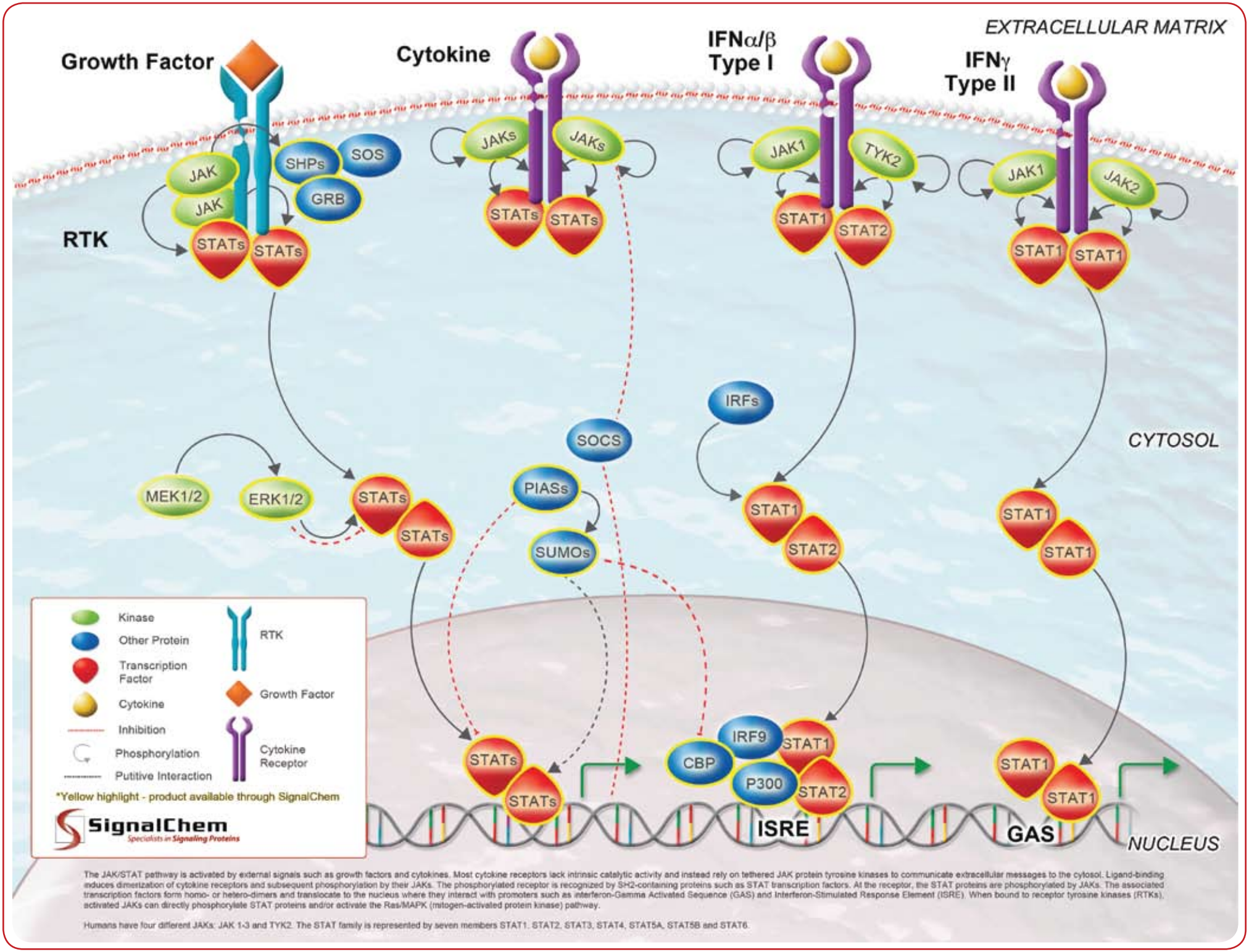

The JAK/STAT pathway is activated by external signals such as growth factors and cytokines. Most cytokine receptors lack intrinsic catalytic activity and instead rely on tethered JAK protein tyrosine kinases to communicate extracellular messages to the cytosol. Ligand-binding induces dimerization of cytokine receptors and subsequent phosphorylation by their JAKs. The phosphorylated receptor is recognized by SH2-containing proteins such as STAT transcription factors. At the receptor, the STAT proteins are phosphorylated by JAKs. The associated transcription factors form homo- or hetero-dimers and translocate to the nucleus where they interact with promoters such as interferon-Gamma Activated Sequence (GAS) and Interferon-Stimulated Response Element (ISRE). When bound to receptor tyrosine kinases (RTKs), activated JAKs can directly phosphorylate STAT proteins and/or activate the Ras/MAPK (mitogen-activated protein kinase) pathway.

Humans have four different JAKs: JAK 1-3 and TYK2. The STAT family is represented by seven members STAT1, STAT2, STAT3, STAT4, STAT5A, STAT5B and STAT6.