The NF-κB signaling protein Bcl10 regulates actin dynamics by controlling AP1 and OCRL-bearing vesicles.

The protein Bcl10 contributes to adaptive and innate immunity through the assembly of a signaling complex that plays a key role in antigen receptor and FcR-induced NF-κB activation. Here we demonstrate that Bcl10 has an NF-κB-independent role in actin and membrane remodeling downstream of FcR in human macrophages. Depletion of Bcl10 impaired Rac1 and PI3K activation and led to an abortive phagocytic cup rich in PI(4,5)P(2), Cdc42, and F-actin, which could be rescued with low doses of F-actin depolymerizing drugs. Unexpectedly, we found Bcl10 in a complex with the clathrin adaptors AP1 and EpsinR. In particular, Bcl10 was required to locally deliver the vesicular OCRL phosphatase that regulates PI(4,5)P(2) and F-actin turnover, both crucial for the completion of phagosome closure. Thus, we identify Bcl10 as an early coordinator of NF-κB-mediated immune response with endosomal trafficking and signaling to F-actin remodeling.