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Researchers describe new functions of cohesin relevant for human disease

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Cohesin is a ring-shaped protein complex involved in the spatial organization of the genome and in mitotic chromosome structure. Vertebrate somatic cells have two versions of cohesin that contain either SA1 or SA2, but their functional specificity has been largely ignored. Researchers of the Spanish National Cancer Research Centre (CNIO) under the direction of Ana Losada have identified new functions of cohesin SA1 that are relevant for two human diseases, cancer and Cornelia de Lange Syndrome (CdLS). These results are published in two papers that appear this week back-to-back in *EMBO Journal*.

The first study shows that SA1 is required for efficient duplication of chromosome ends, the telomeres. In its absence, aberrant telomere structures hinder chromosome segregation during cell division and aneuploid cells (i.e., with an incorrect number of chromosomes) are generated. This aneuploidy likely contributes to accelerate the onset of tumourigenesis in SA1 deficient mice. The appearance of certain types of pancreatic tumours, extremely rare in mice, is particularly striking. This mouse model may turn out to be a very useful tool for the study of pancreatic cancer.

The second study reports for the first time a precise map of the distribution of cohesin SA1 and cohesin SA2 along the mouse genome. Moreover, it uncovers an essential role of cohesin SA1 in the regulation of gene expression during embryonic development. Lack of cohesin SA1 alters the transcription of genes involved in biological processes related to CdLS. This developmental disorder affects 1:30,000 newborns and is

characterized by growth and mental retardation and multiple organ abnormalities. The study offers new clues to understand the origin of the pathologies observed in CdLS patients.

"This work represents an important step towards better understating the role of cohesin in such relevant human diseases as cancer and CdLS", comment Silvia Remeseiro and Ana Cuadrado, co-authors of the two papers.

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