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Functional and mutational landscape of cell polarity complex genes in cutaneous melanoma: A comprehensive bioinformatic analysis

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Cutaneous melanoma is the most aggressive type of skin cancer, known for its high metastatic potential and molecular heterogeneity. This study explores the functional significance of polarity complex proteins in melanoma by analyzing their roles in epithelial polarity maintenance and directional cell migration. Genomic mutation and gene expression data from the TCGA-SKCM cohort were evaluated using bioinformatic tools including PolyPhen-2, SIFT, Mutation Assessor, and AlphaMissense. A total of 347 mutations were identified in 12 polarity-related genes, with 128 predicted as pathogenic or oncogenic. Many mutations were located in PDZ domains and were associated with disruptions in key signaling pathways such as TGF-β and Hippo. STRING-based protein interaction analysis supported these associations. Differential expression analysis revealed significant downregulation of LLGL2, CRB3, PATJ, and PARD3 in melanoma samples compared to normal tissue ($P < 0.01$). Pathway enrichment analysis showed involvement of these genes in cancer hallmark pathways, particularly those related to invasion, metastasis, and immune evasion. The study suggests that polarity proteins can act as either tumor suppressors or oncogenes depending on mutation context. These findings provide valuable insights into melanoma pathogenesis and suggest polarity complex components as potential prognostic biomarkers and therapeutic targets in SKCM.

Keywords: Cell polarity complex, Cutaneous melanoma, mutation, gene expression