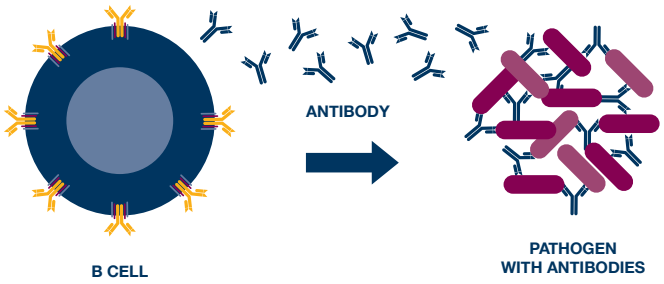
The Role of BTK Inhibition to Disrupt Cancerous B-Cell Function

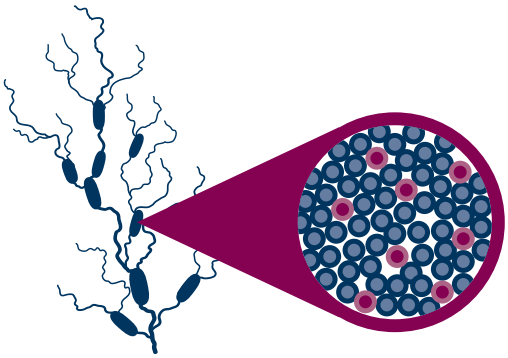
Normal B cells and the immune system



B cell attacking bacteria/virus

B cells play an essential role in the immune system. These lymphocytes, a type of white blood cell, produce antibodies that attack invading pathogens such as bacteria, viruses and toxins.[1]

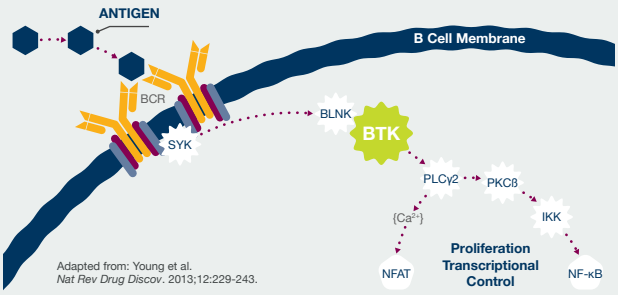
B cells and cancer



Cancerous B cells (purple cells) crowding out normal B cells (blue cells) in a lymph node

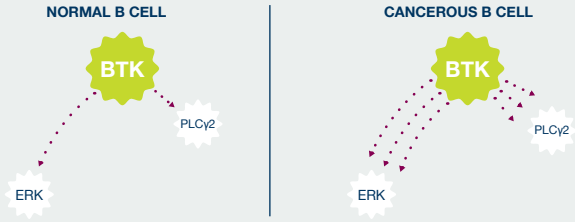
When B cells become cancerous, such as in chronic lymphocytic leukemia (CLL) and mantle cell lymphoma (MCL), some normal cell processes aren't regulated properly, resulting in increased production of B cells. The excess cancerous B cells crowd out the normal cells in the bone marrow and lymph nodes.[2,3]

Normal B cell and BTK



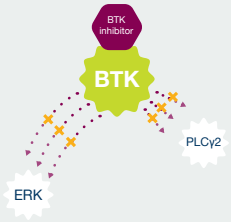
B cells contain an enzyme (or kinase), called the Bruton's tyrosine kinase (BTK), that plays a key role in B-cell receptor signaling. This signaling regulates the development, function and survival of B cells.[4,5]

BTK Expression



The number of BTK receptors on the surface of a B cell (BTK expression) has been reported to be higher in certain B-cell malignancies compared to normal B cells, which may allow cancerous B cells to grow and multiply.[6]

BTK Inhibition



Research has shown that blocking BTK function reduces the growth and cell survival among cancerous B cells.[7]

1. Institute for Quality and Efficiency in Health Care (IQWiG). The defense mechanisms of the adaptive immune system. Cologne, Germany; 2006. https://www.ncbi.nlm.nih.gov/books/NBK279396/. Accessed August 2020. **2.** Horn R. Descending the Helix. 2011, pp. 221. Retrieved from: https://goo.gl/vu57Jw. **3.** American Society of Hematology. Blood Cancers. http://www.hematology.org/Patients/Cancers/. Accessed August 2020. **4.** Maas A, Hendriks R. Role of Bruton's Tyrosine Kinase in B Cell Development. *Dev Immunol*. 2001;8(3-4):171-181. Retrieved From: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2276078/pdf/CDI-08-171.pdf. Accessed August 2020. **5.** Küppers R. Mechanisms of B-cell Lymphoma Pathogenesis. *Nat Rev Cancer*. 2005;5:251-262. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/15803153. Accessed August 2020. **6.** Grassilli E, Pisano F, Cialdella A, et al. A novel oncogenic BTK isoform is overexpressed in colon cancers and required for RAS-mediated transformation. *Oncogene*. 2016;35(33):4368-4378. doi:10.1038/onc.2015.504. **7.** Hendriks RW, Yuvaraj S, Kil LP. Targeting Bruton's tyrosine kinase in B cell malignancies. *Nat Rev Cancer*. 2014;14(4):219-232. doi:10.1038/nrc3702.

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