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Role of fyn in SEB mediated signaling in memory CD4 T cells

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Fyn is an important protein tyrosine kinase in TCR mediated signaling pathway. Earlier it was found that the superantigen, Staphylococcal enterotoxin B (SEB) induces robust activation of naïve CD4 T cells but induces anergy/tolerance in memory CD4 T cells. Interaction of SEB with the antigen receptor on T cells (TCR) leads to altered or impaired signal transduction in memory cells. During signaling a critical tyrosine kinase, ZAP-70, fails to become activated because it does not form a critical coupling with the TCR and therefore ZAP-70 does not become accessible to Lck. It was observed that Fyn activity is elevated in SEB treated memory cells but not in naïve cells. It was shown further that down-regulating fyn activity either by using pharmacological inhibitors or by using fyn knockout mice as a source of memory T cells restores memory cell activation in response to SEB and also promotes proper spatial associations between ZAP-70 and the TCR. We have hypothesized that a fyn-induced signaling pathway controls the association of ZAP-70 with lipid rafts and that this is a critical event which controls initial signaling. We have not completely fleshed out the specific project, but my main aims will address some of the major questions in this model such as determining the mechanism of increased Fyn activation after exposure to SEB and identifying the Fyn mediated signaling pathway that results in anergy.