New piece found in the puzzle of epigenetics

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For many years scientists have known that the numerous biological functions of an organism are not regulated solely by the DNA sequence of its genes: Superordinate regulatory mechanisms exist that contribute to determining the fate of genes. Although they are not anchored in the DNA, they can even be passed on to subsequent generations to a certain extent. Intensive research in recent years has shown that these mechanisms - bundled under the term epigenetics, are very multifaceted and complex.

Professor Dirk Eick and staff members of the Institute of Clinical Molecular Biology and Tumor Genetics of Helmholtz Zentrum München, together with colleagues from the University of Wisconsin-Madison, Wisconsin, USA, have now identified another piece in the puzzle of epigenetics: They showed that the enzyme TFIIH kinase is involved in epigenetic regulation.

The scientists were interested in the fine regulation of the cell nucleus enzyme RNA polymerase II. This transcribes the genetic information of the genetic substance DNA into messenger RNA - mRNA for short - which in turn is the basis for protein synthesis. At the same time RNA polymerase II is also responsible for the production of other kinds of RNA molecules, the so-called snRNA, which are not translated into proteins but take on other tasks. In prior research Eick and his colleagues had observed that a certain region of the RNA polymerase II enzyme - the carboxy-terminal domain - is involved in deciding which kinds of RNA are formed. In humans this domain consists of 52 repeats of a sequence of seven amino acids. For RNA synthesis the determining

factor is whether and how specific amino acids of this region are modified biochemically. Thus, it is absolutely essential for the synthesis of snRNA that the amino acid serine at position 7 of this repeat sequence is provided with an additional phosphate group. If this is lacking, mRNA will be produced, but not any snRNA. The reason for that is presumably that this phosphorylation enables the interaction with a protein complex - the so-called integrator complex - which is necessary for snRNA formation. In other words, the modification of the enzyme RNA polymerase II at defined positions regulates whether this enzyme can produce certain kinds of RNA molecules or not.

In their latest research, the scientists led by Dirk Eick showed that the enzyme TFIIH kinase is responsible for the selective phosphorylation of RNA polymerase II. "With these findings another building block has been identified that plays a key role in epigenetic regulation by means of RNA polymerase II," Professor Eick said. "This is of great significance because knowledge of epigenetic mechanisms is necessary in order to better understand cancer and other diseases and to be able to provide more targeted treatment."

Citation: Md. Sohail Akhtar, Martin Heidemann, Joshua R. Tietjen, David W. Zhang, Rob D. Chapman, Dirk Eick, Aseem Z. Ansari (2009): TFIIH Kinase Places Bivalent Marks on the Carboxy-Terminal Domain of RNA Polymerase II. Molecular Cell 34, 387-393 (Online publication:I DOI 10.1016/j.molcel.2009.04.016)

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