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Functional genomics analysis of the B-Box gene family reveals a possible role in subcellular compartmentalization

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AIM: The genes belonging to the B-box family have been implicated in a variety of processes. Among them, PML, RFP, and Tif1 acquire oncogenic activity when fused to RAR alpha, RET, and B-raf, respectively. Other B-box genes are involved in human diseases, the FMF gene, mutated in Familial Mediterranean Fever, and the MID1 gene, involved in Opitz syndrome. These genes contain a RING, two B-boxes, and a coiled-coil domain. Very little is known about the molecular mechanisms mediating their function and therefore we decided to redefine and characterize the entire family using a systematic approach to efficiently move from sequence/structure information to functional knowledge. METHODS and RESULTS: We identified novel members of the B-box family by a systematic search of the dbEST and we have collected the full-length cDNA 37 novel and known B-box genes. We have defined their chromosomal position and analyzed their expression patterns in adult and embryonic tissues. In addition, we have designed functional assays which allowed us to find that many family members show peculiar subcellular localizations. Moreover, we found that most of the B-box proteins are able to homodimerize and to form large multiprotein complexes. **CONCLUSIONS:** The B-box proteins, through their ability to form multiprotein complexes, appear to play an important role in defining different subcellular compartments suggesting a possible involvement in compartimentalizing other proteins. These data will be useful to better understand the role of this class of proteins during normal development and to assess their role in the pathogenesis of tumors and inherited diseases.

KEY WORDS: PML bodies, RFP-like domain, B-box proteins.

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