Docket #: S19-305

N2N mice - Jackson Labs Stock No. 023607

The N2N allele contains a loxP site and an HA epitope upstream of exon 4, and a Frt-flanked neomycin resistance cassette (neo), followed by a luciferase sequence, downstream of exon 5, of the nuclear factor, erythroid derived 2, like 2 (Nfe212) gene. Nfe212 encodes NRF2, a member of the "cap 'n' collar" (CNC) subfamily of the basic region-leucine zipper transcription factors. NRF2 is a regulator of endogenous antioxidant protection, microglial function, and chronic neuroinflammation. Homozygotes are viable and fertile. In the absence of Cre, reporter gene expression is prevented by the floxed sequence (STOP). After removal of the loxP-flanked STOP cassette via cre-mediated recombination, the luciferase fusion construct behaves similar to wildtype protein where it is bound by Keap1, uibiquitiniated, and degraded by the proteosome; however during oxidative stress or induction by NRF2 activators, the luciferase fusion construct is released from KEAP1 and luciferase luminescence can be observed. As a result, this luciferase fusion construct functions as a reporter of NRF2 activity as well as a knockout for NRF2. Previous NRF2 mice containing inactivation of the CNC, DNA binding, and leucine zipper domains results in age-related macular degeneration (AMD)-like retinal pathology, spontaneous choroidal neovascularization (CNV), increased sensitivity to toxins, impaired adipogenesis, abnormal mitochondria, and an increase in proinflammatory gene expression in microglia and astrocytes. The donating investigator reports that luciferase is functional upon CRE recombination in vitro and in vivo. Functional luciferase activity was found in the skin, intestines, liver, and hindbrain.

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