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Marker Signature for MAPK Inhibitor Resistance in Melanoma

A novel biomarker signature allows stratification of BRAF-mutated melanoma patients for combinatorial targeted or immune therapy.

Keywords Melanoma, BRAF, MAPK inhibitors, resistance biomarker, PTRF, IGFBP7

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Reference Paulitschke, V., et al., EMBO J (2019)38:e95874

Background MAPK inhibitors (MAPKi) show outstanding clinical response rates in melanoma patients with BRAF mutations, but resistance is common. The decision for targeted treatment versus immune therapy is therefore a major clinical challenge: MAPKi-resistant patients undergoing targeted therapy have a risk of high metastatic load that could not be cured even under immune therapy as a second intervention. Predictive markers for MAPKi resistance are therefore urgently needed both in clinical routine and as a tool for the better understanding of resistance mechanisms.

Invention A proteomic signature of MAPKi resistance in melanoma cells was identified by applying a combined approach of high-throughput techniques such as RNAseq and mass spectroscopy. PTRF and IGFBP7 are the two proteins with the highest discriminatory power between MAPKi sensitive and resistant melanoma cells. The proteins were validated as biomarkers by transcriptome data, functional analysis and by evaluation of patient samples.

Fields of Use (a) identification of MAPKi responders and non-responders for determining the best treatment option in BRAF-mutated melanoma patients, (b) identification of resistance-related targets and development of new treatment approaches.

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