Compugen and JHU chart a new course

Collaboration researches first-in-class cancer therapy

BY JENNIFER CLIFFORD

HOLON, Israel—Recently, Compugen Ltd. disclosed new data demonstrating the potential of CGEN-15032 as a target for the development of first-in-class cancer therapy, as well as the extension of its multi-year immuno-oncology research collaboration with Johns Hopkins University (JHU) School of Medicine. The data were the subject of both an oral and a poster presentation at the 3rd Annual CRI-CIMT-EATI-AACR International Cancer Immunotherapy Conference, in Mainz/Frankfurt, Germany.

The data generated as part of this collaboration under the direction of Dr. Drew Pardoll, director of the Bloomberg-Kimmel Institute for Cancer Immunotherapy at Johns Hopkins and chairman of Compugen's scientific advisory board, demonstrate the target's immunomodulatory effect and its effect on tumor growth. The collaboration was initially announced in December 2014, and it will be expanded to include new additional targets discovered by Compugen that have the potential to serve as a basis for the development of cancer immunotherapy treatments.

Dr. Anat Cohen-Dayag, president and CEO of Compugen, said, "The data we achieved with CGEN-15032, together with JHU, exemplifies the tremendous value of our collaboration, providing us with access to world-class immuno-oncology knowledge and expertise to successfully develop our immuno-oncology programs and accelerate their path towards future human testing."

While antibody blockade of CTLA4 and PD-1 immune checkpoints has emerged as a successful treatment option for cancer patients, most do not experience sustained benefits, pinpointing a need for additional immune checkpoints. CGEN-15032, a novel myeloid and epithelial immuno-oncology target which may serve as an immuno-suppressive target within the tumor microenvironment was discovered by the company's immune checkpoint discovery platform, which also served as the cornerstone for the identification of TIGIT and PVRIG, two novel immune checkpoints which are currently in preclinical development by Compugen.

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Compugen recently shared data about the potential of CGEN-15032 as a first-in-class cancer therapy, as well as the extension of its multiyear immuno-oncology research collaboration with Johns Hopkins University School of Medicine.

Data gathered from research on both human and mice in *in-vitro* experimental systems suggest that CGEN-15032 may serve as an immuno-suppressive component of the tumor microenvironment, and that drugs inhibiting CGEN-15032 either alone or in combination with checkpoint inhibitors may activate anticancer immune responses. Ectopically expressed CGEN-15032 dampened anti-melanoma activity of tumor-infiltrating lymphocytes, derived from melanoma patients. In line with the effect observed in human system, overexpression of murine CGEN-15032 in artificial antigen-presenting cells resulted in reduced activity of TCR-transgenic DO11.10 T cells. These functional data, in conjunction with the expression of 15032 on myeloid and tumor cells, suggest that 15032 is a ligand and part of a novel pathway that inhibits T cell function.

To study the immuno-modulatory function of CGEN-15032 and its role in anticancer immunity, researchers generated CGEN-15032 knock-out mice. MC38 tumors grew slower in these relative to wild-type mice. Furthermore, a combinatorial treatment of CGEN-15032-deficient mice with anti-PDL1 antibody resulted in tumor growth inhibition compared with anti-PDL1-treated wild-type mice.

The next step, according to Dr. Yona Geffen, Compugen's vice president of research and validation, is to "Perform mechanistic studies in order to shed more light on the biological significance and the mechanism of action. These studies are being conducted under the multiyear collaboration with Prof. Drew Pardoll's lab at the Johns Hopkins University and Dr. Miriam Merad's lab at the Icahn School of Medicine at Mount Sinai in New York. Mainly, these studies will be focused on *in-vivo* studies and expression in clinical samples."

The Mount Sinai collaboration in question is a multiyear cancer immunotherapy research agreement under Merad's direction. Geffen tells *DDNews:* "This collaboration focuses on the research and target validation of selected myeloid candidates discovered by Compugen for their potential to serve as a basis for cancer immunotherapy treatments, including the validation of their role in innate immunity and involvement in tumor biology."

"Myeloids are a newly rising field in cancer immuno-therapy that is receiving growing interest and investment from both established pharma and biotech companies," she continues. "These myeloid target programs affect T cell immunity through various immunosuppressive mechanisms, and therefore have the potential to serve as the basis for the next wave of cancer immuno-therapies. These targets may offer a complimentary strategy to that of checkpoint inhibitors, and may provide treatment solutions for non-responsive or relapsing patients. A limited number of known myeloid targets are currently pursued in clinical trials, with only initial efficacy results presented to date." ■

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Compugen and Johns Hopkins University are building on the momentum of positive data regarding CGEN-15032 in cancer with the extension of their research collaboration. Pictured here is a Compugen scientist.

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