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Unravelling the Intricate Roles of FAM111A and FAM111B: Exploring their Functions in Health and Disease

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Description

FAM111A and FAM111B, members of the FAM111 gene family, have emerged as critical players in various cellular processes, ranging from DNA repair to cell cycle regulation. Despite their structural similarities and shared evolutionary origins, these proteins exhibit distinct functions and are implicated in different human diseases. This article provides a comprehensive overview of the intricate roles played by FAM111A and FAM111B in cellular physiology, emphasizing their involvement in maintaining genomic stability, regulating cell proliferation, and contributing to disease pathogenesis. The FAM111 gene family comprises two closely related members, FAM111A and FAM111B, which encode proteins that share significant sequence homology and domain architecture. Initially identified through genome-wide association studies, FAM111A and FAM111B have since attracted attention due to their involvement in various cellular processes [1-3]. Despite their structural similarities, recent research has revealed distinct functions for these proteins, shedding light on their unique contributions to cellular homeostasis and disease progression.

Both FAM111A and FAM111B proteins consist of conserved domains, including a metalloprotease domain and an extended C-terminal region. The metalloprotease domain, characterized by the HEXXH motif, suggests a potential role in proteolytic activity, although specific substrates remain elusive. Evolutionary analysis suggests that FAM111A and FAM111B arose from a gene duplication event, resulting in two paralogous genes with divergent functions. One of the key functions attributed to FAM111A and FAM111B is their involvement in DNA repair mechanisms. Studies have implicated FAM111A in the Homologous Recombination (HR) pathway, where it interacts with components of the BRCA1-PALB2-BRCA2 complex to facilitate DNA double-strand break repair. In contrast, FAM111B appears to play a role in base excision repair (BER), participating in the removal of damaged DNA bases and maintaining genome integrity. Dysregulation of these repair pathways due to mutations or aberrant expression of FAM111A/B can lead to genomic instability and predispose cells to oncogenic transformation [4,5].

In addition to their roles in DNA repair, FAM111A and FAM111B influence cell cycle progression through distinct mechanisms. FAM111A has been implicated in the regulation of mitotic progression, where it interacts with cyclin-dependent kinase 1 to ensure proper chromosome segregation and cytokinesis. Conversely, FAM111B appears to modulate the G1/S transition, possibly through its interaction with components of the retinoblastoma protein pathway. Dysregulation of these cell cycle checkpoints can lead to uncontrolled cell proliferation and contribute to tumorigenesis. Mutations in FAM111A and FAM111B have been linked to various human diseases, underscoring their importance in maintaining tissue homeostasis. In particular, mutations in FAM111A have been associated with hereditary fibrosing poikiloderma with tendon contractures, myopathy, and pulmonary fibrosis syndrome. This rare autosomal dominant disorder is characterized by skin abnormalities, joint contractures, muscle weakness, and progressive fibrosis of the lungs. Similarly, mutations in FAM111B have been implicated in Kenny-Caffey syndrome, a rare skeletal dysplasia characterized by short stature, cortical thickening of long bones, and hypocalcemia.

FAM111A and FAM111B represent intriguing targets for further investigation into their roles in cellular physiology and disease pathogenesis. While significant progress has been made in elucidating their functions, many questions remain unanswered regarding their precise molecular mechanisms and physiological significance. Continued research into the intricate roles of FAM111A and FAM111B is essential for understanding their contributions to human health and disease, with potential implications for the development of novel therapeutic interventions.

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Conflict of Interest

There are no conflicts of interest by author.

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