c-Src protein self-association induced by lipid anchoring

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The non-receptor protein kinase c-Src participates in numerous cell signalling pathways that play crucial roles in maintaining the cell physiology. Identified as the first proto-oncogene, its deregulation has been related to several human cancers [1]. Its structure consists of five distinct domains, from N-terminus to the C-terminus: myristoylated SH4, Unique Domain, SH3, SH2 and the Kinase Domain or SH1. c-Src binds to the lipid membrane through the insertion of its myristoyl chain and the electrostatic interaction of the positively charged SH4 domain residues with the negatively charged lipids. Recent studies [2], demonstrated the formation of stable c-Src dimers on supported lipid bilayers. Self-association of the isolated SH4 domain has also been observed and leads to the formation of large clusters, when the domain is directly fused to reporter proteins [3]. The neighbour Src domains, seem to play a role in restricting the oligomerization to discrete dimers. In this study, we use Surface Plasmon Resonance and site-directed mutagenesis to investigate the structural determinants of Src self-association on lipid membranes.

References

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