Abstract

Kinase Src plays an essential role in signal transduction from activated surface receptors. Src is involved in signal pathways that participate in the control of cell proliferation, differentiation or motility. That is why Src activation undergoes strict and complex regulation. Inactive conformation is maintained by intramolecular inhibitory interactions. SH3 domain associates with a polyprolin helix in CD linker whereas SH2 domain binds phosphorylated C-terminal tyrosine 527. Both regulatory domains maintain contacts with the lobes of a kinase domain thereby stabilizing an inactive conformation of the catalytic domain. Transition to an active state is accompanied by a disruption of these inhibitory interactions. Conformation changes are substantially influenced by the phosphorylation status of key tyrosines 416 and 527.

Phosphoproteomic analysis revealed new Src tyrosine residue, which can be phosphorylated *in vivo*. It has been found, that tyrosine works as an additional regulator of Src activity. This is Tyr 90, which forms one of the hydrophobic pockets in the binding surface of Src SH3 domain. Based on the expression of phosphomimic mutant Src 90E in *S. pombe* or in SYF lineage, it has been observed, that Tyr 90 phosphorylation elevates Src kinase activity. The reason is that the phosphate introduces a negative charge into the hydrophobic binding surface of SH3 domain which causes a decrease in the affinity to CD linker. Src 90E has a partial transformational potential. Deregulation of phosphorylation of Tyr 90 could therefore lead to an aberrant Src activation.