A study of the expression and cellular function of the human *FAM111B* gene

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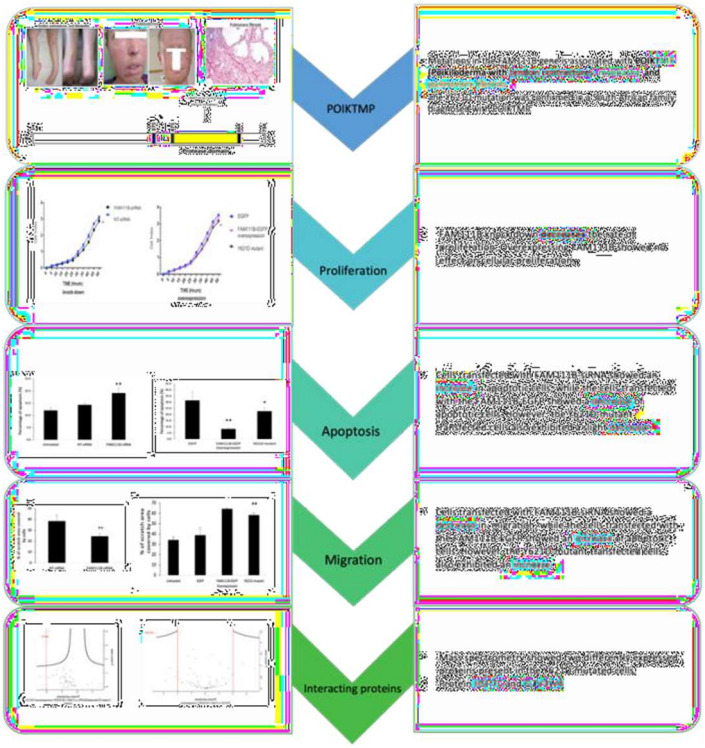

Figure 1. A schematic summary of the introduction and key findings in this study.

Introduction: POIKTMP, a multi-system fibrosing disease, results from mutations in the human *FAM111B* gene. Despite rising interest in the role of *FAM111B* mutations, knowledge of this gene remains limited. Therefore, this study provides insight into the cellular function of *FAM111B,* which is also overexpressed in some cancers, and investigates the pathological effect of the *FAM111B* Y621D POIKTMP-associated mutation.

Methodology: Bioinformatics studies coupled with quantitative PCR and Western blots analysis were employed to assess *FAM111B* gene and protein expression. Subsequently, RNA-interference mediated gene silencing, and recombinant gene expression technologies were used to dysregulate *FAM111B* gene expression in HT1080 cells. Downstream cell-based functional assays were performed to determine the effects of down-and up-regulation of *FAM111B,* respectively, and to determine FAM111B interacting proteins using mass spectroscopy proteomics (MSP). *FAM111B* expression in POIKTMP patient-derived and healthy skin fibroblasts were also evaluated.

Results: The knockdown of *FAM111B* in HT1080 suggests reduced cell proliferation and migration and increased apoptosis. Conversely, the overexpression of *FAM111B* increased apoptosis and cell migration. Furthermore, Y621D *FAM111B* mutant cells showed reduced expression of *FAM111B*, decreased apoptosis, invasion, and an increase in proliferation and migration. Furthermore, our MSP results show that wildtype and mutant FAM111B may interact with proteins HSP7C and G3V3W4, respectively, to minimize apoptosis and accelerate proteolytic cleavage of damaged proteins, including the mutant protein Y621D.

Discussion: Altogether, our data suggest that *FAM111B* promotes cells viability, and FAM111B Y621D mutation may contribute to the rapid proteolytic clearance of *FAM111B*, thereby leading to reduced cellular fitness.

References: (Hoffmann et al., 2020); (Kawasaki et al., 2020); (Khumalo et al., 2006); (Sun et al., 2019),

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