Towards an in vitro stem cell model for Alzheimer's Disease

Abstract

Alzheimer's disease is a neurodegenerative disorder characterized by large amyloid protein aggregates. The causes of aggregate formation are unknown and have been difficult to study with rare human brain samples or current rodent models. An *in vitro* stem cell model for Alzheimer's disease would improve the study of aggregate formation, and here, we derive cell types needed for such a model. First, we generated a double transgenic mouse model with dominant autosomal mutations in the amyloid precursor protein and presenilin genes and affirmed amyloid beta aggregate formation in a nine-month time course in vivo. Second, we derived ernbryonic stem cell and induced pluripotent stem cell lines from these double mutant mice. Third, I differentiated these cells, in addition to Human embryonic stem cells into neurons expressing Emxl, a marker of cortical pyramidal neurons, which are profoundly affected by disease. Finally, I have begun to investigate whether amyloid aggregates are produced in this *in vitro* culture system. If cortical pyramidal neurons can be observed to selectively form aggregates in cells with the disease genotype, these cells could provide a cellular basis for an *in vitro* model of Alzheimer's disease. If so, this model provides a novel and powerful resource to elucidate early pathogenesis of the disease and allow us to screen for chemicals that inhibit aggregate formation and disease progression.