

“Junk” RNA Regulates Important Cellular Processes

Researchers discover a connection between noncoding RNA and the silencing of genes

It has been known for a long time that much of a cell's RNA stems from DNA regions called intergenic spacers (IGS) that lie between two genes and do not code for proteins. A research group headed by Professor Ingrid Grummt of the Division “Molecular Biology of the Cell II” at the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) has now discovered the important role of noncoding RNA molecules originating from IGS regions in a number of control processes including the regulation of ribosomal RNA (rRNA) production. The scientists have published their results in the latest issue of the journal *Molecular Cell*^{*}.

RNA, another type of nucleic acid alongside DNA, is an important carrier of genetic information on the way from gene to protein. Alongside this ‘messenger’ RNA, or mRNA, there are numerous other types of RNA that are very important for the cell. The article deals with a further type of RNA of which the DKFZ researchers have discovered a new function. This discovery is only the tip of the iceberg. “About 95 percent of cellular DNA is noncoding, i.e. contains no information for protein synthesis. Transcripts of these noncoding gene segments, however, are chief regulators of gene activity within the cell and it is likely that they are even more relevant than proteins,” explains Dr. Christine Mayer. The biological value of these results is tremendous: For the first time ever, researchers have come across a mechanism that shows how transcripts that have so far been neglected as “junk” RNA play an active role in regulation processes at the chromatin level. Scientists have known for some time about the existence of this seemingly functionless RNA. What is new is the realization that these molecules are of essential relevance for the cell. The long-held assumption that key regulation processes are controlled only by proteins is no longer valid in this form. “We may even dare to maintain that proteins are presumably responsible only for the basic structure and function of the cell, while RNA is used for its regulation,” says Mayer. Hence, RNA molecules are a central part of cellular regulation processes and more important than previously thought.

The genes from which ribosomal RNA is read are separated by noncoding IGS sequences. The researchers have shown that these IGS sequences are transcribed and the transcripts play an important role in the regulation of its surrounding gene sequences. DNA is found in the cell in the form of chromatin. If it is to be read, special chromatin-modifying protein complexes have to unpack the genetic material to make it accessible for the transcription machine. These complexes are also able to pack DNA in such a way that reading is no longer possible.

Such a function is performed by the nucleolar remodeling complex NoRC. The NoRC complex is capable of switching off those parts of the DNA from which rRNA is read. Grummt's team showed that NoRC can only silence rRNA genes if an RNA component is bound to the protein complex. This NoRC-associated RNA component is an intergenic transcript, i.e. those RNAs that are read from the noncoding regions located between the rRNA genes. This means that those small RNA molecules that were previously regarded as “junk” without special function are able to remodel the chromatin structure and, thus, to switch off the gene activity of the rDNA locus.

* Christine Mayer, Kerstin-Maike Schmitz, Junwei Li, Ingrid Grummt, Raffaella Santoro: Intergenic Transcripts Regulate the Epigenetic State of rRNA Genes. *Molecular Cell*, Vol 22, 351-361

The task of the Deutsches Krebsforschungszentrum in Heidelberg (German Cancer Research Center, DKFZ) is to systematically investigate the mechanisms of cancer development and to identify cancer risk factors. The results of this basic research are expected to lead to new approaches in the prevention, diagnosis and treatment of cancer. The Center is financed to 90 percent by the Federal Ministry of Education and Research and to 10 percent by the State of Baden-Wuerttemberg. It is a member of the Helmholtz Association of National Research Centers (Helmholtz-Gemeinschaft Deutscher Forschungszentren e.V.).

This press release is available at www.dkfz.de/pressemitteilungen

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