A PROTEOMICS VIEW OF MELANOMA PROGRESSION AND DEVELOPMENT OF CHEMORESISTANCE.

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We have recently developed a model system comprised of an immortalized murine melanocyte cell line, melan-a, and two melanoma cell lines derived from this very cell line, TM1 and TM5 (Oba-Shinjo et al., Neoplasia 8:231-241, 2006). Analysis of the proteome and the transcriptome of this model showed that melanoma progression was marked by a prooxidant state, characterized by the massive decrease in molecules involved in reactive oxygen species metabolism (de Souza et al., Proteomics 6:1460-1470, 2006). Differential expression of some of these genes was, at least in part, due to epigenetic events, such as hypermethylation of specific promoter regions. Melanoma cells seemed to be progressively selected for survival under prooxidant conditions, which also rendered cells resistant to chemotherapeutic agents, such as cisplatin. Increased expression of the p53 regulator nucleophosmin and decreased expression of GADD153 could account for survival even when the unfolded protein response was triggered. Indeed, both melanoma progression and development of chemoresistance were followed by a significant increase in the amounts of heat shock proteins. The implications of selected findings towards tumor progression within prooxidant microenvironments will be discussed.

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