Protein Kinase CK2: Functional Proteomic Strategies Reveal New Insights into its Regulation and Functions.

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Protein kinase CK2 is a small family of ubiquitously expressed and highly conserved protein serine/threonine kinases that exhibits oncogenic activity in transgenic mice and is over-expressed in a number of tumors or leukemic cells. Studies in a variety of model systems have implicated CK2 in a diverse series of cellular processes including cell cycle progression, circadian rhythms and cell polarity as well as pathways that regulate cell survival and apoptosis. Despite extensive investigation, one of the most confounding aspects of the CK2 field has been the elucidation of its physiological regulation. It is now evident that CK2 is localized at many discrete sites within cells and that it is likely to have hundreds of potential physiological targets involved in a diverse array of cellular processes. Consequently, it is plausible that cells contain many discrete, and independently regulated, populations of CK2. In this respect, there is now a considerable body of knowledge demonstrating that CK2 is a component of many distinct protein complexes. For example, in yeast, where systematic studies for the isolation and characterization of protein complexes have been performed, the individual subunits of CK2 have been identified in dozens of individual complexes. In an effort to systematically identify the substrates and interaction partners for CK2 in human cells, we have initiated studies using functional proteomics strategies (including the yeast two-hybrid system and TAP-tagging). These studies have led to the demonstration that CK2 interacts with Pin1, a phosphorylation-dependent peptidyl-prolyl isomerase with a role in various cellular processes including mitosis. These studies also led to the discovery of CKIP-1, a novel pleckstrin homology domain-containing protein with a number of protein interaction motifs that localizes primarily to the plasma membrane. In addition to providing new insights regarding the regulation and functions of Pin1 and CKIP-1, our ongoing studies have illuminated previously unappreciated roles and modes of regulation for specific populations of CK2 within cells.