Medical Xpress

Discovery that PARP protein exists in all breast tumors will help target chemo and predict response

March 26 2010

The presence of the protein poly (ADP-ribose) polymerase (PARP) in tumours can help predict their response to chemotherapy, a German scientist will tell the seventh European Breast Cancer Conference (EBCC7) in Barcelona tomorrow (Saturday 27 March). Professor Gunter von Minckwitz, from the German Breast Group Forschungs GmBH, Neu-Isenburg, says that, contrary to current belief that PARP is associated with a limited number of tumours, he and his team found for the first time that PARP expression exists across all breast cancer subtypes, and that such tumours were highly sensitive to chemotherapy.

Professor von Minckwitz and his team set out to investigate the expression of PARP in various hormone receptor subtypes of early breast cancer and to evaluate whether or not it could predict a total response to chemotherapy given before surgery. "We knew that a new class of drug called PARP inhibitors were effective against aggressive types of breast cancer such as those involving BRCA mutations and triple-negative breast cancer, where the tumour does not express genes for the oestrogen or progesterone receptors, or for HER2," he says. "However, we didn't understand whether the presence of PARP would predict the efficacy of these drugs. Before exploring this, we needed to understand whether PARP played any role in breast cancers, whether it was restricted to particular types of tumours, how it correlated to existing prognostic and predictive markers, and whether it could predict the efficacy of chemotherapy."

PARP is a protein involved in a number of cellular processes. One of its important functions is assisting in the repair of single-strand DNA breaks. If one single-strand broken DNA is reduplicated, a double-strand broken DNA results. If PARP is inhibited, cell death occurs; this means that chemotherapy can be targeted precisely at cancer cells, while leaving normal, healthy cells relatively untouched. A recent conference presentation* showed that the simultaneous use of a PARP inhibitor with DNA-damaging chemotherapy in breast cancer could improve overall survival. The potential role of PARP inhibitors as a new anticancer agent is currently under research in a number of other studies.

Professor von Minckwitz's team used tissue from 646 patients in a neoadjuvant Phase III trial (GeparTrio) to look for the presence of PARP and to correlate its existence with other prognostic factors and total response to chemotherapy. Neoadjuvant chemotherapy is given to patients before other treatments such as surgery or radiotherapy. They found that, although PARP was present in all tumour subtypes, it occurred most frequently in HER2 positive and triple negative tumours, and that it correlated with most known prognostic factors, except HER2.

"The relationship to total response was remarkable," says Professor von Minckwitz. "Tumours with a high level of PARP expression had a total response in 26% of cases, whereas those tumours which did not express PARP had a total response in only 9%. Additionally, we found that the presence of PARP can provide more accurate prognostic information than the grade of differentiation or degree of abnormality of tumours. We believe that this is the first study to describe a broad expression of PARP in untreated breast tumours together with a correlation of sensitivity to chemotherapy."

PARP positive tumours could become a new entity in breast cancer, the investigators say. They intend to follow up their initial findings by a trial randomising patients to either chemotherapy alone or chemotherapy plus

a PARP inhibitor. "Particularly in triple-negative tumours there is a great need to improve treatment options," says Professor von Minckwitz. "Apart from chemotherapy, there is no other treatment such as endocrine or anti-HER2 therapy available for this aggressive form of breast cancer."

However, it remains to be seen whether immunohistochemical detection (the process of localising antigens in tissue cells) of PARP is the best method of predicting PARP inhibitor efficacy, the scientists say. "We need more prospective trials to be sure that there is no better way of making sure that the right people are getting the right therapy," says Professor von Minckwitz. "However, it would be fair to say that we believe that we may be on the verge of a major change in the way breast cancer is treated."

Provided by ECCO-the European CanCer Organisation

Citation: Discovery that PARP protein exists in all breast tumors will help target chemo and predict response (2010, March 26) retrieved 4 May 2024 from https://medicalxpress.com/news/2010-03-discovery-parp-protein-breast-tumors.html