Proteins, like people, are often judged by the company they keep. p75, for instance, belongs to the same family as tumor necrosis factor. In addition to regulating neuronal growth, survival, and degeneration and guiding nerve fibers in growing embryos to their final destinations, it was widely thought to mediate cell death in some context.

Various in vitro studies have examined p75 in combination with beta amyloid, seeking evidence that it helps induce nerve cell death in Alzheimer's disease. A team of scientists in Lee's laboratory, however, found that p75 instead has a neuroprotective effect on the sympathetic nervous system.

Scientific interest in the peripheral nervous system has been growing as investigators studying neurodegenerative diseases seek new insights into disease progression. To gather evidence about p75 and the sympathetic nervous system, Lee's group crossed a mouse model for Alzheimer's disease with a line of mice genetically modified to lack the gene for p75. Without p75, they theorized, the neurotoxic effects of beta amyloid would be reduced, and the mice would show fewer Alzheimer's symptoms.

Along with profound motor problems, the p75-deficient mice exhibited severe defects in the wiring of nerves to multiple organs, and the majority died within just three weeks. (Mice normally live up to two years.) But when the researchers scaled down the production of toxic beta amyloid by deleting one copy of BACE1, which encodes the molecular shears that make the first cut in the production of beta amyloid fragments, the nerves in the sympathetic nervous system of p75-deficient mice were substantially restored.

This was the first time the interplay between p75 and beta amyloid in the peripheral sympathetic system has been demonstrated. Lee's findings not only challenge the prevailing view of p75's harmful role in Alzheimer's but could lead to new insights and, ultimately, new protocols for managing the secondary deficits that accompany the condition's hallmark dementia and memory loss.

For more information, please visit salk.edu/faculty/lee.html