Autophosphorylation of carboxy-terminal residues inhibits the activity of protein kinase CK1?

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CK1 constitutes a protein kinase subfamily that is involved in many important physiological processes. However, there is limited knowledge about mechanisms that regulate their activity. Isoforms CK1? and CKl? were previously shown to autophosphorylate carboxy-terminal sites, a process which effectively inhibits their catalytic activity. Mass spectrometry of CKla and splice variant CKl?L has identified the autophosphorylation of the last four carboxyl-end serines and threonines and also for CKl?S, the same four residues plus threonine-327 and serine-332 of the S insert. Autophosphorylation occurs while the recombinant proteins are expressed in Escherichia coli. Mutation of four carboxy-terminal phosphorylation sites of CKl? to alanine demonstrates that these residues are the principal but not unique sites of autophosphorylation. Treatment of autophosphorylated CKla and CKlaS with ? phosphatase causes an activation of 80-100% and 300%, respectively. Similar treatment fails to stimulate t