

Structure, function and localization of NME6 - a member of the NME/NDP kinase family

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NME6 is a member of the nucleoside diphosphate kinase (NDPK/NME/Nm23) family, enzymes that catalyze the transfer of gamma phosphate from ATP to other nucleoside diphosphates. The family has attracted considerable interest due to the involvement of its members in metastasis suppression. The family is divided into two groups. Group I (NME1-NME4) are highly conserved in their amino acid sequence and exhibit the NDPK activity, while Group II (NME5-NME9) members display less homology and seem to lack NDPK activity. Some of the Group II members (NME5-7) arose very early in the evolution of Metazoa, therefore, it is presumed that they participate in one or more basic cellular process. Since little is known about Group II members, we focused our studies on revealing the subcellular localization, quaternary structure and function of the Group II human NME6 protein. The expression of NME6 was screened in several human tumor cell lines by Western blot, using specific anti-NME6 antibodies. All of them express significant amounts of NME6. Fluorescent reporter systems coupled with confocal microscopy as well as cell fractionation were used to assess the NME6 subcellular localization. NME6 colocalizes with mitochondria although it does not possess the mitochondrial signaling sequence. Crosslinking with glutaraldehyde as well as size exclusion chromatography revealed that the NME6 is present mostly in the monomeric, or, in a smaller portion, in a dimeric state. The NDP kinase activity was tested using a coupled pyruvate kinase-lactate dehydrogenase assay which confirmed that the NME6 does not possess traceable NDPK activity. Further studies will be focused on studying the precise submitochondrial localization of the protein, its possible function in mitochondrial respiration and potential interacting partners.