USING PROTEOMICS TO UNRAVEL THE MOLECULAR PATHWAY OF SPARC-MEDIATED TUMORIGENICITY

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SPARC is a glycoprotein from the extracellular matrix normally expressed during development and in wound healing. SPARC is also overexpressed in different tumors, in association with tumor progression. We have showed that downregulation of SPARC expression by antisense and RNAi techniques in human melanoma cells abolished tumorigenicity in an in vivo immunodeficient murine model, through still not clear molecular mechanisms. In the pursuit of molecular mediators of SPARC activity that may explain its role in tumor progression, we have performed a proteomic analysis of proteins secreted by L2F6 clone cells (MEL-LES human melanoma cells with RNAi-mediated inhibition of SPARC expression) and compared it to its control cell line LBLAST. Overall, around 12% of detected spots in conditioned media were significantly up- or down-regulated by changes in expression levels of SPARC. After identification of differential spots using MALDI-TOF/TOF, a selected group of these proteins was chosen for technical, biological and functional validation. Differences in these proteins were confirmed not only in the aforementioned cells but also using transient (i.e. adenoviral) restoration of SPARC expression on MEL-LES cells. Most interestingly, several of the validated proteins are well-known mediators of tumor progression but were not previously related to SPARC. In particular, we have collected experimental evidence that confirm the role of SPARC as an important inductor of proteins involved in tumor invasion. Our results constitute the first evidence that SPARC and these proteins may participate in a single molecular network that leads to tumor progression.