

Researchers identify a disordered region of Src protein that regulates its oncogenic capacity

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The Src protein takes part in the regulation of many physiological processes such as the survival, migration or cell adhesion as a response to



stimuli received from several receptors of the membrane. Although it is demonstrated that its deregulation is involved in the proliferation of cancer in humans, many aspects of this function are still unknown, especially regarding its disordered region.

Now, a collaboration between the teams of the University of Barcelona and the University of Montpelier has enabled them to determine the role of a disordered region of the Src protein in the regulation of this protein's oncogenic capacity.

A published article in the journal *Oncogene* gathers the results of the study. According to the research, mutations of the disordered region, called ULBR, inhibit by more than 50% the transforming activity of this protein in colon cancer cells and the growth of Src-dependent tumors in mice.

"This study reveals the relevant role of this intrinsically disordered region in the malignant cell transformation and it suggests a novel layer of Src regulation by this unique region", notes Miquel Pons, professor at the Department of Inorganic and Organic Chemistry and director of the Biomolecular NMR Research Group (BIO-RMN) located at the Barcelona Science Park (PCB).

The ULBR region has been found by the BIO-RMN group thanks to the tools provided by the <u>nuclear magnetic resonance</u> (NMR), a technique in which the UB is at the forefront. The study was carried out with researchers from the University of Montpellier (France), experts on <u>colorectal cancer</u>, thanks to a collaboration that started with a project of La Marató de TV3 on cancer.

Most eukaryotic proteins have intrinsically disordered regions (IDR) that challenge the classical structure-function paradigm. Therefore, the classical strategies based on the determination of structures or



inactivation of whole domains had made it impossible for researchers to find the regulating role of the Src disordered region, probably because "it may contain opposite regulatory sequences", as Pons notes.

Following this idea, the team inactivated specifically a small <u>region</u> within the disordered domain that showed a unique response by NMR, showing its essential role in the tumoral activity of the <u>protein</u>.

More information: Emilie Aponte et al, Regulation of Src tumor activity by its N-terminal intrinsically disordered region, *Oncogene* (2022). DOI: 10.1038/s41388-021-02092-x

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