# TMU 脳神経研究会

# 第 10 回セミナー

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12 号館階 101 号室

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## Title: Central Mediator Of Neurodegeneration Upon Traumatic Brain Injury That Is Blocked By Antibody

（外傷性脳障害が引き金となる神経変性、そのキー因子）

脳障害とタウオパチー神経変性をシスタウの抗体が阻止するという話です。昨年の Nature Article に発表されました（Nature. 2015 523:431-6）。要旨を添付します。お時間ありましたら、お出でください。

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# Central Mediator Of Neurodegeneration Upon Traumatic Brain Injury That Is Blocked By Antibody

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Traumatic brain injury (TBI) is the best-known environmental risk factor for Alzheimer's disease (AD), whose defining pathologic features include tauopathy made of hyperphosphorylated tau (PHF-tau) and is characterized by acute neurological dysfunction. However, tauopathy is undetectable acutely after TBI and how TBI leads to tauopathy which in turn would increase risk of AD is unknown. Here we identify a neurotoxic *cis* conformation of phosphorylated tau at Thr231 as a major early driver of TBI and neurodegeneration that is effectively blocked by the conformation specific monoclonal antibody. We found robust *cis* p-tau after sport- and military-related TBI in humans and mice. Acutely after TBI in mice and stress *in vitro*, neurons prominently produce *cis* p-tau, which disrupts axonal microtubule network and transport, spreads to other neurons, and leads to apoptosis, a pathogenic process, which we nominated "cistauosis" that appears long before known tauopathy. Treating TBI mice with *cis* antibody not only blocks early cistauosis, but also prevents tauopathy development and spread, and restores brain histopathological and functional outcomes. These results uncover cistausosis as an early precursor of tauopathy and an early marker of neurodegeneration after sport and military TBI. We anticipate that *cis* p-tau will be a new early biomarker and that *cis* p-tau antibody or vaccines may be used to treat or even prevent TBI, chronic traumatic encephalopathy and AD.