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MG53 suppresses tumor growth via transcriptional inhibition of KIF11 in pancreatic cancer

Abstract: Pancreatic ductal adenocarcinoma (PDAC) poses a formidable challenge in oncology due to its limited treatment options and poor long-term survival rates. Our previous work identified MG53, a member of the tripartite motif family protein (TRIM72), as a key player in tissue repair with potential applications in regenerative medicine. Despite the focus on MG53's cytosolic functions, its nuclear role in suppressing pancreatic cancer remains unknown. Through orthotopic and subcutaneous transplantation studies in mice, we observed enhanced tumor growth in MG53-deficient mice compared to wild-type counterparts. The overexpression of KIF11, a motor protein crucial for cell mitosis regulation, has been linked to the aggressive proliferation of pancreatic cancer cells. Confocal imaging confirmed MG53's presence in the nucleus of human pancreatic cancer cells, while functional assays demonstrated its impact on KIF11 expression and subsequent cell proliferation. Mechanistically, we revealed MG53's transcriptional control over KIF11, leading to cell cycle arrest. Our findings position MG53 as a promising tumor suppressor in PDAC, offering a novel avenue for therapeutic intervention by regulating KIF11 expression.

Keywords: TRIM72; nuclear translocation; cell proliferation; syngeneic orthotopic transplantation

Biography: Dr. Chuanxi Cai was trained (PhD) in the Institute of Biophysics, Chinese Academy of Sciences (Beijing), and he joined Rutgers University in the USA as a postdoctoral Fellow and was awarded a postdoc fellowship by American Heart Association. He initiated the discovery of a muscle-specific protein named MG53 (TRIM72) in cell membrane repair. This important finding resulted in several landmark papers published in Nature Cell Biology, Science Translational Medicine, Nature Communication and Journal of Biological Chemistry. He then joined the Faculty of Medicine at the University of Louisville in Kentucky as an Assistant professor. He was recently recruited to the Department of Surgery at the University of Virginia as a tenured Associate Professor. The research in his lab mainly focusses on cancer research and myocardial repair with different animal models.

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