

Public Abstract

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Title: Characterization of PGAM5

In this work reported in this dissertation, the function of the PGAM5 protein has been characterized on several levels. At the organismal level, a mouse model containing a PGAM5 allele that has been rendered non-functional by a gene trap insertion has been characterized, demonstrating that PGAM5 is required for embryonic development. At the cell biological level, a mouse embryo fibroblast cell line that does not express PGAM5 was characterized, demonstrating that PGAM5 protects cells from apoptotic stimuli. At the biochemical level, the ability of PGAM5 to function as a Ser/Thr phosphatase was characterized. The active enzyme formed a multimeric complex that was dependent on a conserved WDXNWD motif. Deletion or mutation of this motif abolished both multimer formation and enzymatic activity. Taken together, these results suggest that PGAM5 functions as a Ser/Thr protein phosphatase that protects cells from apoptotic cell death.