X-ray crystal structure analysis of tyrosine kinase

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Introduction

The Src family kinases (SFKs) play a critical part in cell signaling by phosphorylating tyrosine residues of various cellular components. SFKs have a regulatory tyrosine residue in their carboxyl terminal (Tyr 527) that is phosphorylated by carboxyl terminal Src Kinase (Csk), which results in decrease in their kinase activity. Most of the non-receptor type tyrosine kinases, including SFKs and Csk, have homologous catalytic domain as well as regulatory peptide binding modules such as SH2 (Src Homology 2) domain and SH3 domain.

Until today structures of inhibitory form of SFKs and SH2 and kinase domains of Csk are reported. In SFKs the interaction between phosphotyrosine tail and SH2 domain is thought to have crucial role in maintaining overall conformation and other interactions between catalytic and modular domains. On the other hand, Csk does not have any regulatory tyrosine residues, and some biochemical data have suggested that domain interactions are different between SFKs and Csk.

To elucidate inter-domain interactions in Csk, we started crystallographic study. After extensive crystallization screening and its condition optimisation we have finally succeeded in obtaining crystals of full length Csk.

Results

The crystal belongs to orthorhombic space group of C2221 with unit cell dimensions of a=145, b=187,c=162 (Å). Diffraction data collection was done using the CCD detector Quantum 4R (ADSC) at the beam line of BL6A. It diffracts X-rays with a maximum resolution of 3 Å, but strong anisotropy was observed. The data were processed by the programs MOSFLM and SCALA(Table).

Table

Space group		C2221
Unit cell (Å)	a	145
	b	187
	c	162
Resolution (Å)		3.1
Completeness (%)		99.9
Redundancy		4.7
Rsym (%)		5.8

Reference

Nada,S. and Okada,M., *et al*., ***Nature***, 351, 69-72 (1991)

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