AlphaLISA[®] SureFire[®] Ultra[™] technology as a unique platform to demonstrate TREM2/DAP12 signalling cascade activation in the neuroinflammatory disease space abcam

TGR BioSciences an abcam company

1. Overview

- The triggering receptor expressed on myeloid cells-2 (TREM2), is one of the hottest targets in the neuroinflammatory disease space.
- TREM2 signals through its association with DAP12 with the stimulation of TREM2 and the subsequent phosphorylation of DAP12 resulting in the activation of spleen tyrosine kinase (SYK).
- TREM2/DAP12 pathway activation plays a key role in clearing neuronal debris and Aβ aggregates, thereby protecting the brain from neuroinflammation. Mutations in both TREM2 and DAP12 have been associated with Alzheimer's disease, Parkinson's disease and other neurogenerative disorders.
- The TREM2/DAP12/SYK signalling cascade has become highly important for the study of neurodegenerative diseases.
- This study highlights the utility of AlphaLISA® SureFire® Ultra™ technology to specifically measure TREM2 activation, with assays developed for TREM2/DAP12 Complex, Phospho DAP12 (Y91), Phospho SYK (Y525/526), TREM2 Aggregate & DAP12 Aggregate.

3. Results

Stimulation of TREM2 with a specific TREM2 Activator induces TREM2/DAP12 Complex formation and downstream cascade activation 3.1



TREM2 Activator stimulates the TREM2/DAP12 pathway in a dose-dependent manner 3.2



3.3



4. Conclusions

- development of TREM2 based therapeutic strategies.



Activation of TREM2 with an Anti N-terminal TREM2 Antibody triggers cascade phosphorylation and protein aggregation

• Here-in we describe the development of novel assays that specifically measure: TREM2/DAP12 (Y91), TREM2 Aggregate and DAP12 Aggregate. • Stimulation of TREM2 with a TREM2 Activator led to downstream phosphorylation of DAP12 (Y91) and SYK (Y525/526) proteins while also inducing TREM2 and DAP12 aggregation. ■ AlphaLISA[®] SureFire[®] Ultra[™] Technology has provided new tools for the study of TREM2 related mechanisms underlying neurodegenerative disease pathogenesis that could promote the

- Induction of TREM2 Aggregation TREM2 Aggregate DAP12 Aggregate 10000-**1000** 7500-750-NS 500-250-2500-Unstim Ab Unstim Ab

