



Investigation of EGF effects on HER2 lysosomal accumulation

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Cancer is the bane of existence for multicellular organisms. There are numerous drugs to treat cancer; however, treatments are harmful to both the cancerous cells and healthy cells. Targeted drug therapy has the potential to reduce toxic, off-target effects by delivering a cytotoxic drug directly to cancerous cells. One emerging strategy is to combine the targeting of an antibody with a therapeutic payload. These hybrid systems, called antibody drug conjugates (ADCs), bind to a cell receptor, are taken into the cell and trafficked to the lysosome, and then release the drug cargo. Preliminary studies suggest that the efficacy of ADCs is bottlenecked because of failure to be trafficked to the lysosome (Owen, 2013). Under the direction of Dr. Shawn Owen (Pharmaceutics), I investigated the effects of increasing the lysosomal accumulation of an ADC into the lysosome by co-treatment with Epidermal Growth Factor (EGF). Increasing the localization of the ADC into the lysosome will increase potency and enable precision therapeutic medicine. SKOV3 cells were dosed with a pH activated dye conjugated to an antibody directed against the membrane protein HER2. Once translocated to the lysosome, the pH activated dye fluoresces in the low pH environment. Antibody internalization and fluorescence was detected by flow cytometry. The dosing time and EGF dosing concentrations for SKOV3 cells was optimized at 12 hours incubation time and 100 nM of EGF. The EGF dosed cells were compared against a negative control, cells dosed with only conjugated dye, and a positive control, cells dosed with 100 nM DMAG, a drug known to increase lysosomal accumulation (Chen, 2018). The positive control showed higher intensity fluorescence than the negative control, however the cells dosed with EGF showed no significant difference in fluorescence intensity compared to the negative control indicating no increase in lysosomal accumulation. In conclusion, co-treatment with EGF is not a candidate treatment to increase lysosomal accumulation.

Works Cited

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