MELANOMA AND MELANOCYTIC NAEVI

AUTOPHAGY-GENES ARE SUITABLE MARKERS OF MELANOMA

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Introduction: The role autophagy plays in cancer setup and progression is currently under intense investigation. However, the exact way how it influences melanoma biology is still debated.

Objective: The aim of the present study was to investigate whether genes related to autophagy may act as effective markers of melanoma and possible therapeutic targets, by implementing a multiple validation-steps approach.

Materials and Methods: Data regarding the expression of genes and proteins were derived from the public databases GEO, IST Online, Human Protein Atlas and Oncomine, from a total of 572 human samples. Two hundred twenty-two autophagy-related genes were considered; their expression was compared in controls vs melanoma-samples and analyzed by Mann-Whitney test and ROC analysis. Data obtained by GEO analysis were first validated on IST Online human samples, then on Human Protein Atlas, and finally on Oncomine and on a different GEO dataset. Molecular/functional relationships were investigated via Chilibot, STRING and Gene-ontology enrichment analysis.

Results: Analyzing expression of 222 genes on 63 human samples from GEO database identified 9 genes with very high ability to discriminate controls from melanoma (AUC >0.85, $p < 0.0001$). A first round validation on IST Online database validated 4 genes differentially expressed in controls vs melanoma, on 355 human samples. A second round validation on protein expression in 80 histological sections from Human Protein Atlas database led to the validated selection of 3 genes. A third round validation on 74 samples in another GEO dataset and in Oncomine database further confirmed the identification of BAG1, PEX3 and WIPI1. The molecular network connecting these genes to melanoma was then investigated by Chilibot- and STRING analysis.

Conclusions: BAG1, PEX3 and WIPI1 autophagy-related genes show validated and very

high ability to discriminate human melanoma from control samples. They represent suitable markers of melanoma and potential therapeutic targets.