

Dr. Durakoglugil Murat and Dr. Florian Plattner

Alzheimer's disease (AD) is a devastating and unfortunately currently incurable disease. In the US, 1 in 9 people over age 65 have AD. In the population over the age of 85, the proportion goes up to 1 in 3 (Alzheimer's Association Statistical Report 2013). The current cost of treating AD in the U.S. is \$200 billion per year. As our nation ages and the number of affected individuals increases, that number is expected to rise to \$1 trillion by 2050 (Alzheimer's Association Statistical Report 2013). With no treatment or cure available, the impending AD epidemic imposes an unsustainable socioeconomic strain on our nation. New pathways and therapeutic targets must be found to develop a treatment for this terrible disease.

There are specific receptors on the surface of brain cell cells (NMDA receptors) which play fundamental role in memory formation, and perhaps not surprisingly their loss has been observed in AD patients. We recently characterized a novel molecular mechanism that controls the cell surface levels of these receptors. Based on this novel mechanism, we developed small drug-like compounds (NR2B-siP).

We hypothesized that these compounds might be useful for examining the role of NMDA receptor function in AD-related processes in rodent experiments but also more importantly may alleviate neuronal deficits and memory impairment in models of familial AD. Thus, we performed a biochemical and neurophysiological analysis of older AD mice that exhibit neuropathological hallmarks of AD such as plaques and deficits in NMDA receptors and memory. We evaluated the effect of NR2B-siP on these AD mice models and found that NR2B-siP treatment could, in fact, increase parameters for learning and memory. This memory enhancement effect could be maintained during the course of the experiments. Our results indicate that the molecular mechanism targeted by the NR2B-siP is not disrupted in AD mice and hence may be indeed targeted to enhance memory. Recently we are teasing out the different molecular components of these pathways.