Universität Basel

Publication

Architecture and activation of phosphatidylinositol 3-kinase related kinases

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The phosphatidylinositol 3-kinase related protein kinases (PIKKs) are key to the regulation of a variety of eukaryotic cellular processes including DNA repair and growth regulation. While these massive proteins had long resisted structural analysis, recent advances in electron cryo-microscopy have now facilitated structural analysis of the major examples of PIKKs, including mTOR, DNA-PK, ATM, ATR and TRAPP/Tra1. In these PIKKs, the carboxy-terminal kinase domains and their proximal regions are structurally conserved. The structural organization of their extensive amino-terminal repeat regions, however, as well as their oligomeric organization and their interactions with accessory proteins, differ markedly amongst PIKKs. This architectural divergence provides the structural basis for the complex regulatory roles and functional diversity of PIKKs.
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