Exploring BTK Further to Address the Specific Molecular Processes Behind B-Cell Malignancies

- Our growing understanding of the relationship between BTK and the tumor microenvironment may help to further unravel the molecular processes underlying B-cell malignancies.
- Understanding these molecular processes may help guide research into resistant disease and highly targeted therapeutic strategies.
- Pharmacyclics, Inc., and Janssen Biotech, Inc., are currently investigating BTK in search of insights that could improve the lives of patients with B-cell malignancies.

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References:

Defining new directions in B-cell malignancies*

A Critical Connection Between B-Cell Signaling and the Tumor Microenvironment

The evolving understanding of the microenvironment and Bruto's tyrosine kinase (BTK) is helping to elucidate specific molecular targets that drive B-cell malignancies.1
In B-cell malignancies, the tumor microenvironment includes the stromal cells, T cells, soluble factors, and other cells in the lymph nodes and bone marrow that continuously influence B-cell development and growth. Interactions between the microenvironment and multiple signaling pathways within B cells suggest an important role in B-cell homing, adhesion, and migration, and help to maintain the normal, balanced functioning of B cells. When the interactions become dysregulated, they can promote the progression of B-cell malignancies.

BTK, an essential component of the B-cell receptor (BCR) and other pathways, appears to play a critical role in these dysregulated interactions.

**BTK signaling pathways and the microenvironment**

**Adhesion and Migration**

Adhesion molecules expressed by cells in the microenvironment bind to receptors on the surface of B cells to allow them to migrate through lymphoid tissues. These adhesion molecules also help to retain B cells within the lymph node microenvironment, where the B cells can proliferate. BTK is an essential mediator of multiple adhesion and migration processes.

**Intracellular Pathways Reliant on BTK Exploit Microenvironment Cues to Drive B-Cell Malignancies**

Creative representation of select simplified signaling pathways.

**Prosurvival Signals**

Normal B cells rely on a complex network of prosurvival pathways, such as the BCR pathway, to avoid apoptosis. In B-cell malignancies, microenvironmental cues may inappropriately activate some of these pathways. This initiates signaling cascades through several kinases, including BTK, driving uncontrolled growth and survival of malignant B cells.