

## ABSTRACT

Based on these data, Btk:ER is thought to regulate downstream signaling pathways in B cells primarily via PLC2 (i.e., regulatory protein coupled with nuclear protein chainase inhibitor PLSI 2), and thus it is not known whether activated BukR/STK copy-pasteurs interact with activated Btky receptor expressed as a "conditional system", but this condition will probably allow for the dissection of Btk's (and other) role in various biological processes in many cell types.

## INTRODUCTION

The B cell lymphocytes (BCL) are the most common type of lymphocyte in the human body, and they play a key role in the host's immune response. BCLs have been shown to be able to express multiple kinases such as tyrosine kinase (TRK) and phosphatidylinositol 3-kinase (PI3K), which are involved in a wide range of biological functions. However, their role in the host's immune response is poorly understood; the functional roles of BCLs in the immune response have been largely ignored.

Our aim is to develop a conditional form of tyrosine kinase (TYK) that can activate multiple downstream signaling pathways via PLC Gamma 2 in Btk mutations, which are responsible for the human disease X-linked agammaglobulinemia (reviewed in reference), cause a severe blockage in the pro-B cell transition and result in no mature B cells. It is hypothesized that a two-way process involving PI 3-kinase and Src family PTK Lyn activates Btk upon cross-linking of the BCR. This enzyme causes Btk to become phosphorylated upon binding to the PH domain of Btk. The significance of Btk in BCR-induced phospholipase (PLC2) phosphatidyltransferase, calcium mobilization, ERK, and NF- $\kappa$ B activation and JNK-mediated signaling in deficient B cells has been established through biochemical analyses. However, it is not clear whether all downstream signals mediated by BTK are PLC2-dependent or if Btk alone can perform these functions. By combining the full-length Btk protein with the hormone-binding domain of the estrogen receptor (Btk:ER), we have produced a conditional variant of BTK. We demonstrate that Btk:ER kinase inhibitor BKT-1, KAL1, PLC-2, and PKC-K2 activation alone can activate various downstream signaling pathways in B cells, including calcium mobilization, ERK and JNK MAPK, as well as cellular death by mice.

## CONCLUSION

Remarkable conclusions The Btk mutations observed in XLA patients and the xid mouse indicate that Btk is essential for B cell development, but the important pathways activated by Btk remain unresolved. In our paper, we demonstrate that a conditional form of Btk can activate multiple signaling pathways downstream of the antigen receptor, including PLC2 phosphorylation, calcium mobilization (MS) activation or ERK and JNK activation, and that all Btk-mediated responses are dependent on Btk genes.