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Mass spectrometry reveals protein kinase CK2 high-order oligomerization via the circular and linear assembly

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CK2 is an intrinsically active protein kinase that is crucial for cellular viability and exists as a heterotetrameric holoenzyme (α_2/β_2) composed of two catalytic α subunits (denoted as CK2 α or α) attached to a central, regulatory dimer of β subunits (denoted as CK2 β or β_2). However, conventional kinase regulatory mechanisms do not apply to CK2, and its mode of regulation remains elusive. Interestingly, CK2 is known to undergo reversible ionic-strength-dependent oligomerization. Furthermore, a regulatory mechanism based on auto-inhibitory oligomerization, driven by the inter-holoenzyme electrostatic interactions between the acidic loop of CK2 β and the basic substrate-binding regions of CK2 α , has been postulated based on the observation of circular trimeric oligomers and linear CK2 assemblies in various crystal structures. Here, native mass spectrometry (MS) was employed to monitor the assembly of oligomeric CK2 species in an ionic-strength-dependent manner. Subsequently, ion mobility spectrometry-MS (IMS-MS) was used to examine the conformational state of the CK2 oligomers. To validate the findings from IMS-MS, hydrogen–deuterium exchange mass spectrometry (HDX-MS) was used to analyze the solution-phase conformation of CK2 oligomers. Through the use of a suite of orthogonal mass spectrometric techniques (native MS, IMS-MS and HDX-MS), it was shown that CK2 undergoes ionic-strength dependent oligomerization to form both circular and linear supramolecular assemblies, thus, representing a novel mechanism of regulation for protein kinases. The results were consistent with previously proposed models of CK2 oligomerization derived from X-ray crystallographic analysis and *in vivo* evidence of CK2 aggregation.

Biography

Dijana Matak-Vinković has completed her PhD at University of Zagreb, Croatia. She is a Senior Technical Officer and Head of Mass Spectrometry Service in Department of Chemistry, University of Cambridge. She has published more than 30 papers in reputed journals.

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