

Fam111b Gene Dysregulation Contributes to the Malignancy in Fibrosarcoma, Poor Clinical Outcomes in Poiktmp and a Low-cost Method for Its Mutation Screening

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Abstract : Introduction: The human FAM111B gene mutations are associated with POIKTMP, a rare multi-organ fibrosing disease. Recent studies also reported the overexpression of FAM111B in specific cancers. However, the role of FAM111B in these pathologies, particularly fibrosarcoma, remains unknown. Materials and Methods: FAM111B RNA expression in some cancer cell lines was assessed in silico and validated in vitro in these cell lines and skin fibroblasts derived from the South African family member affected by POIKTMP with the heterozygous FAM111B gene mutation: NM_198947.4: c.1861T>G (p. Tyr621Asp or Y621D) by qPCR and western blot. The cellular function of FAM111B was also studied in HT1080 using various cell-based functional assays and a simple and cost-effective PCR-RFLP method for genotyping/screening FAM111B gene mutations described. Results: Expression studies showed upregulated FAM111B mRNA and protein in the cancer cells. High FAM111B expression with robust nuclear localization occurred in HT1080. Additionally, expression data and cell-based assays indicated that FAM111B led to the upregulation of cell migration and decreased cell apoptosis and cell proliferation modulation. FAM111B Y621D mutation showed similar effects on cell migration but minimal impact on cell apoptosis. FAM111B mRNA and protein expression were markedly downregulated ($p \leq 0.05$) in the patient's skin-derived fibroblasts. Lastly, the PCR-RFLP method successfully genotyped FAM111B Y621D gene mutation. Discussion: FAM111B is a cancer-associated nuclear protein: Its modulation by mutations may enhance cell migration and proliferation and decrease apoptosis, as seen in cancers and POIKTMP/fibrosis, thus representing a viable therapeutic target in these disorders. Furthermore, the PCR-RFLP method could prove a valuable tool for FAM111B mutation validation or screening in resource-constrained laboratories.

Keywords : FAM111B, POIKTMP, cancer, fibrosis, PCR-RFLP

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