

Newly engineered monoclonal antibody moves toward clinical testing

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(Medical Xpress)—Using monoclonal antibodies to fight cancer is a complex, yet promising area of study. At Memorial Sloan Kettering Cancer Center, physician-scientists have focused their attention on expanding the current therapeutic antibody repertoire, and believe a newly developed platform will do just that – ultimately leading to new and innovative treatments for cancer patients with a broad range of malignancies.

Unlike other human therapeutic monoclonal antibodies that can only target proteins found on the outside of [cancer cells](#), the new antibody series, called ESK, is capable of recognizing the presence of WT1, a protein that is nestled within a [cancer](#) cell and is overexpressed in a range of leukemias and other cancers. WT1 is a critically important target for anticancer drugs because it is a widely expressed oncogenic protein, meaning that it supports the formation of cancer. WT1 is rarely found in healthy [cells](#), so toxic side effects are also less likely.

Memorial Sloan Kettering and Eureka Therapeutics recently entered into a licensing agreement with Novartis to develop this unique monoclonal antibody. Under the terms of the agreement, Memorial Sloan Kettering and Eureka Therapeutics grant Novartis an exclusive, world-wide license to develop ESK antibodies for all indications. In return, Memorial Sloan Kettering and Eureka Therapeutics receive an up-front payment and potential future payments upon achievement of development, regulatory, and sales milestones, and annual net sales royalty payments. Novartis will fund and execute the development and commercialization of the drug.

"There has not been a way to make small molecule drugs that can inhibit WT1 function before now," said David A. Scheinberg, MD, PhD, Chair of the Sloan Kettering Institute's Molecular Pharmacology and Chemistry Program, and an inventor of the antibody. "Our ongoing research shows that we can use a monoclonal antibody – which works alone to activate the immune system – to recognize a cancer-associated protein from inside a cell and to kill that cell. There are many other similar cancer-related intracellular proteins that are now new potential targets."

Discovered during a joint research effort led by Dr. Scheinberg, his colleagues at Memorial Sloan Kettering, and Dr. Cheng Liu from Eureka Therapeutics, Inc., ESK was engineered to mimic the binding properties of a T cell receptor, a key component of the body's immune system. T cells have a receptor system that is designed to recognize proteins inside cancer cells. As these internal proteins break down as part of the regular cellular process, receptors known as HLA molecules carry fragments of those proteins – called peptides – to the surface of the cell. When T cells recognize certain peptides as abnormal, the T cell kills the diseased cell.

Research published in March 2013 by Dr. Scheinberg's lab, in collaboration with Eureka Therapeutics, showed that ESK antibodies were able to recognize the WT1 peptide even though the antibody itself did not enter the cells. ESK killed cancer cells in mouse models for several different types of human leukemias and cancers. At the 2013 American Society of Hematology annual meeting, the teams also reported on the development of new versions of the ESK antibody that directly activated human T cells or [natural killer cells](#) more effectively. In animal models, the ESK antibodies were more effective than several traditional tyrosine kinase inhibitors (TKI) against highly TKI-resistant leukemias.

"We are excited to enter into this licensing agreement with Novartis that

will help to bring this new agent into clinical testing, and our work will continue in developing methods to optimize the use of [monoclonal antibodies](#) to treat cancer, until its full potential has been met," said Dr. Scheinberg.

Provided by Memorial Sloan-Kettering Cancer Center

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