Identification of Thymidine Kinase I as a Universal Cell Surface Target for Treating Cancer and Development of a Novel Antibody Drug Conjugate

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The next generation of cancer drug therapeutics involve molecular targets to replace antiquated methods of treatment such as chemotherapy and radiation. Previous studies have shown the protein Thymidine Kinase I (TK1) to be elevated in cancer patient serum. Diagnostic tests using TK1 as a biomarker have been developed. In this project, I examined the potential for using TK1 as a molecular target by discovering its presence on the surface of different types of cancers through gold nanoparticle immunolabeling. Scanning electron microscopy imaging analysis showed TK1 to be present on the surface of various cancer cell lines, but absent on the surface of normal lymphocytes. After confirming the presence of TK1 on the surface of cancer cells, I chemically engineered a novel antibody drug conjugate targeting TK1. IgG antibodies binding to distinct epitopes on the TK1 protein were linked to the ribosome inhibiting toxin saporin and assessed for in vitro efficacy. Saporin-cysteine mutations, gel filtration, and ion exchange chromatography were tested in order to produce the most efficient conjugate. Over 70% cell death at 10 nM conjugate concentrations and near complete cell death at 100 nM conjugate concentrations was observed in MCF-7 breast cancer cells, PC3 prostate cancer cells, and HT-29 colon cancer cells, while normal lymphocytes were unaffected. There was a significant difference between the saporin conjugated treated and untreated samples ($p < 0.001$). These promising results suggest the development of a novel antibody drug conjugate that may in the future revolutionize the ways in which we treat cancer: a drug that will selectively target cancer cells.

Awards Won:

First Award of $5,000

Philip V. Streich Memorial Award to the London International Youth Science Forum