PROGRESS IN NEUROSCIENCE PINS

Seminar Series of the
Brain & Mind Research Institute
Weill Cornell Medical College (WCMC)
&
The Graduate Program in Neuroscience of
WCMC and Sloan Kettering Institute

Thursday, 4/13/17, 4 PM, coffee at 3:45 PM
Weill Auditorium

"Tau Proteostasis Imbalance and Toxicity in Neurodegeneration"

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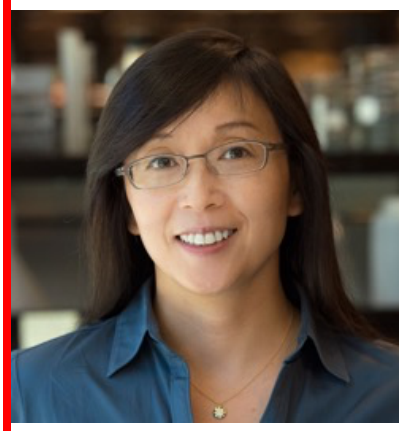
Abstract



Alzheimer's disease is characterized by accumulation of amyloid β (Aβ) and microtubule binding protein tau. Toxic forms of tau have emerged as a major therapeutic target in AD and other tauopathies. Over the past decade, most of studies have been focused on how hyperphosphorylation affects tau accumulation and aggregation. We discovered that acetylation of tau is a critical posttranslational mechanism and represents a novel therapeutic direction. We developed highly specific antibodies against acetylated-tau and identified aberrant tau acetylation sites that are elevated in AD brains. Our recent finding revealed a novel mechanism by which acetylated tau impairs synaptic plasticity. Using small molecule inhibitor of p300/CBP, acetyltransferases for tau, we provided proof-of-principle that inhibition of tau acetylation could reduce pathogenic accumulation of tau and protect against tau-mediated cognitive deficits and neurodegeneration. Immunotherapy targeting pathogenic acetylated tau species will also be discussed.

Recent Relevant Publications:

1. Min SW, Cho SH, Zhou Y, Schroeder S, Haroutunian V, Seeley WW, Huang EJ, Shen Y, Masliah E, Mukherjee C, Meyers D, Cole PA, Ott M, Gan L. (2010) Acetylation of tau inhibits its degradation and contributes to tauopathy. ***Neuron*** 67:953–966. PMCID: PMC3035103
2. Min S*, Chen X*, Tracy TE, Sohn PD, Shirakawa K, Devidze N, Minami SS, Lee BH, Wang C, Schiling B, Cong X, Ellerby L, Gibson BW, Johnson J, Ponnusamy R, Zhou Y, Li Y, Shamloo M, Masliah E, King R, Finley, D, Verdin E and Gan L (2015). Critical Role of Acetylation in Tau-mediated Neurodegeneration and Cognitive Deficits: Therapeutic Implications. ***Nat Med.*** 21(10):1154-1162. PMCID: PMC4598295 (*Co-first author)
3. Tracy TE, Sohn PD, Minami SS, Wang C, Min SW, Li Y, Zhou Y, Le D, Lo I, Ponnusamy R, Cong X, Schilling B, Ellerby LM, Huganir RL, Gan L. (2016) Acetylated Tau Obstructs KIBRA-Mediated Signaling in Synaptic Plasticity and Promotes Tauopathy-related Memory Loss. ***Neuron*** 90(2):245-60. PMCID: PMC4859346

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