Genome & Company
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New immuno-oncology personalized therapies

Genome & Company is developing a microbiome-based add-on therapy for programmed cell death 1/programmed cell death 1 ligand 1 inhibitors. It is also developing novel targeted immune checkpoint inhibitors and believes these two approaches could be combined for personalized therapy.

Genome & Company is developing immuno-oncology (I-O) medicines designed to address the limitations of existing immunotherapies for advanced solid tumors. It is currently progressing its research and development (R&D) pipelines to the early stages of clinical development.

"We are one of the few companies in the world focusing on the development of microbiome-based I-O medicine," said Shawn Sungyeul You, head of business development. "We are also developing ICI [immune checkpoint inhibitor] candidates designed for novel targets that we have identified."

Founded in 2015 in the Republic of Korea, Genome & Company has achieved more than a tenfold increase in market capital since it went public in December 2018. With a strong background in scientific research and medicine, the company is expanding its global presence by working with big pharma collaborators such as Merck/Pfizer and LG Chemical, and through its subsidiaries in the US and Australia.

Microbiome-based therapy

The company's lead program, GEN-001, is a microbiome-based therapy. Growing evidence shows that modulating the gut microbiome could improve therapeutic responses to cancer immunotherapy. "We believe our microbiome asset could improve the response rate and efficacy if used as an add-on therapy with existing anti-PD-1/PD-L1 [programmed cell death 1/programmed cell death 1 ligand 1] drugs," said Hansoo Park, CTO at Genome & Company.

GEN-001 is a single-strain bacterium isolated from a healthy human. The R&D program involved carrying out 16S ribosomal RNA profiling of the gut microbiome using stool samples from participants in a clinical trial. By comparing the bacterial composition in healthy controls with that of patients with lung cancer—both responders and nonresponders to immunotherapy—Genome & Company identified immune-related microbiome species and isolated more than 100 bacterial strains.

"We then conducted in vivo efficacy studies to verify whether these bacteria had an antitumor effect alone or had a synergistic effect in combination with anti-PD-1, and found that several bacteria had a very good antitumor effect," said Park.

Promising preclinical data

Genome & Company's clear mode of action for GEN-001 using a multiomics approach has identified several metabolites that are crucial for immune cell activity. "We suspect these metabolites can activate dendritic cells and macrophages in the gut, leading to increased expression of the cytokines IL-15 [interleukin-15] and IL-7," said Park. "These cytokines are known to activate other immune cells, and can turn an immunologically 'cold' tumor into a 'hot' tumor that is more amenable to treatment."

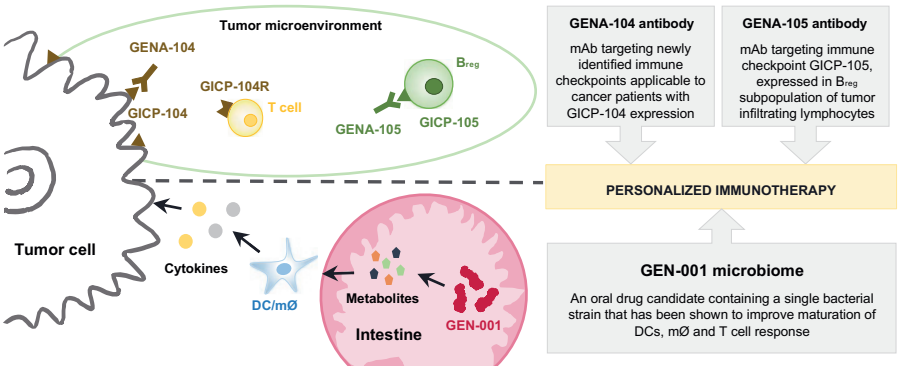

Fig. 1 | Genome & Company's therapeutic candidates in action. B_{reg}, regulatory B cell; DCs, dendritic cells; GENA, anti-GICP monoclonal antibody; GICP, Genome & Company's immune checkpoint inhibitor target code; mØ, macrophages; mAb, monoclonal antibody

Preclinical data from syngeneic mouse models show a significant effect for GEN-001 in suppressing the growth of anti-PD-1-sensitive tumors, which is enhanced when used in combination with a PD-1 inhibitor. GEN-001 has also shown an anticancer effect in anti-PD-1-resistant mouse models.

GEN-001 is being developed for daily administration as an oral enteric capsule containing lyophilized bacteria. In April and May 2020, the company received investigational new drug (IND) clearances by the US Food & Drug Administration and the South Korean Ministry of Food and Drug Safety (MDFS). The clearance came for phase 1/1b trials to commence in both the US and South Korea to assess the immunologic and clinical efficacy of GEN-001 in combination with Merck KGaA/Pfizer's Bavencio (avelumab), an anti-PD-L1 therapy for advanced solid tumors. A phase 1b/2a study is also being planned in South Korea for GEN-001 that will include patients with gastrointestinal cancers which are known to be 'cold' tumors with low overall response rates to PD-1/PD-L1 inhibitors. Also, an investigator-led study of GEN-001 for phase 1 single-dose safety is currently ongoing in South Korea.

Novel targeted ICI

Genome & Company is also progressing an R&D pipeline of novel targeted ICIs designed for a broader population than existing immunotherapy drugs (Fig. 1). The company has been researching more than ten novel targets to induce tumor cell death and is developing therapeutic antibody candidates to target them. Patent applications are in progress for these newly identified novel targets. Potential indications include T cell-inflamed 'hot' tumors as well as non-T cell-inflamed 'cold' tumors.

The company's most advanced ICI project is an antibody to GICP-104, a member protein of the subfamily of immunoglobulin (Ig) domain-containing cell adhesion molecules with high homology of human and mouse. GICP-104 expressed in several human cancer tissues binds to the surface of T cells and regulates their functions negatively. Early studies show that the lead candidate has a potent neutralizing effect for GICP-104 mediated inactivation of T cells, as well as a significant inhibition of tumor growth in syngeneic mouse models. Lead optimization of anti-GICP-104 monoclonal antibody (GENA-104) is ongoing, and an IND-enabling study will be initiated in the first half of 2021.

Genome & Company is also exploring synergies between its microbiome-based therapy and novel ICIs. "We believe these different approaches could work together, as the microbiome bacteria can reprogram the protein expression of immune checkpoint proteins," said Park. "Therefore, we could combine the microbiome asset and novel ICIs for personalized therapy." The company has recently acquired a US microbiome biotech, Scioto Biosciences, and is expanding its personalized therapy approach to neuroscience R&D as well.

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