Taiwan Genomics Research Team Discovers IL-17RB Antibody Blocks Migration of Pancreatic Cancer

A research team led by Academician Wen-Hwa Lee, a Distinguished Research Fellow from the Genomics Research Center, Academia Sinica and the President of China Medical University of Taiwan, recently discovered a protein (IL-17B receptor, IL-17RB) that is strongly associated with migration of pancreatic cancer to other organs after surgery. Using an antibody against IL-17RB, the researchers were able to block tumor metastasis and improve the survival of mice. Pancreatic cancer has an extremely high mortality rate due to its aggressive nature. These findings shed light on a key mechanism underling the highly aggressive nature of pancreatic cancer and also provide a possibility for a future therapy. The discovery was published in the *Journal of Experimental Medicine (JEM)* on March 3, 2015.

Pancreatic cancer is considered largely incurable, even when diagnosed at an early stage. Due to a lack of early symptoms and the aggressive nature of pancreatic tumors, pancreatic cancer patients are often diagnosed at a late stage, when metastasis has already occurred. It is believed that factors derived from both genetics and the surrounding microenvironment may contribute to the aggressive nature of the disease.

The current research confirmed the association of the IL-17RB receptor and its counterpart ligand IL-17B in pancreatic cancer malignancy. A receptor is a protein molecule usually found embedded in the plasma membrane of a cell, and a ligand is a molecule binds to the receptor on the cell surface. When the two types of molecule unite, signals are produced that activate changes inside the cell.

There are many IL-17RB receptors on the pancreatic cancer cell surface, rendering the cell extremely sensitive to IL-17B ligands. In collaboration with Dr Tu-Wen Tien and Dr Yung-Ming Jeng at National Taiwan University Hospital, the research team analyzed 111 pancreatic cancer specimens. They found strong positive correlation (relation) between overexpression of IL-17RB and tumor malignancy in pancreatic cancer patients. They also proved that IL-17B binding to IL-17RB on the cancer cell surface activates the cells.

Then the research team, working with Dr. Alex Che Ma, an Associate Research Fellow of the Genomics Research Center, further developed a new antibody to counteract IL-17RB in mice. The antibody-treated mice had a significantly extended life span, and tumor growth and lung metastasis were also significantly suppressed.

The first author Dr. Heng-Hsiung Wu said: “Since IL-17RB has a much less significant role in other parts of the human body, targeting this receptor with an antibody is likely to cause minimum side effects”.

Academician Lee added that compared with other tumor cells, pancreatic cancer cells are more dynamic and very difficult to understand. He emphasized that the success of the current research was due to close teamwork and cooperation, and the antibody has already been patented.

The current discovery is based on Dr. Lee's previous research outcomes regarding the IL-17RB receptor on the surface of breast cancer cells. He was the first scholar to identify the human tumor suppressor gene, retinoblastoma, in the late 1980s and one of his breast cancer drugs has reached the clinical trial phase.

The complete article entitled "Targeting IL-17B/RB signaling with an anti-IL-17RB antibody blocks pancreatic cancer metastasis by silencing multiple chemokines" can be found at the JEM website at: http://jem.rupress.org/content/early/2015/02/24/jem.20141702.full.

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