

## New function of a protein involved in colon cancer is identified

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Researchers from IMIM, Hospital del Mar Medical Research Institute, have succeeded in determining the function of a new variant of enzyme IKKalpha (IKK $\alpha$ ) to activate some of the genes taking part in the tumor progressions of colorectal cancer. In the future, this fact will make it possible to design new drugs that inhibit this enzyme specifically and are less toxic for the remaining body cells, hence improving the treatment for this disease.

The study is the culmination of previous research by the IMIM Research Group on <u>Stem Cells</u> and Cancer that had proven the existence of a link between the activation of the IKK $\alpha$  enzyme and occurrence of colorectal cancer in humans. "We studied the particularities that distinguish the pre-tumor activity of IKK $\alpha$  from its normal physiological activities, which are known to be essential for the survival of non-cancerous cells and can therefore not be pharmacologically inhibited without causing great harm to the body" explains Dr. Lluís Espinosa, a member of the group and the director of this study.

IKK $\alpha$  is a specific type of enzyme, known as kinase. These enzymes are proteins that act on other proteins adding to them a <u>phosphate</u> and thus modifying their function. The p45-IKK $\alpha$ , which we identified, is located in the nucleus of cancer cells and their action is essential for the progression of the tumor. Lluís Espinosa adds: "The most important novelty of our findings is the identification of a new form of the IKK $\alpha$  kinase, which is mainly involved in activating genes that take part in the <u>tumor progression</u>, and that differs from the main activity of this kinase



in normal cells".

For this research a total of 288 human samples of colorectal cancer were analyzed, identifying the presence of p45-IKK $\alpha$  in most of them and proving that specifically blocking this new form of IKK $\alpha$  avoids the growth of this particular <u>cancer cells</u>.

The results of this work open the door to multiple research lines aiming to discover the mechanisms that generate and activate this p45-IKK $\alpha$  enzyme, and identifying possible inhibitors that are more effective against tumor cells, that are less toxic for the remaining body cells. However, it is important to note that while these results represent an important advance towards understanding the mechanisms of tumor progression, further research will be needed before considering future therapeutic applications of this type of drugs in patients with colorectal cancer.

**More information:** "A novel truncated form of IKK is responsible for specific nuclear IKKα activity in Colorectal Cancer". Pol Margalef, Vanessa Fernández-Majada, Alberto Villanueva, Ricard Garcia Carbonell, Mar Iglesias, Laura López, María Martínez-Iniesta, Jordi Villà-Freixa, Mari Carmen Mulero, Montserrat Andreu, Ferran Torres, Marty W Mayo, Anna Bigas, Lluis Espinosa, *Cell Reports*.

## Provided by Hospital del Mar Medical Research Institute

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