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Data Published in PNAS Show Engineering the Fc Region of Antibodies Makes Them More Toxic to Cancer Cells

Monrovia, CA – March 7, 2006 – Engineering the “Fc“ region of monoclonal antibodies (mAbs) increases their toxicity to cancer cells, potentially improving the utility of targeted cancer therapies, according to research conducted at Xencor, which will be published in the March 14 print issue of the Proceedings of the National Academy of Sciences (PNAS).

Monoclonal antibodies have important advantages over chemotherapy and small molecule drug treatments for cancer, such as their specificity in targeting tumor cells and low toxicity. There are currently eight approved anticancer antibody products on the market today and many more are in development. Unfortunately, many marketed treatments lack the desired potency against tumor cells, providing only incremental improvements in therapeutic success, and many development-stage antibodies fail in clinical trials due to lack of demonstrated efficacy.

Scientists at Xencor, a biotherapeutics company developing protein and antibody therapeutics, said the changes it made to the antibody Fc regions increased antibody effector functions such as activation of immune cells for tumor lysis, called Antibody-Dependent Cell-mediated Cytotoxicity (ADCC), by more than two orders of magnitude. Studies conducted in in vivo models demonstrated that these antibodies were greater than ten times more toxic to target cells. The enhanced antibodies also were able to kill tumor cells that are typically “invisible“ to other antibodies because they express low levels of target antigen.

While antibodies such as Genentech’s Rituxan are well known for their role in the treatment of cancer, many other promising antibodies are sub-optimal for use as therapeutics. “They just aren’t powerful enough,“ said Bassil Dahiyat, Ph.D., President and CEO of Xencor. “The work we published in PNAS shows that specific changes to the Fc regions of antibodies have the potential to greatly improve the effectiveness of next-generation antibody therapeutics, and may mean that many more antibodies can be used in the treatment of cancer than ever before.“

Xencor’s Fc variants were engineered using the company’s XmAb™ technology, which couples computational design algorithms with high-throughput screening to rationally design the antibody constant region. The Fc portion of the constant region of the antibody has been shown in previous studies to be responsible for mediating antibody-dependent cell-mediated cytotoxicity and has been the target of Xencor’s XmAb technology. Xencor has leveraged its XmAb technology to develop therapeutic antibodies, for which it plans to begin clinical testing next year.

We’ve already applied the XmAb technology used in this research to generate a suite of patented Fc antibody variants that have optimized antibody-Fc receptor affinity, which translate into increased effector functions and improved cell cytotoxicity. “These can be used to enhance the potency of nearly any antibody under development today,“ Dahiyat added. Xencor’s research was published in an article entitled “Engineered Antibody Fc Variants with Enhanced Effector Functions“ (Greg A. Lazar, et al.).

About XmAb™ Antibodies

Xencor’s XmAb engineered Fc domains are designed to enhance the therapeutic properties of monoclonal antibodies and form a leading proprietary position in Fc engineering. Xencor’s Fc domains can be inserted into antibody candidates against any target antigen and may improve one or more important effector functions, including enhanced antibody-mediated tumor cell killing, sustained half-life and increased structural stability. XmAb antibodies are produced using conventional expression and manufacturing processes. Xencor is creating a pipeline of XmAb antibody drug candidates with enhanced potency and pharmaceutical properties.

About Xencor

Xencor, Inc., engineers superior biotherapeutics using its proprietary Protein Design Automation® technology platform. The company is internally advancing both XPro™ protein therapeutic candidates and XmAb™ antibody drug candidates optimize for activity against biologically validated targets. Xencor’s product development is led by a protein therapeutic drug candidate, XPro1595, for the treatment of arthritis and other rheumatic disorders and antibody candidates for the treatment of cancer. With multiple partners, such as industry leaders Genentech, Roche, Centocor and MedImmune, Xencor is applying its suite of XmAb antibody Fc domains to improve antibody drug candidates for traits such as potency and sustained half-life. Xencor also develops therapeutic protein variants in collaboration with major pharmaceutical partners. For more information, please visit www.xencor.com.