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Author

Toland, Amanda Ewart

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Abstract

Frequent somatic mutations of chromatin remodeling genes in metastatic cutaneous squamous cell carcinoma

Amanda Ewart Toland

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The Ohio State University

Exome and targeted sequencing studies have identified potential driver mutations for a variety of tumor types. Cutaneous squamous cell carcinoma (cSCC) is one of the most highly mutated cancers but is typically correlated with high survival rates and low rates of metastasis. Nevertheless, metastatic cSCC is a significant health threat; up to 8800 individuals are estimated to die yearly from this disease. As it is difficult to predict which cSCCs are more likely to metastasize, and because there are no targeted therapies specifically designated for metastatic cSCC, we performed exome and targeted sequencing of 18 metastatic and 10 primary cSCCs to identify mutations with potential therapeutic benefit. Genes previously shown to be mutated in primary cSCC as well as aggressive tumors such as *TP53* and NOTCH pathway genes were mutated at high rates in both metastatic and primary tumors. We compared our results to published sequencing results of an additional 223 primary tumors and 68 aggressive cSCCs. We identified several genes showing higher mutation frequencies in metastatic cSCC relative to primary tumors including the chromatin remodeling gene *KMT2D*, AKT/PI3K pathway gene *PIK3CG*, and the classic skin tumor suppressor *TP53*. These studies uncover potential pathways important in metastatic cSCC that may lead to new therapeutic strategies and understanding of the biology leading to more aggressive tumor behavior.