Suppression of Malonyl-CoA: ACP Transacylase as a Treatment for Squamous Cell Carcinomas

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Malonyl-CoA:ACP Transacylase (MCAT) is a mitochondrial enzyme needed for the functionality of pyruvate dehydrogenase (PDH). PDH is known to play a critical role in a tumor suppressor network known as oncogene-induced senescence. Studies have found that inhibiting PDH expression in healthy keratinocytes results in more cancerous phenotypes and increased proliferation. Thus, an absence of MCAT expression in squamous cell carcinomas (SCCs) should reduce PDH activity and also promote increased cell proliferation. In this project, I knocked down MCAT expression in two SCC cell lines using lentiviral infection of MCAT short hairpin RNAs (shRNAs). MCAT knockdown was confirmed using qPCR, and the resulting cell proliferation was analyzed using a colony formation assay and a crystal violet stain. However, my results indicate that suppression of MCAT actually decreases SCC proliferative potential as well as its capacity to repopulate. Cells with lower MCAT expression showed little growth compared to wild-type SCCs, and formed only 35% as many colonies. Thus, suppressing MCAT activity in SCCs significantly prevents cell proliferation, indicating that MCAT is actually crucial to SCC development. However, it has been shown that knocking out MCAT in healthy skin tissue has absolutely no effect. As a result, suppressing MCAT serves as a potential method to selectively treat only skin cancer cells without affecting any surrounding healthy tissue.

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