New advances in the understanding of cancer progression

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Researchers at the Hospital de Mar Research Institute (IMIM) have discovered that the protein LOXL2 has a function within the cell nucleus thus far unknown. They have also described a new chemical reaction of this protein on histone H3 that would be involved in gene silencing, one of which would be involved in the progression of breast, larynx, lung and skin tumours.

Led by Dr Sandra Peiró and published in *Molecular Cell* journal, the study is a significant advance in describing the evolution of tumours and opens the door to researching new treatments that block their activity. "LOXL2's action on the intra-cellular level and its interaction with histone H3 stimulates tumour growth. The fact that the protein LOXL2 is an enzyme and is overly expressed in many types of cancer makes it a very good therapeutic target. Now that we know how it acts, we need to keep working to develop chemical inhibitors that counteract its activity", the researcher explained.

Previous studies had identified the extra-cellular function of the protein LOXL2, and it was being studied as a possible therapeutic target for avoiding metastasis in certain kinds of tumours. However, this study has described the presence of this protein at the level of the cell nucleus for the first time.

The process of gene expression in cells consists of transforming the information of the DNA into the proteins necessary to carry out different functions. The DNA molecule has been found to form a certain

structure due to its interaction with some proteins called histones. When these histones are modified, the structure of the DNA is also modified and the final result is the expression or non-expression of a certain group of genes.

In the case of tumour cells, the protein LOXL2 acts upon one of these histones (histone H3) and modifies it, eliminating the lysine 4 amino group, a change never described before. As a result of its action, the genes modulated by histone H3, modified by LOXL2, stop expression, preventing the cells from behaving normally and favouring tumour development.

The work of Sandra Peiró's team is the conclusion of three years of effort focused on the biochemical characterisation of the protein LOXL2 and the study of its role in the modification of histone H3. Since this modification had never been described before, the data obtained open many lines of research. The location on the genomic level of the protein LOXL2 and histone H3, modified by LOXL2, and the possible existence of some enzyme that might neutralise its function, are two of the questions that the group aims to tackle in the years to come.

More information: "Lysyl Oxidase-Like 2 (LOXL2) deaminates lysine 4 in Histone H3" Nicolás Herranz, Natàlia Dave, Alba Millanes-Romera, Lluís Morey, Víctor M. Díaz, Víctor Lórenz-Fonfría, Ricardo Gutierrez-Gallego, Celia Jerónimo, Luciano Di Croce, Antonio García de Herreros, Sandra Peiró. MOLECULAR-CELL-D-11-01044R3.

Provided by IMIM (Hospital del Mar Research Institute)