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ABS105: REACTIVE OXYGEN SPECIES PLAY A ROLE IN ENDOSOMAL B CELL ANTIGEN RECEPTOR (BCR) SIGNALING

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Ligation of the B cell receptor (BCR) initiates B cell signaling and internalization to endosomes. BCR ligation also generates reactive oxygen species (ROS). ROS may act as a secondary messenger in cell signaling. This study addressed the role of ROS in endosomal B cell antigen receptor (BCR) signaling.

Anti-IgM stimulation of Quasi Monoclonal (QM) mouse B cells strongly induced ROS which was detected by flowcytometry using carboxy-H₂DCFDA assay. BCR ligated B cells treated with NADPH oxidase inhibitor resulted in clear reduction of ROS while, in unstimulated cells mitochondria inhibition significantly reduced cellular ROS. Following ligation more than 80% BCR was internalized within 1 hour. The internalized BCR entered early endosomes by 10 minutes and translocated to late endosomes by 2 hours. Internalized IgM was found to remain in the late endosome even at 24 hours. Cell proliferation assay of QM mouse B cells stimulated with anti IgM antibody after 48 hours showed markedly reduced cell proliferation in the presence of ROS inhibitor N-acetyl cysteine (NAC) indicating that ROS is involved in late BCR signaling. BCR mediated Calcium signaling was not dependent on ROS. Anti IgM antibody ligation induced phosphorylation of tyrosine and Akt at the endosome which was retarded in the presence of NAC, suggesting the potential involvement of the endosome in ROS generation and ROS dependent signal transduction. In conclusion the findings suggest that ROS was not required for early BCR signaling but plays a role in later stages of B cell signaling and cellular proliferation.