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Singapore:Ã?Â A team of scientists from National University of Singapore (NUS) has established novel insights into the relationship between breast cancer tumour intracellular redox environment and the cancer cells' ability to become invasive.

The study by Dr Alan Prem Kumar from the Cancer Science Institute of Singapore (CSI Singapore) at NUS and NUS Yong Loo Lin School of Medicine, together with Professor Shazib Pervaiz and Associate Professor Marie-Veronique Clement from NUS Yong Loo Lin School of Medicine, found that high levels of Manganese Superoxide Dismutase (MnSOD), a key enzyme involved in regulating the cellular redox milieu, has a role to play in causing breast cancer cells to turn aggressive, especially in triple negative breast cancer subtype tumours. These aggressive cells are able to invade other sites in the body, resulting in secondary tumours.

"Our group's work over the years has highlighted the critical role of cancer cells' oxidative metabolism in drug resistance and cell survival. This study underscores the importance that MnSOD plays in the biology of breast cancer," said Assoc Prof Clement.

The new findings build on the group's previous discovery of the presence of a significantly higher MnSOD levels in triple negative breast cancer patients.

"MnSOD expression is decreased during the initial stages of cancer development. However, as the cancer advances, MnSOD expression increases and such high MnSOD levels are typically observed in triple negative breast cancer patients. In fact, we have shown that less aggressive tumours, when artificially made to increase MnSOD protein levels, adopt an aggressive behaviour. Our study shows that the amount of MnSOD levels in the tumour cell determines the predominant reactive oxygen species that will tell the tumour cells whether to stay put or to transform into an invasive form that is capable of moving to distal parts of the body," explained Dr Loo Ser Yue, a former graduate student from NUS Yong Loo Lin School of Medicine and the first author of the study.

Triple negative breast cancer is a subtype of estrogen-independent breast cancer. Among female patients diagnosed with various subtypes of breast cancer in Singapore and worldwide, about 13 per cent of them are triple negative. While considerable progress has been made in the diagnosis and treatment of estrogen-dependent breast cancer, triple negative breast cancer is associated with poor diagnosis due to a lack of targeted therapeutic options. By studying the underlying cause of this subtype of breast cancer, the NUS research team hopes to design and develop effective therapeutic strategies to combat this disease.

"Our study provides a novel mechanism for exploiting cancer's Achilles heel with potential implications for the design of target-specific therapies against aggressive breast cancer," said Professor Pervaiz.

As part of their earlier study, the NUS team had shown a novel strategy of targeting this enhanced MnSOD expression and therefore its activity using other FDA-approved drugs to make the aggressive tumours more sensitive to conventional anti-cancer drugs. They also showed that this strategy would re-sensitise patients who develop resistance to conventional breast cancer drugs such as Docetaxel or Doxorubicin.