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Press Release

New diagnostic method improves treatment options for breast cancer - Protein test finds hidden molecule

Immunotherapy can be a successful treatment option for breast cancer patients. The method uses antibodies, which bind to the surface molecules of the tumor, hindering its growth. One of these antibodies targets the HER2 protein, which is not actually present in all variants of the tumor. Now researchers have developed a sensitive new diagnostic method that could allow more patients to benefit from the treatment. This new test also detects cancer cells that appear to be free of HER2 – but which do actually carry the molecule.

HER2 occurs in many somatic cells. The molecule is a growth hormone receptor that gives cells the signal to divide. This causes tumor cells to multiply also – with the difference that they are carrying considerably more HER2 molecules and so the cells reproduce at an uncontrollable rate. Since not all breast cancer cells are HER2-positive, pathologists analyze samples of the tumor tissue prior to any immunotherapy. However, these tests do not always produce an accurate result, as NGFN-scientists from the Technische Universität München (TUM) and scientists from the George Mason University in the USA have demonstrated.

The researchers developed their own diagnostic method to analyze 223 tissue samples: “We were able to detect HER2 in 37 patients, even though they had previously been tested negative,” relates Prof. Karl-Friedrich Becker from TUM’s Institute of Pathology. The difference is that this new method is able to detect HER2 even when the molecule is active and in the process of transmitting signals. “When it is active, phosphate groups are attached to the molecule. It could be these groups that cause the conventional antibody test to produce a negative result.” The researchers are hopeful that more patients can be treated with the Trastuzumab antibody, which switches off HER2.

The new technique has been developed in conjunction with the National Genome Research Network (NGFN-Transfer). During the process, the researchers succeeded in tracking the HER2 signal pathway at protein level. For the first time, they were able to extract intact proteins from formalin-fixed, paraffin-embedded tissue samples. “These ‘FFPE’ tissue samples are used as standard in all hospitals,” explains Prof. Becker. “However, up to now it has been very difficult to extract proteins from them.” In order to detect the active HER2 phosphoproteins, the researchers used a combination of biopsies and an automated analysis method known as protein arrays.

The research team compared their results with protein analyses of frozen tumor tissue. Unlike FFPE tissue samples, proteins are relatively easy to detect in frozen, untreated biopsies. The activated HER2 molecule was also found in many frozen tumor samples that were previously classified as HER2-negative. "Fresh or frozen tissue samples are rarely found in hospitals," explains Prof. Becker. "In the future, pathologists will be able to use FFPE tissue, which is routinely prepared during every biopsy, to perform more accurate testing for HER2 using our method. This will give breast cancer patients a better chance of receiving successful treatment." The methodology is also suitable for other biomarkers, in particular in tissue samples of other types of tumor.

Original Publication:

Clin Cancer Res. (2012). **Molecular analysis of HER2 signaling in human breast cancer by functional protein pathway activation mapping.** Wulffkuhle JD, Berg D, Wolff C, Langer R, Tran K, Illi J, Espina V, Pierobon M, Deng J, Demichele A, Walch A, Bronger H, Becker I, Waldhor C, Höfler H, Esserman LJ, Liotta LA, Becker KF, Petricoin EF 3rd.
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National Genome Research Network (NGFN)

The federal ministry of education and research (BMBF) is funding the investigation of breast cancer markers within the national genome research network (NGFN) since 2008 in the field NGFN-Transfer of the Program of Medical Genome Research. The present study was conducted by the Innovation Alliance "Protein analysis of formalin-fixed breast cancer tissues for diagnosis, prognosis, and therapy guidance". Within this Innovation Alliance the Institute of Pathology at TU München (lead management) cooperates with the Women's Clinic of the University Hospital rechts der Isar, Munich, the Institute of Pathology, Klinikum Rosenheim, the Women's Clinic of the Hospital of Rosenheim, and the company Quiagen GmbH, Hilden.

<http://www.ngfn.de/en/>

Technische Universität München (TUM) is one of Europe's leading universities. It has roughly 480 professors, 9,000 academic and non-academic staff and 32,000 students. It focuses on the engineering sciences, natural sciences, life sciences, medicine and economic sciences. After winning numerous awards, it was selected as an "Elite University" in 2006 and 2012 by the German Council of Science and Humanities (Wissenschaftsrat) and the German Research Foundation (DFG). The university's global network includes an outpost with a research campus in Singapore. TUM is dedicated to the ideal of a top-level research-based entrepreneurial university.

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Clinical tissue sample - fixed in formalin and embedded in paraffin.

image: S. Willax/TU Munich

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Production of tissue sections

image: S. Willax/TU Munich

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