Press Release

Whole Genome Sequencing Finds Therapeutic Targets for Linitis Plastica-type Gastric Cancer

Prospects towards developing treatments for intractable cancer

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National Cancer Center Japan
Keio University School of Medicine
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A group comprising Division of Cellular Signaling (Chief: Hiroyuki Mano) and Department of Translational Oncology, Fundamental Innovative Oncology Core (Chief: Fumitaka Takeshita) at the Research Institute, National Cancer Center Japan (President: Hitoshi Nakagama) and Department of Pathology, Keio University School of Medicine (Professor Yae Kanai) analyzed the whole genome of cancerous cells of ascitic fluids to elucidate the carcinogenic mechanism of linitis plastica-type (also known as scirrhous-type) gastric cancer (LPGC) and to look for targets for its treatment. LPGC is difficult to treat, and little is known of its associated genetic alterations.

The study found many genetic abnormalities associated with LPGC, a quarter of them very likely to respond to molecularly targeted drugs already available. Model mice were implanted with cell lines derived from cancerous cells from the ascites. When specific inhibitors were given, suppression of cancer progression or disappearance of peritoneal dissemination was observed.

Rarely diagnosed early, and often disseminating in the peritoneal cavity, LPGC treatments are challenging, summoning measures to contain peritoneal dissemination, and for prevention. The findings will be directly taken to a wide range of clinical development, from off-label use of molecular targeting drugs, to implementation in cancer gene panel tests and to developing novel compounds.

The results have been published online at *Nature Cancer* on 17 August 2021.

Prospects

The study found detailed genomic information on LPGC, of which highly amplified genes in the receptor-type tyrosine kinase-RAS-MAPK pathway stand out. As mouse models responded to corresponding targeted drugs, inclusion in cancer gene panel tests and development of target drugs are anticipated. A TEAD pathway inhibitor could be the new LPGC treatment drug.

Publication

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