New molecule protects heart from toxic breast cancer drugs

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A new molecule has been found that protects the heart from toxic breast cancer drugs and also kills the cancerous tumor. The research from Italy addresses the burgeoning problem of heart disease in cancer survivors and is announced by the European Society of Cardiology today on World Cancer Day.

Dr Alessandra Ghigo, first author and research fellow in the Department of Molecular Biotechnology and Health Sciences, University of Torino, Italy, said: "Cardiotoxicity of cancer drugs has become an increasing problem in the last decade due to the increasing success of anticancer therapy and aggressive use of these drugs. More people are now surviving cancer but it is estimated that 32% of them could die of heart disease caused by their treatment. This has led to a new field of medicine called cardio-oncology."

Professor Patrizio Lancellotti, chair of the ESC EACVI/HFA Cardiac Oncology Toxicity Registry, said: "Patients with some forms of breast cancer are at greater risk of dying from heart disease than from cancer. A number of breast cancer treatments are toxic for the heart notably chemotherapy with anthracyclines, such as doxorubicin, or with trastuzumab (Herceptin). Radiation therapy can make anthracyclines even more cardiotoxic, as can the sequence of anthracylines followed by trastuzumab. The latter combination for metastatic breast cancer can cause severe heart failure in up to 27% of patients."

The theme of World Cancer Day 2015 is 'Not beyond us'. New research

from Dr Ghigo presented for the first time at the Heart Failure Winter Research Meeting shows that solutions to cardiotoxicity of cancer drugs are within reach.

Dr Ghigo's research focuses on the enzyme phosphoinositide 3-kinase gamma (PI3Kγ) which regulates heart function. She previously showed that inhibiting the activity of PI3Kγ protected mice with hypertension from developing heart failure.

For the current study she used genetically modified mice expressing an inactive form of PI3Kγ to mimic the use of an enzyme inhibitor. When the mice were treated with the anthracycline doxorubicin, they survived more than normal mice and their heart function was completely preserved. Normal mice, who had the active form of PI3Kγ, developed severe heart failure within 2 months of beginning treatment with doxorubicin.

To see if the findings could be applied to humans the next step was to treat normal nice with doxorubicin plus a drug to inhibit the activity of PI3Kγ. Dr Ghigo said: "The inhibitor was able to completely protect the mice from developing heart failure after doxorubicin treatment."

The same experiment was then performed on mice with breast cancer to ensure that the PI3Kγ inhibitor did not interfere with the anticancer activity of doxorubicin. Again the mice were treated with both doxorubicin and the PI3Kγ inhibitor.

Dr Ghigo said: "The PI3Kγ inhibitor protected the mice from developing heart failure. Importantly, the inhibitor was able to synergise with the doxorubicin and help to delay tumour growth. This means we could use an inhibitor of PI3Kγ to both protect the heart from doxorubicin and prevent tumour growth. Our research shows that inhibiting PI3Kγ stops inflammation in the tumour and kills the tumour."

She added: "One of the main problems with the cardiotoxicity induced by chemotherapy is that the anticancer regimens need to be modified. We may have to use lower doses of agents to prevent the cardiotoxicity or stop the treatment. By using this inhibitor of PI3Kγ together with the chemotherapy we could allow a wider and safer use of anticancer therapies because we don't need to lower the dose or change the treatment."

She concluded: "The mechanisms underlying heart failure induced by anticancer therapies are different to those underlying heart failure from other causes such as hypertension. For this reason there are no effective drugs on the market to prevent this new kind of heart failure. Our study shows that PI3Kγ could be a novel way to prevent heart failure caused by cancer drugs while also helping to kill the tumour itself."

More information: The ESC EACVI/HFA Cardiac Oncology Toxicity Registry was launched in September to collect data on practices for identifying and treating cardiotoxicity of breast cancer drugs. More information can be found here: www.escardio.org/guidelines-su … ry.aspx?highlight-on

Provided by European Society of Cardiology