Oral squamous cell carcinoma (OSCC) is the most common oral cancer and most common subtype of head and neck cancer, with a patient 5-year survival rate of approximately 50%. OSCC cells that overexpress the Sphingomyelin Phosphodiesterase 3 (SMPD3) gene have been found to resist chemotherapy. An important aspect of cancer growth is cell-to-cell signalling, which is accomplished by packaging of information within extracellular vesicles (EVs). MicroRNAs (miRNAs) are packaged within EVs to communicate information between cells. This study aimed to uncover which miRNAs display an increase or decrease in expression between SMPD3 overexpressing OSCC cells and EVs, relative to control OSCC cells and EVs. Extracellular vesicles were isolated through ultracentrifugation, followed by analysis of miRNA expression in cells and extracellular vesicles using TaqMan Low-Density Array cards. Ultimately, nine miRNAs were identified to have at least a four-fold change in expression in SMPD3 overexpressing cells and their extracellular vesicles relative to the expression in control cells and their respective extracellular vesicles. One miRNA that showed a significant increase in EVs released by the SMPD3 overexpressing OSCC cells was MiR-636. Interestingly, MiR-636 has been linked to Transforming Growth Factor Beta signalling, which is a known mechanism of chemotherapy resistance in squamous cell carcinoma. This study helps explain how SMPD3 overexpression in cancer cells changes the miRNA content of extracellular vesicles and their cells of origin. Further exploration of the role of these miRNAs could facilitate the development of gene targeting drugs in order to treat OSCC more effectively.