

The COMM-domain containing protein 1 interacts with the Guanine-rich RNA sequence binding factor 1 and regulates its subcellular distribution

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Background: The guanine-rich RNA sequence binding factor 1 (GRSF1) is an RNA-binding protein of the hnRNP H/F family and has been implicated in different cell functions. GRSF1 can also be located in the mitochondria and plays an important role in mitochondrial RNA metabolism (Jourdain et al. 2013, Cell Metabolism, 17(3), 399-410). COMMD1 belongs to the family of COMM-domain containing proteins and has been implicated in different cellular processes such as copper homeostasis, the function of the epithelial sodium channel or cell proliferation. Recent studies suggest the possibility that regulation of the ubiquitin pathway may constitute the functional basis for the biological activity of COMMD1 (Maine et al. 2007, Cell and Mol Life Sciences, 64(15), 1997-2005).

Methods: We employed the yeast two-hybrid system to search for GRSF1-binding proteins and carried out co-immunoprecipitation experiments to confirm this protein-protein interaction in living cells. To further characterize this protein-protein interaction, we performed siRNA mediated knock-down in human cell lines followed by co-immunoprecipitation experiments and differential centrifugation experiments.

Results: Using the yeast two-hybrid system we identified the COMMD1 protein as GRSF1 binding partner. It interacts with the alanine-rich domain of GRSF1 in reconstituted in vitro system but also in cells expressing the two proteins. Lack of COMMD1 has no effect on GRSF1 ubiquitination but reduces the mitochondrial GRSF1 content.

Conclusion: These data indicate that COMMD1 specifically interacts with GRSF1 in mammalian cells. Lack of COMMD1 prevented mitochondrial import of this RNA-binding protein.

General significance: This is the first report describing a protein-binding partner for GRSF1, which modifies the subcellular distribution pattern of this RNA-binding protein. (Dumoulin et al. 11/2020, Biochem Biophys Acta - General Subjects)