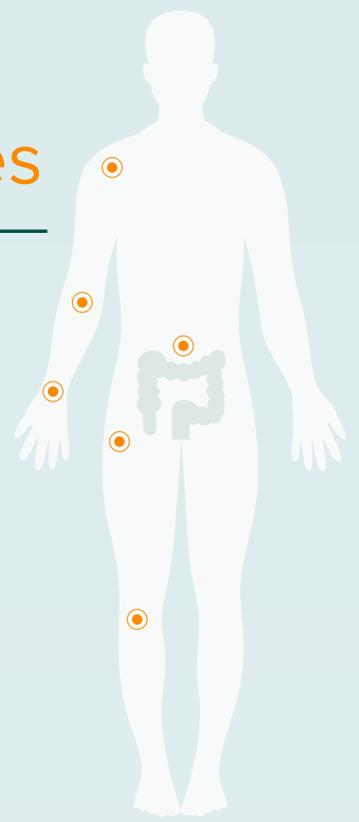


# JAK INHIBITORS

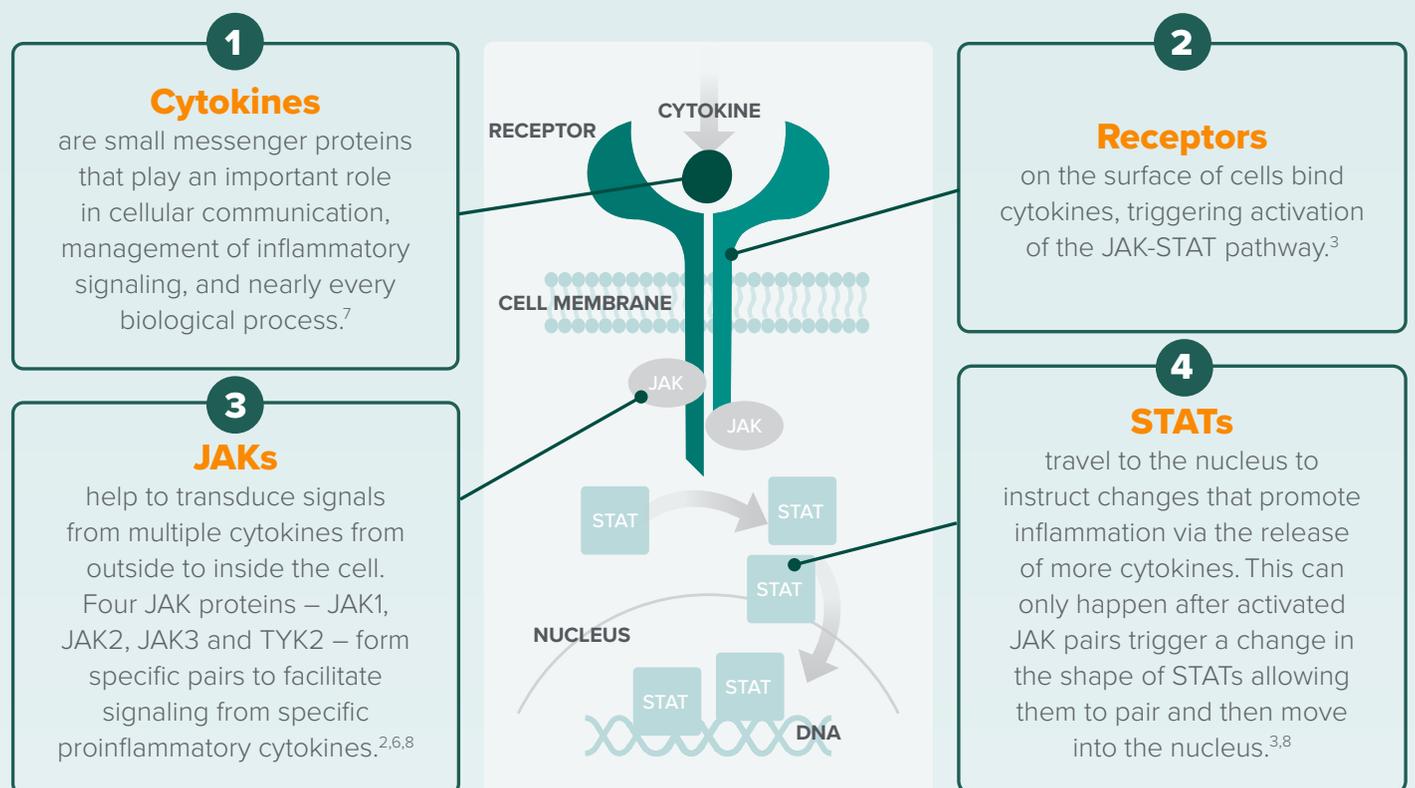
## in Chronic Inflammatory Diseases



People with chronic inflammatory diseases have excessive levels of proinflammatory cytokines.

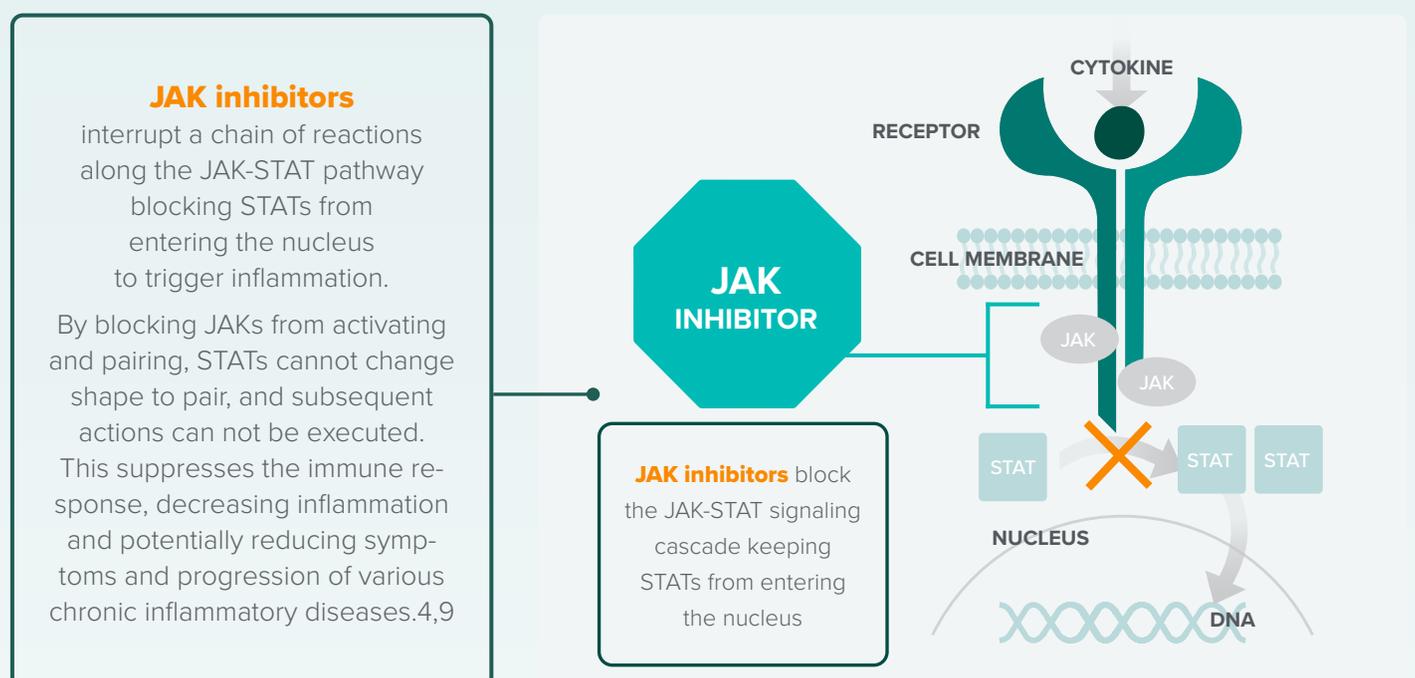
Cytokines bind to the receptors on the surface of immune cells and activate the Janus Kinase Signal Transducer and Activator of Transcription, or JAK-STAT, pathway. Activation of the pathway triggers the production of greater levels of proinflammatory cytokines perpetuating a cycle of chronic inflammation.<sup>1,2,3</sup>

The JAK-STAT pathway is critical for important functions within the body and is associated with numerous chronic inflammatory diseases such as rheumatoid arthritis, psoriatic arthritis, ulcerative colitis, and Crohn's disease.<sup>3,4,5,6</sup>



### JAK INHIBITORS MAY HELP NORMALISE EXCESSIVE CYTOKINE SIGNALING

Left unchecked, excessive cytokine signaling via JAK-STAT will continue, contributing to the chronic inflammation that underlies the typical signs of inflammatory disease.<sup>5</sup>



#### References

- Clark, J., et al. Discovery and Development of Janus Kinase (JAK) Inhibitors for Inflammatory Diseases. *Journal of Medicinal Chemistry*. 2014;57(12):5023–5038. Available at: <https://pubs.acs.org/doi/10.1021/jm401490p>. Accessed May 2021.
- Gadina, M., et al. Janus Kinases to Jakinibs: from basic insights to clinical practice. *Rheumatology (Oxford)*. 2019;58(1):i4-i6. Available at: <https://pubmed.ncbi.nlm.nih.gov/30806710/>. Accessed May 2021.
- Schwartz, D. M., et al. Type I/II cytokines, JAKs, and new strategies for treating autoimmune diseases. *Nature reviews. Rheumatology*. 2016;12(1):25–36. Available at: <https://doi.org/10.1038/nrrheum>. Accessed May 2021.
- O'Shea JJ., et al. Janus kinase inhibitors in autoimmune diseases. *Ann Rheum Dis*. 2013;72:2(0:2):ii111-ii115. Available at: <https://pubmed.ncbi.nlm.nih.gov/23532440/>. Accessed May 2021.
- Malemud, C.J. The role of the JAK/STAT signal pathway in rheumatoid arthritis. *Integr Mol Med*. 2016;3:1-9. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6009092/>. Accessed May 2021.
- Winthrop KL. The emerging safety profile of JAK inhibitors in rheumatic disease. 2017;13:234-243. *Nature Review Rheumatology*. Available at: <https://www.nature.com/articles/nrrheum.2017.23>. Accessed May 2021.
- Dinarello C. A. Historical insights into cytokines. *European journal of immunology*. 2007; 37:1 (1):S34–S45. Available at: <https://doi.org/10.1002/eji.200737772>. Accessed May 2021.
- O'Shea, JJ., et al. The JAK-STAT pathway: impact on human disease and therapeutic intervention. *Annu Rev Med*. 2015;66:311-328. Available at: <https://pubmed.ncbi.nlm.nih.gov/25587654/>. Accessed May 2021.
- Banerjee, S. et al. Drugs. JAK-STAT Signaling as a Target for Inflammatory and Autoimmune Diseases: Current and Future Prospects. 2017;77(5):521-546. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7102286/>. Accessed May 2021.