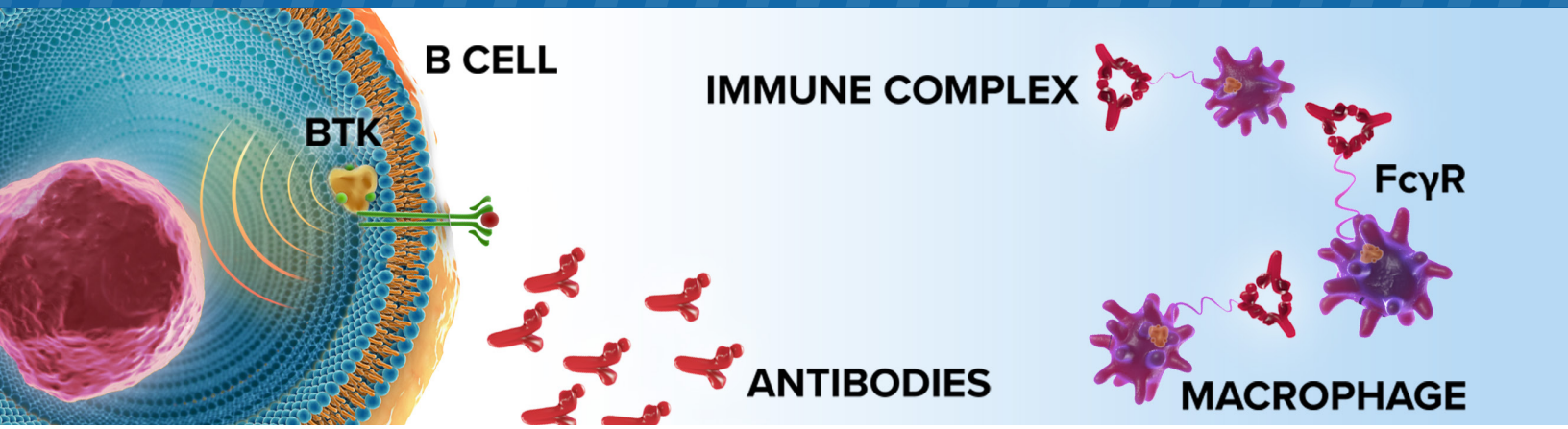
Bruton's Tyrosine Kinase (BTK) Pathway Fact Sheet



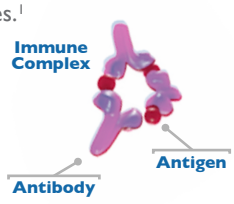
About BTK

Bruton's tyrosine kinase (BTK) is an enzyme found inside certain immune cells that plays a fundamental role in the immune response to antigens, which are proteins recognized as foreign materials in the body.[1,2]

BTK works with activated receptors on the surface of immune cells to transfer signals into the cell and inform immune responses.

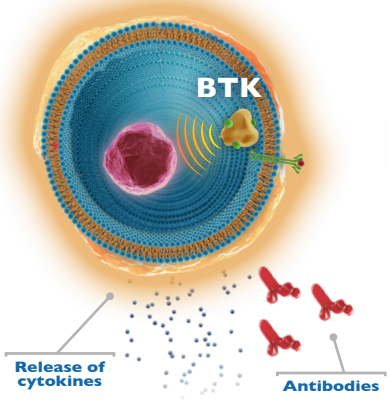
BTK and Immune Function

- BTK pathway signaling is fundamental for the functionality and survival of B cells, a type of specialized immune cell.
- In the B cell, immune responses to antigens are mediated through BTK interaction with B cell receptors (BCR).
- When B cells recognize antigens through BCR, BTK interacts with BCR and initiates a signaling cascade critical to the production of antibodies, proinflammatory cytokines and chemokines, as well as influencing antigen presentation on B cells.[2]
- BTK is also expressed to high levels in certain myeloid cells, such as macrophages and granulocytes. In these cells, receptor activation by immune complexes promotes BTK signaling and expression of proinflammatory cytokines and cell adhesion molecules.[1]
- Collectively, these actions allow the immune system to selectively target antigens for destruction.



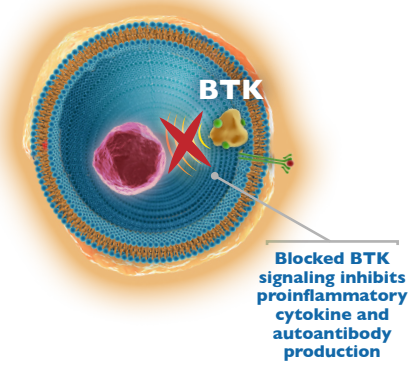
BTK and Disease

- While these actions enable antigen destruction, when the immune system mistakes self-proteins as foreign antigens and activates these destructive pathways, this action can lead to autoimmunity.
- The BTK pathway's role in the production of autoantibodies and proinflammatory cytokines has been linked to a number of autoimmune disorders, including rheumatoid arthritis and lupus.[1,3]



Clinical Implications and Interactions

- Loss of BTK functionality in certain immune cells modulates multiple signalling pathways simultaneously, and has been linked to compromised inflammatory responses or protective effects in preclinical models of autoimmune diseases.[1,4]



The BTK pathway is one of many pathways under investigation at Bristol-Myers Squibb. Learn more about our work in immunoscience by visiting:
https://www.bms.com/researchers-and-partners/areas-of-focus.html

[1] Chu AD, Chang BY. B-cell kinase inhibitors in rheumatoid arthritis. OA Arthritis 2013 Oct 27;1(2):17. [2] Pablo Engel, José A. Gómez-Puerta, Manuel Ramos-Casals, Francisco Lozano, Xavier Bosch. Therapeutic targeting of B cells for rheumatic autoimmune diseases. Pharmacol Rev. 2011 Mar; 63(1): 127–156. Published online 2011 Jan 18. doi: 10.1124/pr.109.002006 [3] A. Rankin, et al. Selective Inhibition of BTK Prevents Murine Lupus and Antibody-Mediated Glomerulonephritis. The Journal of Immunology November 1, 2013, 191 (9) 4540-4550; DOI: 10.4049/jimmunol.1301553 [4] Cheung TT, McInnes IB. Future therapeutic targets in rheumatoid arthritis? Seminars in Immunopathology. 2017;39(4):487-500. doi:10.1007/s00281-017-0623-3.

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