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【Overview presentation】

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Plasma endogenously cleaved MTBR-tau243 measured by an automated immunoassay is associated with tau PET-based Braak staging

Authors	Masanori Kurihara[1,2], Kengo Ishiki[3], Shun Murakami[3], Yuki Hoshina[3], Tomoko Ohashi[3], Mayu Fujita[4], Yoshifumi Shima[4], Chihiro Suminaka[3], Masahiro Miura[3], Toshiyuki Sato[3], Kenji Ishii[2,5], Ryoko Ihara[1], Shigeki Iwanaga[3], and Atsushi Iwata[1,2] [1] Department of Neurology, Tokyo Metropolitan Institute for Geriatrics and Gerontology [2] Department of Biomarkers, Integrated Research Initiative for Living Well with Dementia, Tokyo Metropolitan Institute for Geriatrics and Gerontology [3] Central Research Laboratories, Sysmex Corporation [4] Reagent Engineering, Sysmex Corporation [5] Research Team for Neuroimaging, Tokyo Metropolitan Institute for Geriatrics and Gerontology
Overview presentation	**Objectives** Endogenously cleaved microtubule-binding region tau containing residue 243 (eMTBR-tau243), identified by immunoprecipitation–mass spectrometry (IP-MS), has been shown to reflect advanced neurofibrillary pathology in Alzheimer's disease. However, the lack of scalable and automated immunoassays has limited the clinical translation, and the utility of plasma eMTBR-tau243 for estimating tau PET-based Braak staging using immunoassay platforms remains unclear. In this study, we investigated whether novel automated immunoassays for plasma eMTBR-tau243 can be used to estimate tau PET-based Braak staging. **Methods** Plasma samples were obtained from 129 participants of the Tokyo Metropolitan Institute for Geriatrics and Gerontology (TMIG) biobank, who had tau PET data using [^{18}F]MK 6240. Plasma eMTBR-tau243 concentrations were quantified using the Automated Immunoassay System HISCL™-5000. PET-based Braak

	stages were assigned according to established criteria. Associations between plasma eMTBR-tau243 concentrations and Braak stages were assessed, and receiver operating characteristic (ROC) analyses were performed to evaluate the ability to discriminate tau PET-based Braak stages. **Results** In the total cohort of 129 participants, plasma eMTBR-tau243 concentrations increased with advancing tau PET–defined Braak stage. Of these participants, 112 were classified as Braak stage <V and 17 as Braak stage ≥V by tau PET. Plasma eMTBR-tau243 showed high discriminative performance for distinguishing participants with Braak stage ≥V from those with Braak stage <V, achieving an area under the receiver operating characteristic curve (AUC) greater than 0.9. **Conclusion** Using an automated immunoassay platform, we demonstrate that plasma eMTBR-tau243 is associated with tau PET-based Braak staging. These findings support the feasibility of translating mass spectrometry–based discoveries into scalable immunoassays suitable for large-scale clinical and research applications and highlight the potential utility of plasma tau biomarkers for biological staging in Alzheimer's disease.
Session	Developing Topics: Biomarkers (Sunday-1152)