

SYK (Spleen Tyrosine Kinase)

SYK is a cytoplasmic tyrosine kinase involved in innate and adaptive immune signaling. It plays a critical role in the activation of immune cells such as B cells, macrophages, microglia, and mast cells.

General Information

- **Full name:** Spleen Tyrosine Kinase
- **Gene:** SYK (Chromosome 9)
- **Protein type:** Non-receptor tyrosine kinase
- **Location:** Cytoplasm
- **Expressed in:**
 - B cells
 - Myeloid cells (e.g., macrophages, microglia, dendritic cells)
 - Mast cells
 - Platelets

Functions

- Transduces signals from ITAM-bearing receptors such as:
 - B Cell Receptor (BCR)
 - Fc receptors (FcγR, FcεR)
 - TREM1 (via DAP12 adaptor)
- Activates key intracellular signaling pathways:
 - **PI3K/AKT**
 - **MAPK/ERK**
 - **NF-κB**
 - **PDK1 → STAT3**

In the Central Nervous System

- In microglia, SYK mediates:
 - Inflammatory activation
 - Cytokine release
 - Phagocytosis
- In glioblastoma (GBM):
 - Activated via TREM1 on microglia
 - Promotes tumor-supportive immune environment via SYK-PDK-STAT3 axis

Pathological Involvement

- **Autoimmune disorders:** rheumatoid arthritis, lupus
- **B-cell malignancies:** lymphomas

- **CNS disorders:**
 - Glioblastoma progression
 - Alzheimer's disease (via microglial dysfunction)
- **Allergy:** mast cell degranulation

Therapeutic Targeting

- **Fostamatinib:** FDA-approved SYK inhibitor (for chronic ITP)
- Clinical trials for:
 - Autoimmunity
 - Cancer
 - Neuroinflammation

SYK Signaling Pathway (Simplified)

1. Receptor activation (e.g., TREM1)
2. ↓ ITAM phosphorylation
3. ↓ SYK recruitment and activation
4. ↓ Downstream signals:
 - **PDK1 → STAT3** (proinflammatory transcription)
 - **PI3K-AKT** (cell survival, metabolism)
 - **NF-κB** (cytokine expression)

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