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## Removal of C-terminal Src kinase from the immune synapse by a new binding protein

Tomas Mustelin, Souad Rahmouni, Andres Alonso, Scott Williams,  
Marianne van Stipdonk, Chiara Soncini, and Stephen P. Schoenberger

Author Affiliations

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**Abstract**

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The Csk tyrosine kinase negatively regulates the Src family kinases Lck and Fyn in T cells. Engagement of the T cell antigen receptor results in a removal of Csk from the lipid raft-associated transmembrane protein PAG/Cbp. Instead, Csk becomes associated with a ~72-kDa tyrosine phosphorylated protein, which we here identify as G3BP, a phosphoprotein reported to bind the SH3 domain of Ras GTPase activating protein. G3BP reduced the ability of Csk to phosphorylate Lck at Y505 by decreasing the amount of Csk in lipid rafts. As a consequence, G3BP augmented T cell activation as measured by IL-2 gene activation. Conversely, elimination of endogenous G3BP by RNA interference reduced TCR signaling. In antigen-specific T cells, endogenous G3BP moved into an intracellular location adjacent to the immune synapse, but well inside the cell, upon antigen recognition. Csk co-localization with G3BP occurred in this 'parasynaptic' location. We conclude that G3BP is a new player in TCR signaling that acts to reduce the amount of Csk in the immune synapse.

**Footnotes**

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