FC fusion protein for the treatment of autoimmune diseases, in two peer-reviewed papers.

BY MEL J. YEATES
TEL AVIV, Israel—Compugen Ltd. announced in early February the publication of the discovery and validation of the ILDR2 protein as a novel immune checkpoint, and its use as an Fc fusion protein for the treatment of autoimmune diseases, in two peer-reviewed papers in The Journal of Immunology.

According to Dr. Zurit Levine, vice president of research and discovery at Compugen, body against the membrane protein ILDR2. Since we have shown that CGEN-15001T is a negative regulator of T cell activity, targeting this protein with an antibody therapeutic would overcome CGEN-15001T’s suppressive effect within the tumor microenvironment and result in a robust antitumor immune response,” Levine notes in regards to Bayer’s interest in ILDR2.

 “[T]he unique mechanism of action of CGEN-15001 combines immunomodulation with restoration of immune homeostasis and re-establishment of antigen-specific immune tolerance, underlying its ability to ameliorate autoimmune. Both these traits are highly desired for a broad range of autoimmune diseases and are not well addressed with currently available therapeutics, which are often globally immunosuppressive or employ only one of these traits,” Levine continues. “Tolerance induction represents a paradigm shift in the treatment landscape across multiple autoimmune diseases, addressing high unmet need, in either early intervention, treatment or remission in an established autoimmune disease—or even when thinking about drug-free remission.”

“Unlike current therapies, ILDR2-Fc combines immunomodulation and regulation of immune homeostasis by downregulating pro-inflammatory T cells while enhancing anti-inflammatory and regulatory T cells. ILDR2-Fc has been shown to re-establish Ag-specific immune tolerance, leading to durable disease amelioration following a short period of therapeutic intervention. The long-term therapeutic effect of ILDR2-Fc appears to be associated with its ability to enhance the differentiation of regulatory T cells (Tregs).”

The publication led by Compugen’s scientists describes the computational discovery approach leading to the discovery of ILDR2 as a novel immune checkpoint. The experimental validation of the role of this protein as a negative regulator of T cell activity was established internally at Compugen, as well as in collaboration with scientists from three leading academic institutions. The paper reports the beneficial effects of CGEN-15001 in an animal model of rheumatoid arthritis (RA), as well as in a translational assay utilizing blood cells from RA patients, which mimics the deleterious interactions of immune cells in the RA synovium.

“Understanding the potential of ILDR2-Fc fusion protein to address autoimmunity and inflammatory conditions, as well as the mechanism of action underlying this activity. The data show the potent and long-lasting immunomodulatory activity of ILDR2-Fc fusion protein in animal models of multiple sclerosis (R-EAE) and type 1 diabetes, and its ability to promote engrainment in an animal model of bone marrow transplantation.

“CGEN-15001 was previously shown to be effective in treating several autoimmune diseases in animal models, including models of multiple sclerosis, rheumatoid arthritis, type 1 diabetes and psoriasis. In some of these models, a short period of treatment with CGEN-15001 was shown to induce a durable long-term response suggestive of an immune tolerance mechanism. In addition, CGEN-15001 enhanced graft survival in a model of bone marrow transplantation, demonstrating induction of donor-specific tolerance. The MOA of CGEN-15001, which affords restoration of immune homeostasis and re-establishment of immune tolerance, could be beneficial in a broad range of autoimmune and inflammatory conditions,” McInnes said.

Preclinical research led by Compugen’s scientists—along with Prof. Stephen Miller and Joseph R. Podojil from the Department of Microbiology-Immunology and Interdepartmental Immunobiology Center, Feinberg School of Medicine, Northwestern University—was published in an additional paper demonstrating the potential of ILDR2-Fc fusion protein to address autoimmune and inflammatory conditions, as well as the mechanism of action underlying this activity. The data show the potent and long-lasting immunomodulatory activity of ILDR2-Fc fusion protein in animal models of multiple sclerosis (R-EAE) and type 1 diabetes, and its ability to promote engrainment in an animal model of bone marrow transplantation.

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