# Synthesizing peptide-conjugated prodrugs that specifically target irradiation-induced drug transporter to eliminate radioresistant breast cancer cells

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Radiotherapy is commonly used in combination with various chemotherapies, and has emerged as one of the most cost-effective treatments for cancers. More than 50% of cancer patients with solid tumour are treated with radiotherapy worldwide. However, effectiveness of radiotherapy has been greatly hampered by developed chemoresistance and radioresistance. Tumour cells that developed chemoresistance frequently acquire elevated efflux of chemotherapeutic drugs that decreases intracellular drug activity and consequently long-term drug insensitivity. Enormous effects have not only been made in the discovery of chemosensitizer but also radiosensitizer. Small molecular inhibitors have been the central focus of drug development in the battle with undesired chemo- and radioresistance. For instance, numerous studies have focused on modulating drug efflux transporters that are highly expressed during and after acquisition of chemoresistance. Despite initial optimism from *in vitro* and preclinical studies using inhibitors against those transporters, the results of clinical trails have recently been disappointing. Influx drug transporters that are composed of the solute carriers (SLC) superfamily, however, have only been well recognized in their critical impact on cancer therapies in recent years. This is due to their differential expression patterns of SLC transporters by favouring higher expression in tumour cells than normal tissues. Our preliminary data provided first evidence that SLC15A1/2 are significantly elevated at both mRNA and protein levels in breast cancer cells that had been treated with ionizing radiation. Members of SLC15A are shown to have higher expression in pancreatic and colon, but not breast cancer. SLC15A is a family of five proteins known for their ability of di- and tri-peptide cellular uptake. We thus strategize a prodrug chemical synthesis scheme that takes advantage of elevated expression of SLC15A1 and consequently enhanced peptide uptake ability in irradiated breast cancer cells. We employed biochemical protein purification of SLC15A1, peptide phage-display/biopanning, and identified 35 potential candidate peptides that will be used as targeting promoiety for more effective delivery of well-established anti-breast cancer drug, doxorubicin. In this project, we expect to identify peptide(s) that can serve as exceptional promoiety to significantly boost therapeutic effect of parental doxorubicin against radioresistant breast cancer cells.