Genome & Company
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New immuno-oncology personalized therapy approaches

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 pharmaceuticals," said Shawn Sungyeul You, director 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 a tenfold increase in market capital since it went public in December 2018. With a strong background in scientific research and medicine, the company has established development partnerships with leading medical institutes and university hospitals in Korea. It is also expanding its global presence by working with renowned scientific advisers in the field of I-O.

Microbiome-based therapy

Genome & Company's lead development program, GEN-001, is a microbiome-based therapy (**Fig. 1**). There is growing evidence 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 Kyoung Wan Yoon, CSO at Genome & Company.

GEN-001 is a single-strain bacterium isolated from healthy humans. 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 Kyoung Wan Yoon.

Promising preclinical data

Genome & Company has established a clear mode of action for GEN-001 using a multiomics approach, which 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 Kyoung Wan Yoon. "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."

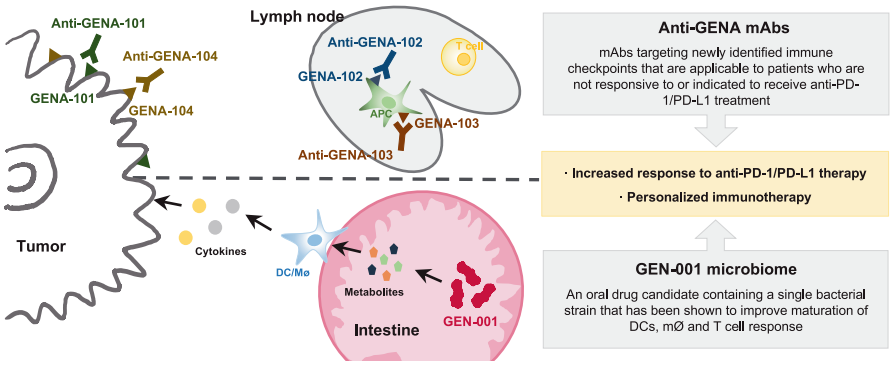

Fig. 1 | Genome & Company's therapeutic candidates in action. APC, antigen-presenting cell; DCs, dendritic cells; GENA, undisclosed novel target; mØ, macrophages; mAb, monoclonal antibody; PD-1, programmed cell death 1; PD-L1, programmed cell death 1 ligand 1.

The company is preparing to submit an investigational new drug (IND) application to the US Food & Drug Administration in Q4 of 2019. GEN-001 is being developed for daily administration as an oral enteric capsule containing lyophilized bacteria. Early clinical development is due to begin in 2020 with a phase 1/2 study in the US to assess the safety, immunologic efficacy and clinical efficacy of GEN-001 in combination with anti-PD-1/PD-L1 therapies for advanced solid tumors. A second phase 1/2 study in Korea for GEN-001 will include patients with gastrointestinal cancers which are known to be 'cold' tumors with low overall response rates to PD-1/PD-L1 inhibitors.

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 validated more than ten novel targets to induce tumor cell death, and is developing therapeutic antibody candidates to target these. 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 novel ICIs are designed to be efficacious in patients who are either nonresponders to PD-1/PD-L1 inhibitors, or may not be eligible for treatment with these therapies. In non-small-cell lung cancer, for example, approximately 10–20% of patients show a durable response to PD-1/PD-L1 inhibitors, thus there is still a large unmet need for new approaches. Lead optimization is complete, and an IND-enabling study is ongoing. Early studies show that the lead candidate has a potent T cell-inhibiting effect, as well as a synergistic effect in combination with PD-1/PD-L1 inhibitors.

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 Kyoung Wan Yoon. "Therefore, we could combine the microbiome asset and novel ICIs for personalized therapy."

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