Revision 1

Store at -20C

#92114

Human TREM2 Activity Antibody Sampler Kit

1 Kit (6 x 20 microliters)

Cell Signaling TECHNOLOGY®

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Product Includes	Product #	Quantity	Mol. Wt	Isotype/Source
TREM2 (D8I4C) Rabbit mAb	91068	20 µl	28 kDa	Rabbit IgG
TREM2 (E9U8L) Rabbit mAb (Amino-terminal Antigen)	70551	20 µl	28 kDa	Rabbit IgG
CD33 Antibody	77576	20 µl	70-80 kDa	Rabbit
Syk (D3Z1E) XP® Rabbit mAb	13198	20 µl	72 kDa	Rabbit IgG
Phospho-Syk (Tyr525/526) (C87C1) Rabbit mAb	2710	20 µl	72 kDa	Rabbit IgG
DAP12 (E7U7T) Rabbit mAb	97415	20 µl	10, 12 kDa	Rabbit IgG
Anti-rabbit IgG, HRP-linked Antibody	7074	100 µl		Goat

Please visit cellsignal.com for individual component applications, species cross-reactivity, dilutions, protocols, and additional product information.

Description

The Human TREM2 Activity Antibody Sampler Kit provides an economical means of evaluating key members of the human TREM2 signaling pathway using phospho-specific and control antibodies. The kit includes enough antibodies to perform two western blot experiments with each primary antibody.

Storage

Supplied in 10 mM sodium HEPES (pH 7.5), 150 mM NaCl, 100 µg/mL BSA, 50% glycerol, and less than 0.02% sodium azide. Store at –20°C. *Do not aliquot the antibodies.*

Background

Alzheimer's Disease (AD) is one of the most common neurodegenerative diseases worldwide. Clinically, it is characterized by the presence of extracellular amyloid plaques and intracellular neurofibrillary tangles, resulting in neuronal dysfunction and cell death. Triggering receptor expressed on myeloid cells 2 (TREM2), a protein localized at the membrane of innate immune cells, including microglia in the brain, has been genetically linked to AD, with specific variants increasing disease risk by as much as threefold (1,2). The TREM2 receptor is a single-pass type I membrane glycoprotein that consists of an extracellular immunoglobulin-like domain, a transmembrane domain, and a cytoplasmic tail. Upon activation, TREM2 interacts with the tyrosine kinase-binding protein DNAX-activating protein 12 (DAP12, TYROBP) to form a receptor-signaling complex. The DAP12 protein structure consists of a short extracellular domain, a transmembrane domain, and a cytoplasmic immunoreceptor tyrosine-based activation motif (ITAM) (2-9). ITAMs function as a binding site for tyrosine kinases, including spleen tyrosine kinase (Syk). Syk is comprised of two tandem amino-terminal Src homology (SH) 2 domains separated by an SH2-kinase linker, and a C-terminal tyrosine kinase domain, separated from the SH2 domains by an inter-domain linker. When Syk binds to an ITAM, it changes conformation, allowing for residues within the inter-domain linker region, including Tyr352, to become phosphorylated. Residues within the activation loop subsequently become phosphorylated, leading to full Syk activation. Tyr525 and Tyr526 are located in the activation loop of the Syk kinase domain and phosphorylation at these residues (equivalent to Tyr519/520 of mouse Syk) is essential for Syk function (10-12). This activation can lead to the mediation of a variety of cellular responses, including proliferation, differentiation, inflammation, and phagocytosis. Evidence suggests that TREM2 and DAP12 may act in a Syk-dependent manner to drive microglial cellular responses in AD (2,4-8,13).

There is also evidence that these processes may be regulated via crosstalk between TREM2 and the cell surface receptor CD33, a sialic acid-binding Ig-like lectin (Siglec-3) type I transmembrane protein. Much like *TREM2*, *CD33* has been identified as a risk gene in AD. CD33 binds preferentially to alpha-2, 6-linked sialic acid, which can be found in sialylated gangliosides in the brain. Activation of CD33 has been shown to be inhibitory to a variety of cellular processes. Evidence suggests that TREM2 may act downstream of CD33 and that TREM2-dependent microglial signaling in AD may be directly inhibited by CD33 activation (14-17).

Background References

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