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Bafilomycin A1 increases the sensitivity of tongue squamous cell carcinoma cells to cisplatin by inhibiting the lysosomal uptake of platinum ions but not autophagy

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The role of autophagy in tongue squamous cell carcinoma (TSCC) cisplatin resistance is unclear. We aimed to identify a possible synergistic effect of autophagy inhibitors and cisplatin in TSCC cells and explore the underlying mechanism. Our results indicate that autophagic flux was high in TSCC cells; Autophagy inhibitor bafilomycin A1 increased cisplatin cytotoxicity in TSCC cells by inhibiting lysosomal uptake of platinum and enhancing intracellular platinum ion binding to DNA; Autophagy gene (Atg5) knockout in TSCC cells did not duplicate the above-mentioned sensitization of bafilomycin A1. Furthermore, we found that cisplatin resistance of TSCC cells was related to cisplatin inducing lysosome biogenesis in a TFEB-dependent manner, which was regulated by c-Abl. In summary, this is the first study to show that Bafilomycin A1 increases the sensitivity of TSCC cells to cisplatin by inhibiting lysosomal function but not autophagy. Lysosomes may be a potential target to increase cisplatin cytotoxicity toward TSCC cells.