P. 73

DIGE PROFILING OF MELANOMA SECRETOME IDENTIFIED MOLECULAR MEDIATORS OF SPARC ACTIVITY

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SPARC is a secreted glycoprotein related to tumor progression and metastasis and overexpressed in different tumors. Its role has been expanded to include tissue remodelling, endothelial cell migration, morphogenesis, angiogenesis and increased aggressiveness of different human cancer types. However, little is known about the molecular mechanisms affected by SPARC during tumor growth. We have showed that stable transfection of tumor cells with antisense SPARC DNA abolished tumorigenicity in an in vivo melanoma murine model through still unclear molecular mechanisms. In order to identify putative secreted proteins that may mediate SPARC biological function, we performed a proteomic analysis of conditioned media of a stable cell clone of human melanoma cells (L2F6) in which SPARC expression was downregulated by the use of a RNAi versus the control cell line LBLAST. For this purpose we applied DIGE (DIfferential Gel Electrophoresis). After analyzing 2D-gel images with DeCyder software, we obtained 98 differentially expressed proteins that were identify by using MALDI TOF-TOF technology. Ontological studies shown that the predominant group of differential proteins belongs to the family of proteases, proteins which have been extensively associated with tumor progression. Functional and biological validation confirmed the differences observed by DIGE. Thus, our results define a set of proteins potentially related to SPARC role in tumor progression, many of them not previously associated with SPARC. Further work is in progress to elucidate the molecular interactions between SPARC and this set of novel proteins.