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Alzheimer's disease is a neurological disorder that is characterized by two major hallmarks—the extracellular aggregation of beta-amyloid (Aβ) peptides to form Aβ plaques and the hyperphosphorylation of microtubule-binding protein tau to form neurofibrillary tangles (NFTs). The R47H loss-of-function variant in TREM2, a microglial transmembrane surface receptor that is important for cell survival and proliferation, was found to strongly increase the risk for developing Alzheimer's. Individuals with the R47H TREM2 variant were also found to have reduced microgliosis around Aβ plaques. These findings suggest that TREM2 induced microgliosis could protect against the aforementioned neuritic dystrophy and NFT formation, thereby slowing the progression of the disease. However, the specific effects of TREM2 activation still remain unclear. This study sought to establish a HEK cell line that expressed a functional TREM2-DAP12 cell membrane reporter to characterize its efficacy as a model for Alzheimer's, using TREM2 mAb agonists.

After establishing a puromycin kill curve to select 2 μg/mL of antibiotic as an optimal concentration for cell selection, TREM2-DAP12 transfected cells were tested at this dose to see whether they had been successfully transfected. High survival rates confirmed that the HEK cells had taken up the plasmid construct. A subsequent qPCR on the TREM2-DAP12 transfected cells and control HEK cells revealed that the transfected cells were able to amplify both TREM2 and DAP12 genes, indicating that they readily expressed both genes, in addition to the puromycin resistance gene. It was then discovered via fluorescence microscopy that hamster mAbs raised against the TREM2 receptor did not specifically bind to the TREM2-DAP12 surface receptor. This finding is insufficient to determine if the receptor is expressed on the cell surface and that the tested antibodies were specific to this receptor. Further testing is necessary to confirm the validity of this model via binding effects of the aforementioned agonists.