positron emission tomography (PET). However, little information is available about ligands for amyloid detection with mganetic resonance imaging (MRI). We have developed two types of potential imaging agents using fluorine (^{19}F)-MRI: ^{19}F-containing benzoxazole derivative (named Shiga-X22) and ^{19}F-containing curcumin derivative (named Shiga-Y5). Following injection of Shiga-Y5 or Shiga-X22 compounds into the tail vein of a transgenic mouse model of AD or control wild-type mice, MR signals were measured using a 7.0 T horizontal-bore MR scanner. After MR measurement, brain sections were prepared for fluorescence microscopy. Both compounds showed marked ^{19}F-MR signals in the area corresponding to the brain of the AD mouse but not controls. Under fluorescence microscopy, AD model mice injected with Shiga-Y5 or Shiga-X22 showed massive fluorescence co-localized with amyloid plaques. Quartz crystal microbalance (QCM) analysis and histochemical examination demonstrated that both Shiga-X and Shiga-Y compounds are bound to Aβ aggregates (with β-sheet) and senile plaques in the brain of AD mice and human subjects. Moreover, QCM analysis showed significant frequency decreases in oligomer-immobilized electrodes following the addition of Shiga-Y5, but not Shiga-X22. These results indicate that we have two types of probes: Shiga-Y5 detects Aβ oligomers as well as Aβ aggregates, while Shiga-X22 only detects Aβ aggregates.

Biography

Ikuo Tooyama completed his Ph.D. at age 32 from Kyoto University and postdoctoral studies from the Kinsmen Laboratory of Neurological Research at the University of British Columbia. He is the director and professor of the Molecular Neuroscience Research center, Shiga University of Medical Science. He has published more than 170 papers in international journals and serves as an executive board member of the Japan Society of Dementia Research.