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Professor Hansoo Park's joint research team identifies microbiome findings and mechanisms that increase the efficacy of immuno-cancer drugs

□ GIST (Gwangju Institute of Science and Technology, President Kiseon Kim) Department of Biomedical Science and Engineering Professor Hansoo Park through joint research with Genome & Company (Professor Hansoo Park and Jisoo Bae, co-representatives), a leading global immunotherapy company that he founded, has discovered microbiomes (intestinal microbes)* that increase the effectiveness of anticancer drugs and investigated the anticancer mechanisms.

> * microbiome: It is a compound word of microbe and biome. It is the sum of all microorganisms, such as living organisms, symbiotic bacteria, and pathogens that share and live in our body and has been overlooked as a cause of health or disease. 95% of the microbiome present in the human body is concentrated in digestive organs such as the intestines.

◦ This study analyzed the intestinal microflora of a total of 235 normal non-small cell lung cancer* patients. As a result, it was confirmed that among Korean non-small cell lung cancer patients, Bifidobacterium bifidum** was significantly distributed at the species level in the group with good anticancer treatment effect.

* non-small cell lung cancer: Lung cancer is largely divided into small cell lung cancer and non-small cell lung cancer according to the tissue type. Types of non-small cell lung cancer include adenocarcinoma of the lung, squamous cell carcinoma, and large cell cancer.

** Bifidobacterium bifidum: It is a bacterial species of the genus Bifidobacterium and resides in the stomach and intestines of humans.

- The research team confirmed that the degree of cancer inhibition was different for each strain of the same Bifidobacterium bifidum species when administered in combination with Bifidobacterium bifidum and an immune anticancer drug (anti-PD-1) in cancer model mice. Bifidobacterium bifidum strains were identified that significantly suppress cancer more significantly than when the strain and the immuno-anticancer agent were administered in combination.

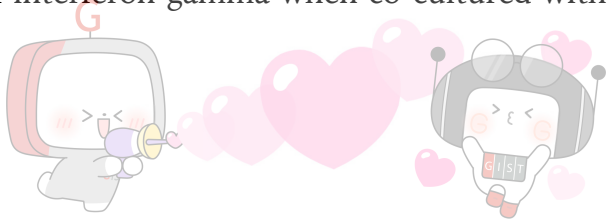
  - The research team identified the anti-cancer mechanism of Bifidobacterium bifidom strains through multi-omics analysis* and the intestinal genome of the mouse. Through transcriptome analysis, it was confirmed that the expression of genes related to regulation of interferon gamma**, one of the anticancer cytokines***, was increased when taking the anticancer strain. Analysis of serum metabolites (metabolomics) and lipid bodies (lipidomics) confirmed that the metabolites that promote the secretion of interferon gamma increased when the strain was administered.

    * multi-omics analysis: a comprehensive and integrated analysis of data generated at various molecular levels such as genome, transcriptome, protein, metabolite, epigenetic, and lipid body

    ** interferon-gamma: As one of the most well-known cytokines, it exhibits biological effects such as antiviral effect, antiproliferative effect of cancer cells, activation of macrophages and B lymphocytes, and increase in expression of main immune complex (MHC) antigens.

    *** cytokine: a glycoprotein used as a signaling substance to control and stimulate the body's defense system

- The research team confirmed that the Bifidobacterium bifidum strains significantly increased the secretion of interferon gamma when co-cultured with



human immune cells (monocyte, CD8+ T cells) compared to the non-effective strains. Through genetic analysis, it was confirmed that the peptidoglycan synthesis pathway was increased in the strains that enhance the efficacy of the immune anticancer agent.

- Experiments using the peptidoglycan receptor TLR2 knock-out mouse demonstrated that differences in peptidoglycan, a component that forms the cell wall of bacteria, are a key mechanism for enhancing the immune anticancer effectiveness of the Bifidobacterium bifidum strain.

□ Professor Hansoo Park said, "This study was the first in the world to discover a microbiome that enhances the efficacy of anticancer drugs in non-cell lung cancer in Asians, and further investigated the mechanism through multi-omics analysis by which the anticancer effect significantly differs depending on the strain of even the same species. Based on the results of this research, we would like to develop a new microbiome drug to give hope to cancer patients to treat carcinomas that are resistant to immune anticancer drugs."

□ This research was conducted by GIST Professor Hansoo Park with support from the National Research Foundation of Korea, the GIST Development Project, and Genome & Company and was published online on January 12, 2021, in *Nature Microbiology* (IF = 15.54, the top 2.9% of the JCR journal rankings).

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