Biosensor to detect tumors at early stages

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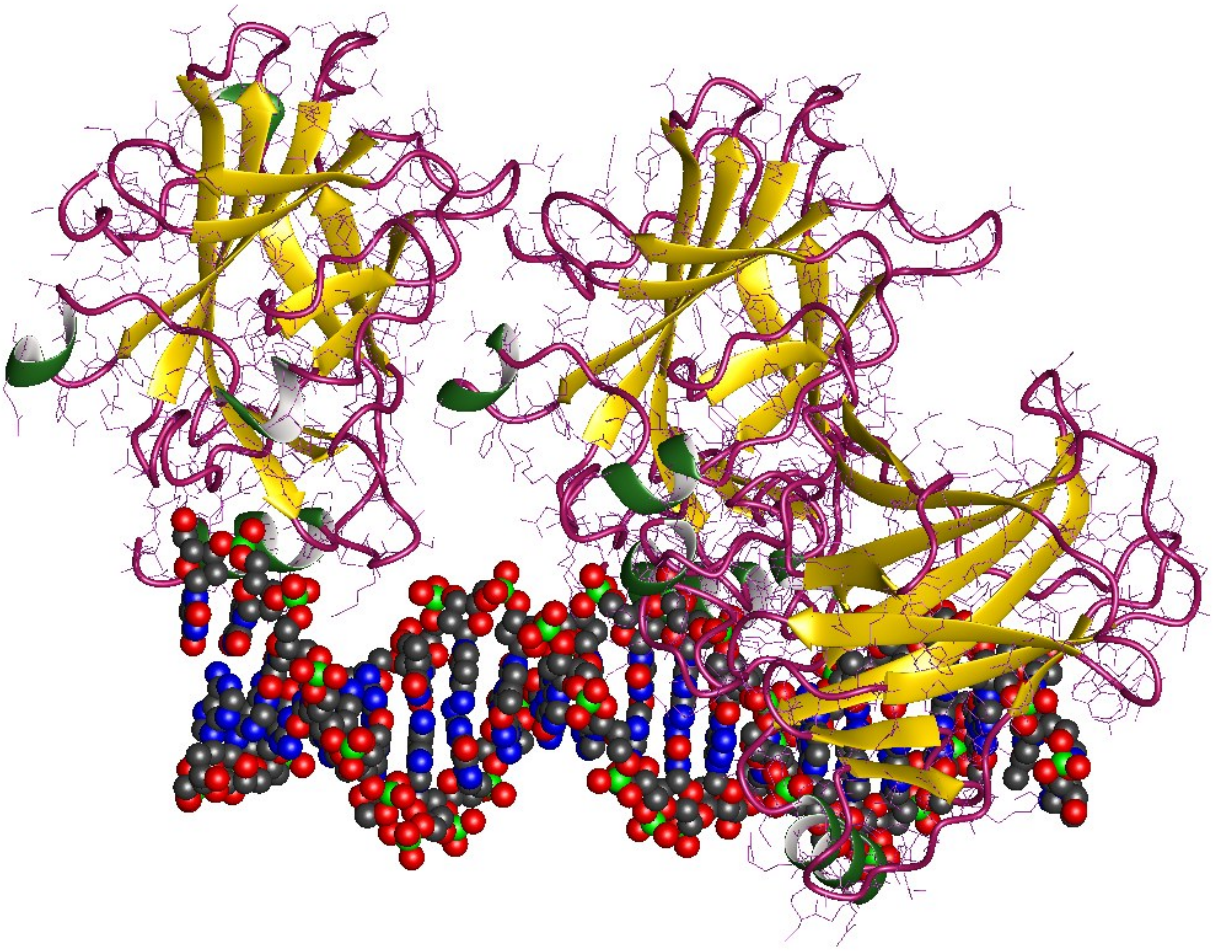

Tumor suppressor p53 trimer and DNA fragment. Credit: Cho, Y., Gorina, S., Jeffrey, P.D., Pavletich, N.P.; Astrojan.

Before a malignant tumor develops, the immune system tries to fight

against its altered proteins by producing certain cancer antibodies. A biosensor developed by scientists from the Complutense University of Madrid is able to detect these defensive units in serum samples of patients with colorectal and ovarian cancer. The method is faster and more accurate than traditional methods.

When healthy cells become tumors, the expression of many proteins is altered. As a defense, the immune system produces certain antibodies against them. The production of these autoantibodies starts several months or even years before the disease is completely developed and detected by the clinicians.

"Our immune system produces these cancer autoantibodies even three years before the first symptoms appear," explains Susana Campuzano, associate researcher at the Department of Analytical Chemistry at the Complutense University of Madrid (UCM).

In collaboration with other hospitals and the Instituto de Investigaciones Biomédicas Alberto Sols (Madrid), scientists at the UCM have designed a biosensor capable of detecting these antibodies in serum samples from both cancer patients and patients at high risk of developing cancer.

To verify their effectiveness, the researchers applied the biosensor to the analysis of serum samples from four patients with colorectal cancer and two with ovarian cancer and treated at Puerta de Hierro and La Paz Hospitals (Madrid). In addition, they also used the biosensor to analyze the sera from 24 patients treated at Hospital Universitario Clínico San Carlos (Madrid) with high probability of developing malignant colorectal tumors due to a familial history of cancer.

With the biosensor, the scientists at UCM detected the autoantibody content generated by the patients against the p53 protein. "This protein is known as the guardian of the genome because it repairs DNA mutations,

avoiding alterations in the cell cycle and the appearance of tumors," says José Manuel Pingarrón, professor of *Analytical Chemistry* at UCM and co-author of the work, recently published in *Analytical Chemistry*.

When p53 is aberrantly mutated and multiplies without control, the immune system of between 10 and 40 percent of all cancer patients produce autoantibodies against p53, depending on the cancer type, signaling a possible malignant transformation.

"The presence of antibodies against p53 could be indicative of the existence of a neoplastic disease already initiated or of the risk of developing cancer in the near future," says Rodrigo Barderas, Ramón y Cajal fellow at the Biochemistry and Molecular Biology I Department of the Chemistry Faculty of the UCM and co-author of the work.

Management of the disease

Compared with other methods that also detect autoantibodies against p53, the biosensor demonstrated a 440-fold higher sensitivity and a better discrimination between positive and negative serum samples to p53 autoantibodies.

Another advantage of the biosensor is its simplicity and speed. In less than six hours, the test is completed, including the expression and purification of p53, in contrast to the weeks or months necessary for traditional methods in which the protein is produced and purified separately from the assay. "Its simplicity of handling, portability and time to complete the full procedure make it suitable for application in clinical routine," says Campuzano.

In addition to application as an early diagnostic method in liquid biopsies, the biosensor can be used to monitor the course of the disease in patients with autoantibodies to p53. It has been demonstrated that

when the tumor burden disappears, the levels of these antibodies to p53 decrease to normal values.

The study participants with high probability of developing colorectal malignant tumors are currently undergoing exhaustive follow-up by clinicians at the Hospital Universitario Clínico San Carlos (Madrid).

More information: María Garranzo-Asensio et al, Toward Liquid Biopsy: Determination of the Humoral Immune Response in Cancer Patients Using HaloTag Fusion Protein-Modified Electrochemical Bioplatforms, *Analytical Chemistry* (2016). DOI: 10.1021/acs.analchem.6b03526

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