**////Title: A New Biological Tool to Assess the Efficacy of Chemotherapy in Breast Cancer**

**////Stand-first**: There is an urgent need for prognostic tools that can accurately predict the outcomes of patients undergoing treatment for breast cancer. Dr Fatima Rehman and her colleagues investigated the relationship between breast cancer prognosis and the secretion of a biological marker called Galectin-3 to drive forward the development of optimised treatment regimes. This work was conducted at Shaukat Khanum Memorial Cancer Hospital and Research Centre in Pakistan.

**////Body text:** While there have been significant advances in the technology used to diagnose breast cancers, less progress has been made in developing tools or methods to allow clinicians to accurately monitor a patient’s prognosis while they are undergoing treatment.

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Depending on a patient’s type and grade of cancer, the treatment that they require will vary. While a lower grade (slower growing) or localised tumour may be treated with minimal amounts of chemotherapy following surgery, a higher grade cancer that is spreading more rapidly may require more aggressive chemotherapy to shrink the mass before it is removed surgically. Sometimes, the cancer responds so well that there is no visible tumour remaining once therapy is complete. However, even in these cases, there are plenty of tumour cells still circulating in the body that could lead to a return of cancer in the future.

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Establishing the ongoing presence of a cancer after it has been treated can be challenging.At present, clinicians use a variety of techniques that include magnetic resonance imaging and computerised tomography scanning. These methods are less useful as tools once all signs of the visible tumour have been removed. However, it is crucial to monitor how effective a treatment regimen is likely to be and to ensure that it is being continually optimised to reduce the remaining cancer burden in a patient and the chance of a relapse, especially in cases with no visible tumour to follow.

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Galectin-3 is a protein that is widely expressed in the nucleus, cytoplasm [sai·tow·pla·zm], cell surface and also outside of cells in the extracellular environment. It plays a pivotal role in numerous biological processes, including cell growth, differentiation, adhesion, inflammation and programmed cell death.

The absence of Galectin-3 has been associated with higher growth of breast tumours in mice and also with a poorer prognosis in women with breast tumours that have spread to the underarm lymph nodes.

Studies have produced conflicting results regarding the function of Galectin-3 in tumour formation, growth and progression, depending on its localisation. While Galectin-3 inside the cell can help in tumour cell survival, secreted Galectin-3 can actually induce tumour cell death instead.

In fact, extracellular Galectin-3 in patient plasma and surrounding matrix of tumours has been implicated in the process of programmed cell death, leading Dr Fatima Rehman (at Shaukat Khanum Memorial Cancer Hospital and Research Centre in Pakistan) to speculate that it might play an important role in determining tumour response to chemotherapy treatments in patients.

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Dr Rehman and her colleagues investigated whether soluble Galectin-3 was elevated in breast cancer patients receiving chemotherapy and whether it could be used as a biological tool to assess the prognosis of breast cancer patients while they were undergoing treatment. They hypothesised that increased levels of Galectin-3 would be found in the stromal [stro-mal] tissues – which include the fatty and fibrous connective tissues of the breast – as well as the plasma of patients whose tumours were responding well to chemotherapy treatment.

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A total of 88 women attending the Shaukat Khanum Memorial Cancer Hospital and Research Center in Pakistan were recruited into the study, which took place between March 2007 and 2008. All had a first-time breast cancer diagnosis and none had undergone any prior treatment for their cancer.

Patients were divided into two groups: those receiving minimal amounts of chemotherapy following surgery and those who received more aggressive chemotherapy to shrink the mass, before surgery. All patients received the conventionally used taxane-based chemotherapy as part of their treatment protocol.

Stromal and plasma levels of Galectin-3 were measured in each patient at the time of diagnosis and then throughout the study. Blood samples were also obtained from 63 healthy women to establish baseline levels of plasma Galectin-3.

Patients were followed up for 84 months after the end of their treatment to enable the researchers to calculate how long they remained free from disease.

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Before treatment, analysis of tumour tissue from newly diagnosed breast cancer patients showed that significant levels of extracellular Galectin-3 were observed in the stroma of low-grade tumours but that these levels decreased dramatically with increasing grade of malignancy.

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Dr Rehman and her colleagues then analysed stromal and plasma Galectin-3 levels in women undergoing two different treatment methods for newly diagnosed breast cancer and followed the expression and localisation of Galectin-3 throughout the treatment period in these patients.

Enhanced levels of plasma Galectin-3 in women who had received chemotherapy treatment following surgery were found to be predictive of how effective their chemotherapy treatment had been. In women who had received more aggressive chemotherapy treatment before their surgery, enhanced levels of Galectin-3 present in their stromal tissue was also found to bepredictive of chemotherapy efficacy. However, no enhancement or significant change in plasma levels of Galectin-3 was observed in these patients.

Patients with chemotherapy-induced increases of extracellular Galectin-3 experienced longer disease-free intervals and a significantly lower rate of disease recurrence during the 84-month follow-up period, compared to patients who demonstrated unchanged or reduced secretion of extracellular Galectin-3.

For patients who have been initially treated with surgical removal of their tumour before any chemotherapy treatment, these findings support the use of Galectin-3 measurements in plasma samples as a way to assess treatment efficacy when there is no visible tumour left to image.

For those patients receiving chemotherapy to shrink their tumour before its surgical removal, Dr Rehman also concluded that levels of Galectin-3 present in the stroma of any remaining tumour can also be used to help predict the long-term prognosis of a patient.

In summary, Dr Rehman and colleagues demonstrated that increased Galectin-3 secretion, seen in response to chemotherapy treatment, indicated a better prognosis and longer disease-free survival in newly diagnosed breast cancer patients.

The researchers propose a potential mechanism of action for chemotherapy-induced extracellular Galectin-3 but note that more research is required to understand the process fully. Dr Rehman cautions that although the findings indicate that Galectin-3 might be a useful biological marker, furtherresearch is required to validate the results from this study, which will allow for the translation of the method into clinical practice. Nevertheless, these results have exciting implications for monitoring the prognosis of women while they are undergoing treatments for breast cancer.

This SciPod is a summary of the paper ‘Elevated Soluble Galectin-3 as a Marker of Chemotherapy Efficacy in Breast Cancer Patients: A Prospective Study’, from the International Journal of Breast Cancer. DOI: https://doi.org/10.1155/2020/4824813.

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