

Publication

Activity of the human centrosomal kinase, Nek2, depends on an unusual leucine zipper dimerization motif

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Nek2 is a human cell cycle-regulated kinase that is structurally related to the mitotic regulator, NIMA, of *Aspergillus nidulans*. Localization studies have shown that Nek2 is a core component of the centrosome, the microtubule organizing center of the cell, and functional approaches suggest a possible role for Nek2 in centrosome separation at the G2/M transition. Here, we have investigated the importance of an unusual leucine zipper coiled-coil motif present in the C-terminal noncatalytic domain of the Nek2 kinase. Glycerol gradient centrifugation indicated that endogenous Nek2 is present in HeLa cells as a salt-resistant 6 S complex, the predicted size of a Nek2 homodimer. Recombinant Nek2 overexpressed in insect cells also formed a 6 S complex, whereas a Nek2 mutant specifically lacking the leucine zipper motif was monomeric. Using yeast two-hybrid interaction analyses and coprecipitation assays, we found that Nek2 can indeed form homodimers both in vivo and in vitro and that this dimerization specifically required the leucine zipper motif. Moreover, deletion of the leucine zipper prevented a trans-autophosphorylation reaction on the C-terminal domain of Nek2 and strongly reduced Nek2 kinase activity on exogenous substrates. Finally, we emphasize that the Nek2 leucine zipper described here differs from classical leucine zippers in that it exhibits a radically different arrangement of hydrophobic and charged amino acids. Thus, this study reveals not only an important mechanism for the regulation of the Nek2 kinase but, furthermore, highlights an unusual organization of a leucine zipper dimerization motif.

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