TREM1

(Triggering Receptor Expressed on Myeloid cells 1) It is an immune receptor found predominantly on myeloid lineage cells such as monocytes, macrophages, and microglia. It acts as a powerful amplifier of inflammatory responses.

Key Facts About TREM1

Structure and Expression Type: Cell surface receptor, part of the immunoglobulin superfamily.

Expressed on:

Monocytes/macrophages

Neutrophils

Microglia (especially in pathological states)

Usually low or absent at rest, but upregulated during infection, inflammation, or cancer.

⚙ Function Acts via DAP12, an adaptor protein that transmits activating signals.

Amplifies TLR (Toll-like receptor)-mediated responses → enhances cytokine and chemokine release (e.g., TNF-α, IL-6, IL-1β).

In microglia, it promotes:

Proinflammatory plasticity

Phagocytic activity

Response to brain injury and tumors

TREM1 in Neurological Disease In glioblastoma (as shown in the PNAS 2025 paper):

Tumor-derived extracellular vesicles (EVs) deliver TREM1 or activate its signaling in microglia.

This reprograms microglia toward a tumor-supportive phenotype via the SYK–PDK–STAT3 pathway.

In Alzheimer’s disease, TREM1 has been linked to exacerbated inflammation and worse outcomes.

In stroke and brain injury, TREM1 contributes to secondary neuroinflammation.

Therapeutic Target Potential TREM1 blockade reduces:

Inflammation in sepsis

Tumor progression in GBM (shown in animal models)

Inhibitors:

LP17 peptide (experimental)

TREM1-Fc decoy receptor

Small molecules under development

⚠ Therapeutic targeting must balance immune suppression with retaining antimicrobial defense.

 Pathways Downstream of TREM1 DAP12 → SYK → PDK1 → STAT3

Promotes:

Cell survival

Cytokine expression

Metabolic reprogramming