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The small GTPase hRAB37 acts as a metastatic suppressor via inhibition of MMP/FAK/RhoA signal in lung cancer

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Our previous data demonstrates that a small GTPase hRAB37, which is a member of Rab superfamily, plays a role in lung cancer progression. This study aims to investigate the functions of hRAB37 to regulate vesicle trafficking and its cell signals involved in cell migration. We demonstrated that hRAB37 is a tumor metastatic suppressor protein in lung cancer. Clinical data showed that low hRAB37 protein expression and promoter/exon1 hypermethylation of *hRAB37* gene correlated markedly with poor progression-free survival and overall survival in lung cancer patients. Overexpression of hRAB37 resulted in loss of migration/invasion ability in CL1-5 lung cancer cells-based assays and remarkably reduced lung tumor metastasis in animal models. Migration/invasion ability of CL1-5 cells was inhibited under the treatment of conditional medium taken from hRAB37 overexpressed CL1-5 cells resulting from an increased protein level of secreted TIMP-1 protein, which is an inhibitor of matrix metalloproteinases (MMPs). In addition, the decreased expression of MMP2 and MMP9, and FAK-mediated metastasis pathway, including p-FAK, p-AKT and RhoA activity, provided a potential mechanism for the metastasis suppression effects of hRAB37. Furthermore, confocal analysis demonstrated a co-localization of hRAB37 with the secretory marker VAMP2 and the RAB3a exocytosis protein. Confocal images demonstrated a colocalization between RAB37 and TIMP-1, an MMP inhibitor. Our data provided first compelling evidence from cell, animal, and clinical studies that hRAB37 small GTPase is a metastasis suppressor through exocyticly trafficking the anti-metastatic proteins such as TIMP-1. Low expression of hRAB37 due to promoter hypermethylation leads to poor survival of lung cancer.

Biography

Yi-Ching Wang is currently a Distinguished Professor at National Cheng Kung University, Taiwan. Prof. Wang received her Ph.D. from Genetic Program of Michigan State University in 1993. She studies the molecular mechanisms involved in lung tumorigenesis. Candidate gene study and research on cancer genomics and epigenomics are her main focus. Several potential anti-cancer drugs are also developing in her laboratory. Prof. Wang has published more than 50 SCI papers in prestigious journals such as J. Clin. Oncol., J. Clin. Invest., Cancer Res. and Oncogenes. Prof. Wang was one of the recipients for Excellent Research Award of Taiwan National Science Council.