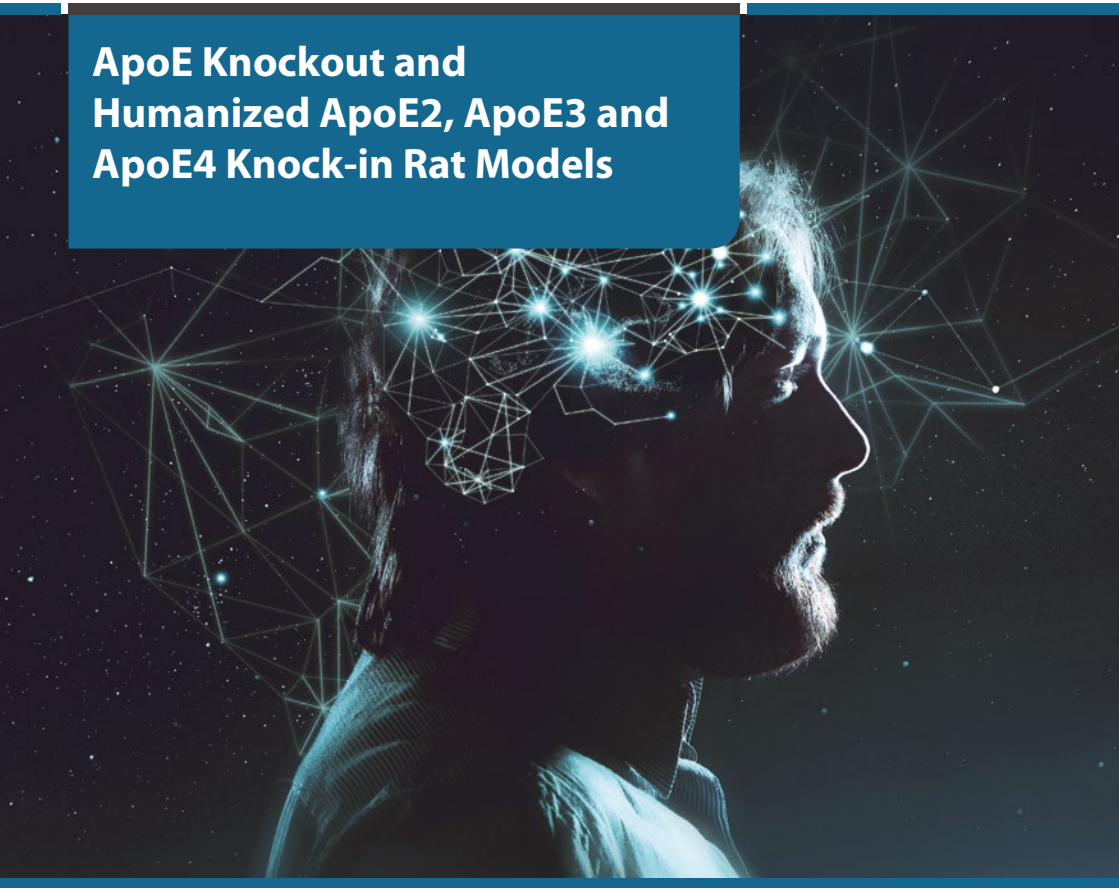
ApoE Knockout and Humanized ApoE2, ApoE3 and ApoE4 Knock-in Rat Models



In vivo models for Alzheimer's Disease

Horizon has generated the first knockout rats of Apolipoprotein E, as well as the first knock-in of humanized ApoE4. ApoE has been demonstrated to play an important role in the development of Alzheimer's disease (AD), and these unique models will be instrumental in further unravelling the role of ApoE, ApoE2, ApoE3 and ApoE4 in the pathology of AD.

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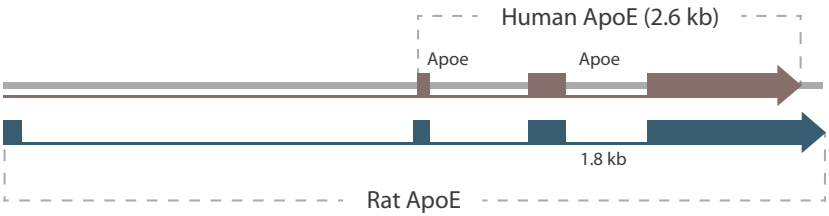
Translational models of Alzheimer's disease

Extensive studies have been conducted for the role of ApoE in cardiovascular disease and lipoprotein transport. ApoE4 has more recently been implicated as a major risk factor in Alzheimer's disease and cognitive degeneration. ApoE knockout rats and the Humanized ApoE2, ApoE3 and ApoE4 rats will be useful models for studies of Alzheimer's, diabetes, atherosclerosis and nerve injury.

The ApoE knockout rats were developed using targeted Zinc Finger Nuclease (ZFN) technology in the Sprague-Dawley strain. The humanized ApoE2, ApoE3 and ApoE4 knock-in rats were developed using CRISPR technology in the Sprague-Dawley strain. The colonies are maintained by mating homozygous males with homozygous females.

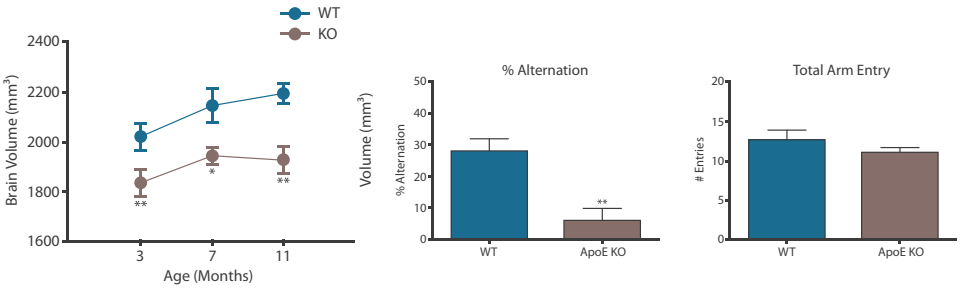
Genotype

Humanized ApoE4 Replacement at the Rat ApoE Locus



- ApoE KO: 16 base pair deletion within Exon 3 on chromosome 1. Frameshift results in premature stop codon
- Humanized ApoE4 KI: Homozygous replacement of the rat ApoE gene with the human ApoE4 gene

Homozygous knockouts display reduced brain volumes and impairments in working memory



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