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Study shows that early-stage breast cancer patients who carry a variation of the BDNF gene are less likely to develop chemotherapy-induced cognitive impairment

A team of researchers from the National University of Singapore (NUS) has established that variation of a gene may have a role in protecting cancer patients from developing chemotherapy-induced cognitive impairment, commonly known as 'chemofog' or 'chemobrain'.

The brain derived neurotrophic factor (BDNF) gene is responsible for producing a protein that controls the growth and function of nerve cells in the brain and spinal cord. Studies have shown that a reduction in blood level of BDNF – due to variation in the BDNF gene – is associated with cognitive impairment in patients with Alzheimer's disease and other neuropsychological disorders.

A recent study led by Associate Professor Alexandre Chan and PhD candidate Mr Terence Ng, who are from the Department of Pharmacy at the NUS Faculty of Science, found that early-stage breast cancer patients who carry a specific variation of the BDNF gene are less likely to develop cognitive impairment after undergoing chemotherapy. This is the first time that the BDNF gene is associated with cognitive changes in cancer patients. The novel discovery was reported in the international scientific journal *Neuro-Oncology* in August 2015.

Chemotherapy-induced cognitive changes

In his earlier studies, Assoc Prof Chan had found that breast cancer patients who undergo chemotherapy may develop a side effect known as 'chemofog' or 'chemobrain', in which they experience cognitive impairment such as memory loss, difficulty in decision making and multi-tasking abilities.

Assoc Prof Chan said, "These cognitive changes affect patients' quality of life, prevent them from returning to work or school and inhibit their social activities. Hence, gaining a better understanding of how 'chemobrain' occurs and how to prevent it is crucial."

Carriers of BDNF gene variant protected against 'chemobrain'

The study was conducted from December 2011 to April 2014 and involved 145 early-stage breast cancer patients from the National Cancer Centre Singapore and KK Women's and Children's Hospital. The patients were monitored before, during and after chemotherapy. The researchers evaluated the cognitive status, quality of life and behavioural symptoms of these patients. They also performed genotyping on patients' blood sample in collaboration with Associate Professor Ho Han Kiat from the NUS Department of Pharmacy.

Of the 145 patients studied, 54 showed cognitive impairment after they underwent chemotherapy. However, patients who are carriers of a variation of the BDNF gene showed less impairment in verbal fluency and/or multitasking ability. The variation occurs when an amino acid in the gene changes its position.

On the significance of the findings, Assoc Prof Chan explained, "We are very excited about the findings as this is the first time that cancer patients who carry the BDNF gene mutation has been shown to be less likely to experience cognitive decline after chemotherapy. This novel discovery can certainly help researchers better understand the underlying mechanisms that lead to the development of this chemotherapy-induced side effect. More importantly, this will provide us with information on whether certain patients who are at high risk for cognitive impairment post-chemotherapy may benefit from early interventions. Further studies need to be conducted to evaluate how the gene mutation is associated with the blood levels of BDNF as well as the precursors of BDNF."

Taking the research forward

Assoc Prof Chan and his team are collecting additional patient samples to conduct further studies to validate their findings, and they are also currently evaluating how cognitive impairment in cancer patients is associated with other physiological and behavioural symptoms, such as cancer-related fatigue and anxiety.

The researchers are also conducting a randomised controlled trial to manage post-chemotherapy side effects and symptoms in breast cancer survivors, including cognitive impairment. They are collaborating with overseas institutions to further their research, and they also hope to work with partners to develop therapeutics for preventing and treating cognitive impairment in cancer patients.

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