Scientists discover a cause of multiple resistance to cancer chemotherapy

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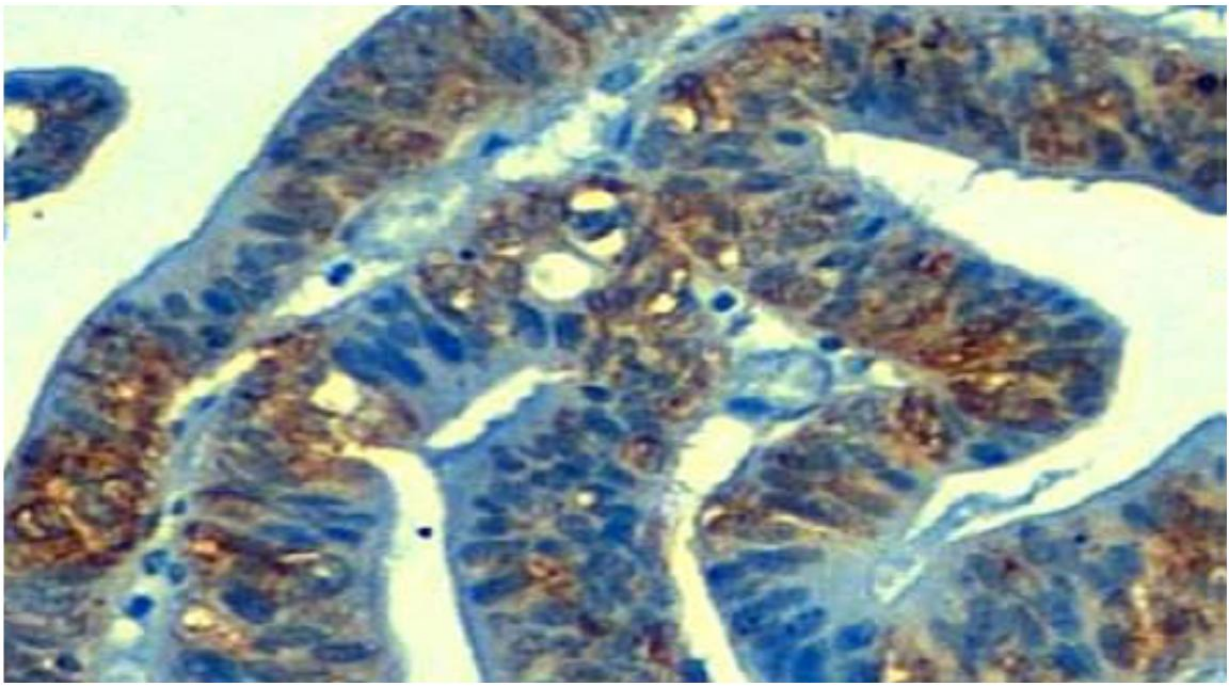

Section of a stomach cancer (seen under a microscope) showing aberrant expression of YBX1 protein (stained brown). Credit: IDIBELL

A new study by researchers at the Bellvitge Biomedical Research Institute (IDIBELL) has found a cause of multiple resistance in cancer chemotherapy. The work, published today in the *Proceedings of the National Academy of Sciences* (*PNAS*) journal, the organ of expression of the United States Academy of Sciences, has been carried out by the

research group of Dr. Manel Esteller, Director of Epigenetics and Cancer Biology Program (PEBC) of IDIBELL, ICREA Researcher and Professor of Genetics at the University of Barcelona.

The introduction of cancer chemotherapy was a revolution for the treatment of this disease in those cases in which the cure is no longer possible only with the mere extirpation of the tumor. Chemotherapy has been shown to be effective in a wide range of patients, but one of its main problems is the emergence of resistance against the anti-tumor drug used. However, it has been known for decades that there are tumors that display cross-resistance against different drugs since its inception, when they have not yet been treated.

"We have found that 10% of colon and stomach tumors present the loss of a molecule called TP53TG1, whose function in healthy cells is to prevent activation of YBX1 protein. Without surveillance of TP53TG1 in these gastrointestinal tumors, YBX1 goes to the nucleus of the cell and is responsible for the activation of hundreds of oncogenes that will prevent the death of malignant cells that antitumor drugs induce", says Dr. Manel Esteller.

The spectrum of resistances induced by this mechanism is extensive and includes drugs commonly used in the treatment of these cancers, such as as 5-fluorouracil, oxyplatinum or irinotecan, but also drugs targeting recent molecular targets such as kinase inhibitors.

After publishing their results in *PNAS*, Dr. Esteller explains, "we want to study if there is any drug that escapes this mechanism of multiple chemoresistance and also to explore whether returning the activity of the molecule TP53TG1 would mean regaining the sensitivity of these tumors to the drugs analyzed, which would represent a clinical benefit for these patients."

More information: Epigenetic inactivation of the p53-induced long noncoding RNA TP53 target 1 in human cancer, *PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1608585113

Provided by IDIBELL-Bellvitge Biomedical Research Institute