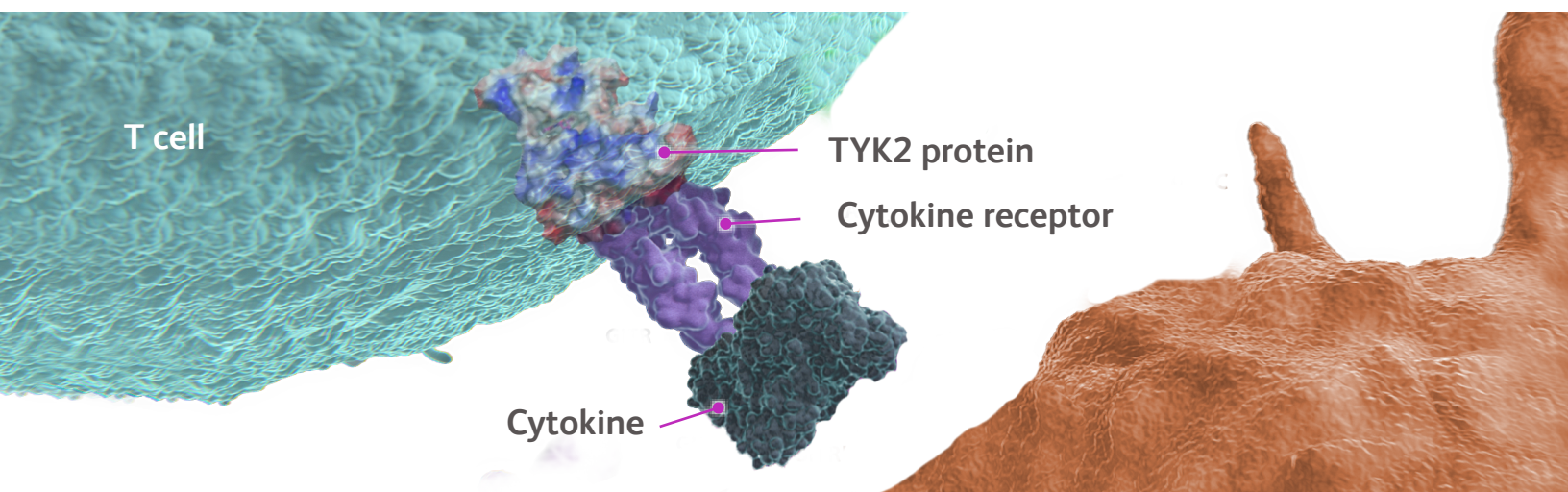


Tyrosine Kinase 2 (TYK2) Immune Pathway



About TYK2

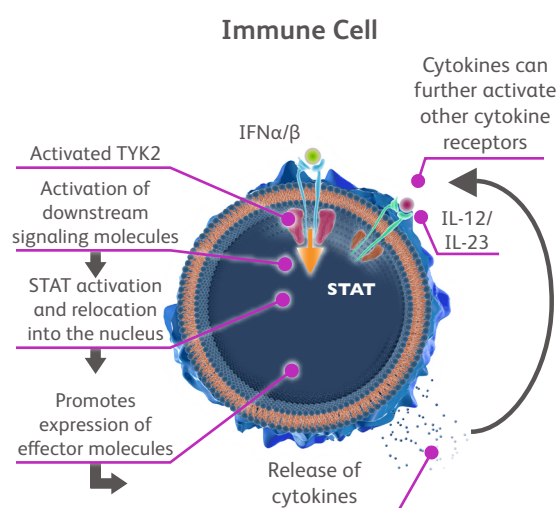
Tyrosine kinase 2 (TYK2) is an intracellular enzyme that mediates immune signaling and inflammatory signaling pathways.¹⁻⁷ TYK2 is important in both innate and adaptive immune cells. In a healthy person, TYK2 is an essential component of maintaining normal immune responses.

TYK2 and Immune Function

TYK2 activates a series of transcription factors called signal transducer and activator of transcription (STAT).⁸

Activated STATs promote expression of cytokines and cellular processes such as cellular division, differentiation and death.⁸

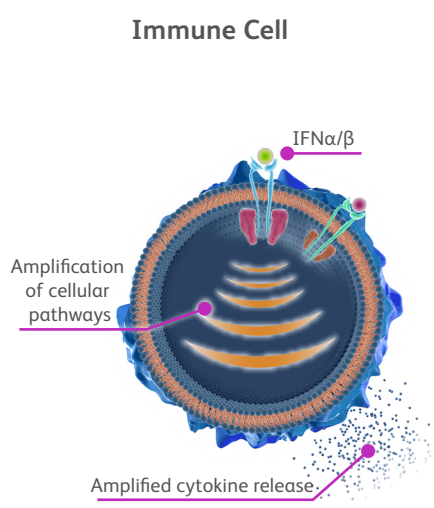
By binding to specific receptors, cytokines signal through TYK2 to regulate the immune system. These cytokines include IL-12, IL-23 and Type I IFNs, which are critical in driving the function of Th1 cells, Th17 cells and the innate immune response.^{8,9}



TYK2 and Pathology

Immune cells are correlated with the pathogenesis of immune-mediated diseases such as psoriasis, lupus, psoriatic arthritis and inflammatory bowel disease.¹⁰

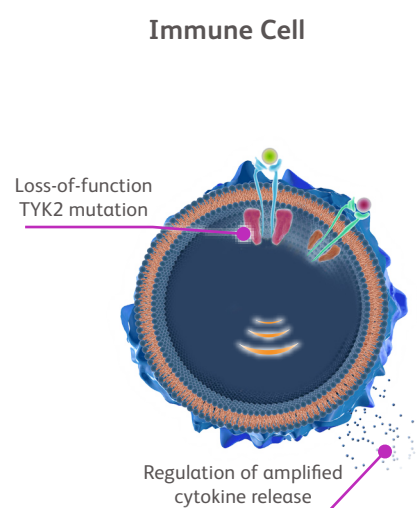
TYK2 plays a critical role in driving these pathways and generating an effect in multiple immune-mediated disorders.¹¹



Research Implications and Interactions

Advancements in the understanding of TYK2 signaling and activation have resulted in the investigation of this pathway for the potential of therapeutic intervention.

Through the regulation of overproduction of immune-inflammatory components, it may be possible to have an effect on immune-mediated diseases.



The TYK2 pathway is one of many pathways under investigation at Bristol Myers Squibb.

Learn more about our work in Immunology by visiting:

www.bms.com/researchers-and-partners/areas-of-focus.html

1. Min X, et al. J Biol Chem 2015;290:27261-27270.
 2. Jani M, et al. Ann Rheum Dis 2014;73:1750-1752.
 3. Smith JA, Colbert RA. Arthritis Rheumatol 2014;66:231-241.
 4. Hofer MJ, Campbell IL. Cytokine Growth Factor Rev 2013;24:257-267.
 5. Paniagua RT, et al. J Am Acad Dermatol 2011;65:389-403.
 6. O'Sullivan LA, et al. Mol Immunol 2007;44:2497-2506.
 7. Burke JR, et al. Sci Transl Med 2019;11:eaaw1736.
 8. Leitner NR, et al. Tyrosine kinase 2 – Surveillant of tumours and bona fide oncogene. Cytokine. 2017; 89: 209-218.
 9. Paunovic V, et al. Crossed signals: the role of interleukin (IL)-12, -17, -23 and -27 in autoimmunity. Rheumatology. 2008; 47:771-776.
 10. Li Z, et al. Two Rare Disease-Associated Tyk2 Variants Are Catalytically Impaired but Signaling Competent. J Immunol. 2013; 190(5):2335-44.
 11. Dendrou et al., Resolving TYK2 locus genotype-to-phenotype differences in autoimmunity. Sci Transl Med. 2016;8:363ra149.