

## Donor Progress Report for the Darrell K Royal Research Fund for Alzheimer's Disease of the Dallas Foundation

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Alzheimer's disease is rapidly becoming a socio-economic burden of sweeping proportions that dramatically affects the lives of millions of Alzheimer's disease sufferers, their family and friends, as well as their caregivers. One of the hallmarks of the disease is the accumulation of a protein fragment, called amyloid- $\beta$ . However, the molecular mechanisms underlying the toxicity of amyloid- $\beta$  remain poorly understood. Here, we are testing a novel hypothesis and focusing on the role of amyloid- $\beta$  in brain function and its effect on processes central to memory formation. In particular we are studying the interplay of amyloid- $\beta$  with a molecule called NR2B that is fundamental for learning and memory. Understanding these molecular pathways in detail is critical to our ability to develop effective therapeutic approaches for this devastating disease.

Our research is focused on the molecular processes that underlie learning and memory in mouse models of Alzheimer's disease and how these processes may be targeted to enhance memory performance. As part of this research project, we gained a deeper understanding of the interplay between amyloid- $\beta$  and molecules that are fundamental for processes underlying learning and memory. Moreover, we characterized a new mouse model of Alzheimer's disease that has a great potential to aid the further exploration of molecular processes underlying memory function and Alzheimer's disease. This mouse model will greatly help to progress our future studies. One significant finding of our research revealed that NR2B would be a suitable target to enhance memory functions and therefore may be used to develop new treatments for Alzheimer's disease.

Funding from the Darrell K Royal Research Fund for Alzheimer's Disease enabled us to conduct an initial set of crucial experiments into the role of amyloid- $\beta$  in memory processes and develop a new mouse model of Alzheimer's disease. These findings are an important first step towards a comprehensive understanding of the molecular basis of Alzheimer's disease and form the basis of our innovative research program. The challenge ahead of us now is to translate these findings into clinical applications for the benefit of Alzheimer's disease sufferers.

We are extremely grateful for the Darrell K. Royal Research Fund for Alzheimer's disease's gift. We would like to thank the Royal family, the directors, officers, advisers and all the supporters of the Fund for their generous contribution to our exploration of the molecular basis of Alzheimer's disease and the development of memory enhancers for the treatment of Alzheimer's disease.