ANNOTATION


Primary News: How New, Phospho-tau? Sparring Synapses, Meeting with Microtubules

Comment by: Fred Van Leuven, ARF Advisor (Disclosure)
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While this study helps us to understand some of the actions of tau, several questions come to mind:

- It is surprising that no effects are noted on spines or dendrites, while synapses are not really analyzed here. The evident neurotoxicity is remarkable in its regional difference since CA1 is the most vulnerable hippocampal region, as the authors properly discuss.
- Do the recombinant "im-E-tau" molecules still bind to microtubules (MT), and is displacement of normal tau from MT part of the problem?
- The S1/T to E mutation is a fairly easy method to assess effects of phosphorylation, but it remains "pseudo-phosphorylation" and therefore not relevant to the real thing, as opposed to the S1/T to A mutations to prevent phosphorylation.
- In our hands, in cellular transfections, when EGFP is fused to tau at either the N- or C-terminus, it interferes with its "normal" behavior, including formation of the MCI epitope. Moreover, this epitope is specific and should in principle not be evident by Western blotting after SDS PAGE.

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Comment by: Alejandra Alonso, Khalid Iqbal

Alzheimer disease (AD), frontotemporal dementia with parkinsonism linked to chromosome 17 (FTDP-17), Guam parkinsonism dementia, cortical basal degeneration, dementia pugilistica, Pick's disease, progressive supranuclear palsy, and tangle-only dementia, among other leukopathies, are linked to the progressive accumulation of filamentous hyperphosphorylated tau inclusions. Besides the accumulation of tau, another distinctive feature is the loss of neural arborization and the disruption of microtubules and synaptic terminals. This neurodegeneration is also present in FTDP-17, diseases linked to tau mutations, pointing to tau and tau function as the origin of dementia. Shahani et al. recently described a very interesting model to test the role of hyperphosphorylated tau in neurodegeneration, they injected neurons in mouse brain slices with pseudo-hyperphosphorylated tau using recombinant Sindbis virus. This method allows the authors to study behavior of hyperphosphorylated tau in living neurons. The expressed tau filled up the neurons highlighting all the processes. In this...

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