An undiscovered code in the intrinsically disordered proteins: Phosphorylation as control of ligand binding and protein structure.

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Intrinsically Disordered Proteins (IDPs) or Intrinsically Disordered Regions (IDRs) have gained ever−increasing relevance during the last years due to their atypical properties. IDPs/IDRs are lacking a tridimensional structure on physiological conditions, and they are able to adopt highly dynamic conformations, allowing in most cases binding to several partners. IDPs play diverse and essential roles in biological systems as signaling processes, transcription, including mineralization of bone and teeth. In globular proteins, phosphorylation can promote conformational changes and also can alter surface recognition. This knowledge has understood in depth by crystallographic studies. However, IDPs can not form protein crystals. Many IDPs are highly phosphorylated via post-translational modifications. Phosphorylation in IDPs induce conformational changes, promote order-disorder transitions, and modulate binding via electrostatic interactions with partners. Nevertheless, the evidence in the literature regarding the role of phosphorylation on the conformational kinetics of IDPs is not conclusive, and which is the effect on molecular recognition with their partners is still elusive. Previous studies have shown that phosphorylation on IDPs has a profound effect on the flexibility that is essential for performing their functions and allowing them to explore different conformations. By performing molecular dynamics simulations (MD) of several IDPs, showed the phosphorylated version of them showed higher affinity to their partners and a more organized structure. The change to a more-ordered structure after phosphorylation and interactions with their partners was verified by circular dichroism, small-angle scattering, and vibrational spectroscopy.