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 CK1? were previously shown to autophosphorylate carboxy-terminal sites, a process which effectively inhibits their catalytic activity. Mass spectrometry of CK1a and splice variant CK1?L has identified the autophosphorylation of the last four carboxyl-end serines and threonines and also for CK1?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 CK1? to alanine demonstrates that these residues are the principal but not unique sites of autophosphorylation. Treatment of autophosphorylated CK1a and CK1aS with 3-phosphatase causes an activation of 80-100% and 300%, respectively. Similar treatment fails to stimulate t