

# **Innovative antibody-fusion-protein delivery of peptide drugs for cancer treatment**

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Cancer is a high mortality disease around the world. Although there are many drugs for cancer patients, clinical survival rates of late stage patients have not significantly improved. Over the last decades, monoclonal antibody therapy offers a useful cancer treatment. Reducing side effects by specifically targeting cancer cells provides a better life quality for patients. However, blocking interaction between receptor and ligand is not sufficient for destroying cancer cells and inhibiting tumor growth. It is still needed to further investigate and design of therapeutic antibodies.

We have developed an innovative bio-drug delivery system, called Antibody Switch-on Cytotoxicity (ASC) platform. ASC platform provides good strategy for cancer therapy. There are three major steps in this design. Step one is antibody specific to cancer cell, we generate cancer-specific antibody and this antibody recognize surface marker in cancer cells. Step two is drug delivering to cancer cell. Linker-X switched-on is using protease secreted from cancer cells to digest linker-X to release peptide drug. This microenvironment provides cancer-specific protease, not normal cell secreting, to specifically target cancer cells. Step three is drug toxicity. Once linker-X switched-on by the protease, peptide drugs are delivered into cytoplasm via penetrating the cell membranes. We select many peptide drugs to destroy cancer cells effectively using ASC platform.

Our results demonstrated that ASC-S9 specifically bound to cancer cells. Flow cytometry showed that linker-X was digested and released in culture condition. Immunofluorescence indicated that releasing peptide drugs delivered into cancer cells. The anchorage-independent growth of cancer cells were inhibited by ASC-S9 with the soft agar colony formation assay. Moreover, xenograft model also proved that tumors with ASC-S9 treatment were smaller than with control. Dependent on our data, we further used the platform to approach the clinical trails.