New biomarker to enable the identification of patients who may develop resistance to hormone therapies for breast cancer

BACKGROUND

Around 80% of breast cancers are ER+ and are treated with anti-oestrogen therapies such as tamoxifen and aromatase inhibitors. But around one in five of these cases recur within 10 years, and nearly all advanced cases develop resistance to hormonal therapies. It is currently not possible to predict which patients are likely to develop resistance at the early stages of treatment.

TECHNOLOGY

A team based at the Institute of Cancer Sciences has found that although short-term treatment with anti-oestrogen drugs decreased tumour growth, it also increased the activity of breast cancer stem cells. They found that these stem cells were driven by a signal called NOTCH4. Studies looking at patient-derived breast cancers in mice and cells grown in the laboratory indicated that it was the presence of NOTCH4 that enabled the cancer stem cells to avoid anti-oestrogen treatment. In patient tumours, having high levels of NOTCH4 before treatment was linked to breast cancer spread and worse survival outcomes.

This suggested that resistance to anti-oestrogen treatment could be overcome by targeting the cancer stem cells with a NOTCH inhibitor.

When patients were treated with both tamoxifen and a NOTCH inhibitor, tamoxifen decreased the tumour growth while the NOTCH inhibitor decreased the numbers of breast cancer stem cells that could form new tumours, compared to treating with tamoxifen alone.

This shows that combining standard hormonal therapies with a NOTCH pathway inhibitor, or other drugs targeting breast cancer stem cells, could improve treatment of ER+ breast cancer patients by preventing relapse due to therapy resistance. General inhibitors of the NOTCH pathway are already being tested in breast cancer clinical trials.

The team has found a link between high levels of NOTCH4 and ALDH1, which means that ALDH1 could act as a biomarker to predict whether a breast cancer patient is likely to be resistant to anti-oestrogen drugs and which patients could benefit most from combined treatment with anti-oestrogen therapies and a NOTCH inhibitor.

OPPORTUNITY

The University is now looking for commercial partners who will be interested in collaborating with the research team to develop the biomarker for use in clinical trials and potentially as a companion diagnostic for Notch inhibitors.

PATENT

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