

CANCER RESEARCH

Molecular and Cellular Biology, Genetics

Abstract 5456: Avoiding chemotherapy resistance in squamous cell carcinomas: anticancer activities of terpenoids and their impact on the regulation of microRNAs

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Abstract

MicroRNAs are small noncoding RNAs that play important roles in cellular biology. They have been implicated in pharmacogenomics by down-regulating genes that are essential for drug function. In this work we verified the potential anticancer activity of the quinone methide triterpenes maytenin and 22- β -hydroxymaytenin, as well as of a quinone methide triterpene-rich extract obtained from cultivated *Maytenus ilicifolia* root cells, and evaluated the associated microRNA expression following half maximal inhibitory concentration (IC_{50}) treatment. Standard selectivity index (SI) for the isolated compounds and the root cell extract was determined by the logarithmic shift in effective concentration (IC_{50}) between cancer cell lines and oral keratinocytes. Both isolated molecules as well as the root cell extract presented pronounced antiproliferative and pro-apoptotic activities in four cell lines derived from head and neck squamous cell carcinomas, including a metastasis-derived cell line. A positive SI, with an average 2-fold increase in potency, was detected for single agents and for the extract. MicroRNA expression profiles were assessed at 24h, 48h and 72h following treatment and an average of 100 molecules presented consistent marked variation in expression levels. Considering associations of microRNAs, genes they regulate, and the drugs effects dependent on these genes, the down-regulation of miR-193a-3p and miR-21 in treated cells is of particular interest. Both microRNAs have been involved in 5-fluorouracil and cisplatin resistance, current agents of standard chemoradiotherapy for locally advanced head and neck cancer. Squamous cell carcinoma of the head and neck is one of the most common cancer types worldwide whereas

treatment options based on conventional therapies or targeted therapies under development have limited efficacy. Plant-derived products are valuable sources for the development of new therapeutic options for cancer treatment or as synergistic agents in existing regular care.

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