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# Swiprosin 1 – regulator of proximal BCR signaling

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The adaptor protein Swiprosin-1/Efhd2 that we identified recently in B cell lipid rafts exhibits its highest expression in immature B cells. Swiprosin-1/Efhd2 consists of a proline rich domain, two EF-hands and a C-terminal coiled-coil domain. Knock-down of Swiprosin-1/Efhd2 in an immature B cell line with a shRNA directed against the 3'-UTR (WEHI231shSw1) impaired spontaneous and BCR-elicited apoptosis. Due to co-clustering of a Swiprosin-1-EGFP fusion protein with the B-cell receptor we expected Swiprosin-1 to be a player in proximal BCR signaling. Indeed, downregulation of Swiprosin-1 attenuated total tyrosine phosphorylation and diminished BCR induced intracellular calcium flux. In contrast, WEHI231 cells ectopically expressing Swiprosin-1 showed increased, but shortened total tyrosine phosphorylation at early time points, as well as increased BCR induced calcium flux. Concomitantly, transient re-expression of Swiprosin-1 in WEHI231shSW1 cells restored BCR-induced calcium flux.

These data suggested interactions of Swiprosin-1 with central elements of the BCR signaling cascade. In fact, GST-pulldown experiments showed that Swiprosin-1 can interact with tyrosine-phosphorylated proteins of ~145 and 70 kDa. With this assay we identified the protein tyrosine kinase Syk in its phosphorylated form as interaction partner of Swiprosin-1. The interaction of pSyk with Swiprosin-1 is mediated by the C-terminal part of Swiprosin-1 because a deletion mutant of Swiprosin-1 lacking the EF-hands and the coiled-coil domain of Swiprosin-1 did not show any interaction with pSyk. We next tested the kinase activity of Syk as a function of Swiprosin-1 levels. Interestingly, immune complex kinase assays showed that BCR-induced Syk activity was reduced in WEHI231shSw1 cells

Hence, Swiprosin-1 could regulate proximal BCR signaling through maintenance of Syk activity.