News Press Research Release

Title

Near-infrared photoimmunotherapy targeting GPR87: Development of a humanized anti-GPR87 mAb and therapeutic efficacy on a lung cancer mouse model

Key Points

- GPR87 is expressed in a variety of cancer cell types, but is rarely expressed in normal cells.
- GPR87 is a potential therapeutic target, but the development of therapeutic agents has not progressed.
- We confirmed that GPR87 is frequently expressed in lung cancer and malignant pleural mesothelioma from surgical specimens.
- We succeeded in developing near-infrared photoimmunotherapy (NIR-PIT) targeting GPR87.
- This study is expected to contribute to the basic knowledge for the application of NIR-PIT targeting GPR87 in humans.

Summary 1

Graduate student **Hirotoshi Yasui (1st author)** at the department of Respiratory Medicine, Nagoya University Graduate School of Medicine, Assistant Professor **Kazuhide Sato (corresponding author)**, at Institute for Advanced Research, Nagoya University, **Keisuke Ishii** at Perseus Proteomics Inc and their collaborators succeeded in developing humanized monoclonal antibody for GPR87 and applying them for near-infrared photoimmunotherapy (NIR-PIT) targeting GPR87 for lung cancer.

GPR87 is a protein found on the cell surface of various cancers but rarely found in normal cells, and is attracting attention as a therapeutic target for cancer. GPR87 is found on the surface of various cancer cells, but is rarely found in normal cells.

NIR-PIT is a new cancer treatment reported in 2011 by Dr Hisataka Kobayashi and colleagues at the National Cancer Institute (NCI/NIH). The antibody bound to photosensitizer, IR700, reacts specifically with tumor cells and destroys them when irradiated with 690nm near-infrared light.

In this study, we generated GPR87 antibodies and synthesized IR700 complexes, and proved the efficacy of NIR-PIT against lung cancer targeting GPR87 in cell and animal experiments.

This research was supported by the JST Grant-in-Aid for Human Resource Development in Science and Technology "Project for Building a Consortium for Human Resource Development in Science and Technology: Start-up Research Funds for Young Researchers", the Ministry of Education, Culture, Sports, Science and Technology's Research University Strengthening Promotion Project, the Ministry of Education, Culture, Sports, Science. The paper was published in EBioMedicine, a scientific journal jointly published by the academic publishers Cell Press and The Lancet (electronic version dated May 13,2021).

Summary 2

Research Background

Lung cancer is the most common cause of cancer death in the world. Malignant pleural mesothelioma is a disease with a very poor prognosis and limited treatment options, although the number of patients is small. Both diseases are in need of new treatments.

GPR87 is a protein that is poorly expressed in normal adult cells, where as it has been found to be expressed in the cell membranes of a variety of cancer cells, including lung, pancreatic, cervical and skin cancers, making it a promising target for cancer therapy. However, its physiological functions remain unclear, and the development of therapeutic agents has not progressed.

NIR-PIT is a new cancer modality reported in 2011 by Dr Hisataka Kobayashi and colleagues at the National Cancer Institute, National Institutes of Health, USA. The antibodies bound to photosensitizer, IR700, specifically react with proteins on the surface of tumor cells.

The reaction of IR700 to near-infrared light at 690nm changes the structure of the antibody-dye conjugate and destroys the cell membrane of the tumor cells. This research group has developed a NIR-PIT targeting GPR87.

Research Results

We performed GPR87 immunostaining to resected specimens from patients pathologically diagnosed with lung cancer or malignant pleural mesothelioma who underwent surgery at Nagoya University Hospital. The results showed that GPR87 was expressed in about 60% of non-small cell lung cancer, 40% of small cell lung cancer, and all cases of malignant pleural mesothelioma.

We developed an anti-GPR87 humanized antibody (GPR87ab) at Perseus and synthesized a complex of anti-GPR87 antibody and photosensitizer IR700 to produce GPR87ab-IR700, which was used for NIR-PIT against lung cancer and malignant pleural mesothelioma cells. Microscopic observation showed rapid cell expansion, rupture, and cell death after NIR light irradiation. Simultaneous irradiation of target and non-target cells with near-infrared light caused cell death only in the target cells, without any effect on the non-target cells. In a mouse model of lung cancer, significant inhibition of tumour growth and prolongation of survival were observed (Figure 1).

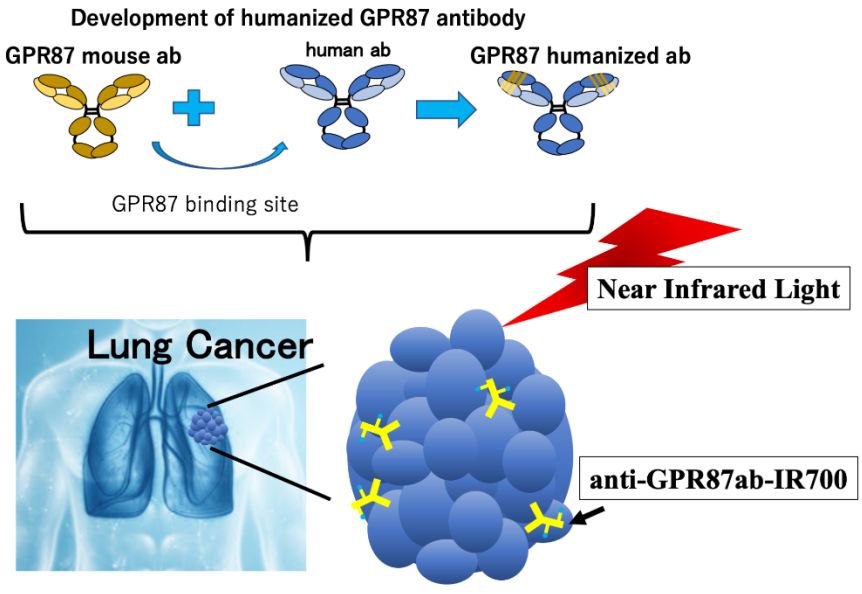

Figure 1. Overview: development of humanized anti-GPR87 ab, and near-infrared photoimmunotherapy for lung cancer targeting humanized GPR87.

Research Summary and Future Perspective

The efficacy of NIR-PIT targeting GPR87 in lung cancer and malignant pleural mesothelioma was confirmed in cell and animal experiments. GPR87 was also found to be highly expressed in lung cancer and malignant pleural mesothelioma. The results are expected to contribute to the basic knowledge for the application of near-infrared photoimmunotherapy to the treatment of lung cancer and malignant pleural mesothelioma in humans. Further applications, such as the development of near-infrared light irradiation devices for thoracic tumors and their combination with conventional therapies, are also being considered in the future.

Publication

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