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## Identification of a New Mechanism for Alzheimer-like Neurodegeneration

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One of the hallmark features of Alzheimer pathology is neurofibrillary tangles. These structures arise from abnormal behavior of a protein called tau. When tau becomes abnormally modified by the addition of phosphate groups (phosphorylation), it abandons its normal function and forms neurofibrillary tangles. Current models of Alzheimer's disease propose that these events are part of the disease process, but their role in that process is not understood.

Contrary to common belief, there is not widespread death of nerve cells in the early stages of Alzheimer's disease, even though conditions in the brain would be expected to cause cell death. Jianzhi Wang, M.D. and colleagues are studying this paradox. They have found evidence that formation of neurofibrillary tangles rather than being a step toward cell death, actually makes the cells less susceptible to death. This model suggests that neurofibrillary tangles are a key cause of nerve cell dysfunction and neurodegeneration, even though they do not cause direct cell death.

Dr. Wang and colleagues have planned a series of experiments to test this concept. They will test whether tau phosphorylation protects nerve cells from death when the cells are exposed to conditions normally causing death. For these studies, they will use mice that have been genetically altered to express Alzheimer-like pathology. These studies could help to define the pathologic mechanisms causing Alzheimer's disease, and possibly some of the molecular targets for potential drug therapy.