The Crystal Structure of Human CDK7 and Its Protein Recognition Properties

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CDK7, a member of the cyclin-dependent protein kinase family, regulates the activities of other CDKs through phosphorylation on their activation segment and hence contributes to control of the eukaryotic cell cycle. CDK7 also assists in the regulation of transcription as part of the transcription factor TFIIH complex. For maximum activity and stability, CDK7 requires phosphorylation, association with cyclin H, and association with a third protein, MAT1.

We have determined the crystal structure of human CDK7 in complex with ATP at 3 Å resolution. The kinase is in the inactive conformation, similar to that observed for inactive CDK2. The activation segment is phosphorylated at Thr170 and is in a defined conformation that differs from that in phospho-CDK2 and phospho-CDK2/cyclin A. The functional properties of the enzyme against CDK2 and CTD as substrates are characterized through kinase assays. Experiments confirm that CDK7 is not a substrate for kinase-associated phosphatase.

Keywords: cyclin-dependent kinase, cell cycle, structure