

A NOVEL PROTEIN INVOLVED IN THYMOCYTE DIFFERENTIATION

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Thymocyte development is marked by differential gene expression that regulates progress of thymocyte precursors through distinct developmental checkpoints. To learn more about genes that regulate differentiation of double positive (DP) thymocytes into single positive cells that eventually develop into mature $\alpha\beta$ T cells, we used a subtractive hybridization approach to clone genes expressed differentially during this transition. We describe a novel gene, MG143, that is upregulated during transition from the double negative (DN) to DP stage. Differential expression of MG143 during thymocyte development was confirmed by Northern blot, quantitative PCR and western blot analyses. MG143 expression appears to be T cell specific. MG143 protein lacks any of the known sequence motifs for functional annotation and bears no significant homology to proteins in the public databases, suggesting a novel function. MG143 protein is distributed in the cytosol as well as in the nucleus. A MG143 polypeptide exhibited binding *in-vitro* to SH3-domains from multiple T cell signaling proteins, indicating a possible role of MG143 in intracellular signaling. *In vivo*, MG143 is phosphorylated and binds Ataxia Telangiectasia Mutated (ATM) kinase, known to play an important but poorly defined role in thymocyte development. Thymocytes from MG143-transgenic mice display improved survival following DNA-damage. Our results suggest that MG143 may participate in signaling pathways involved in thymocyte differentiation and survival.