IN THE NEWS

A use for junk

Researchers from Harvard Medical School, USA, have discovered a new type of gene with a regulatory function, which might help us to understand why 95% of chromosomes are made up of 'junk' DNA.

In *Nature* (3 June 2004), Fred Winston and colleagues show that the *SRG1* gene in yeast represses its next-door neighbour, *SER3*, using a transcription-interference mechanism. *SRG1* transcription across the *SER3* promoter hinders activator binding.

The authors studied the *SER3* gene because it is repressed by a common transcriptional activator complex. When they analysed *SER3*, they were surprised to find that all the factors necessary for transcription were just upstream of the *SER3* promoter, despite the fact that the gene was switched off. However, they then noticed a TATA box upstream of *SER3*, which could signify the promoter of a new gene. They showed that this gene — *SRG1* — is highly transcribed, but that is does not encode a protein. It is the active transcription of *SRG1* that represses *SER3* transcription.

Winston said, "This doesn't explain all junk DNA. It gives a potential use for some junk DNA." "We found one example of a type of regulatory gene that hasn't been found before that might alert investigators to look for it in other cases" (*Reuters AlertNet*, 2 June 2004).

"Our guess is that more examples will be found, and this will be really illuminating", Winston added (*The Scientist*, 3 June 2004). So, the challenge now is to find other examples of this type of regulation and to understand how this type of gene regulation is controlled.

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CELL CYCLE

Time to go our separate ways

Chromosomes that are duplicated during DNA replication are held together by the cohesin protein complex until anaphase, when chromosome segregation is triggered by the cleavage of cohesin. New findings indicate that, in budding yeast, cohesin cleavage is not sufficient to complete chromosome segregation of ribosomal DNA. The segregation of rDNA — and possibly other regions of repetitive DNA on the chromosomes — also requires the Cdc14 phosphatase, which promotes chromosome condensation and subsequent chromosome resolution.

The Amon, Uhlmann and Strunnikov groups all reported that rDNA failed to segregate in *cdc14*-mutant cells. Amon and colleagues found that this was also true for telomeres — which resemble rDNA in that they are regions of repetitive DNA — indicating that this type of chromosome loci has special requirements for segregation. Amon and Uhlmann and their co-workers showed that Cdc14 mediates a chromosome segregation process that is independent of cohesin. Indeed, the removal of cohesin did not promote the segregation of rDNA in *cdc14*-mutant cells. The data reported by all groups clearly indicate that Cdc14 mediates chromosome segregation by targeting condensin to the rDNA and inducing DNA condensation and resolution.

Cdc14 has a well-known function in promoting exit from mitosis, and is released by two regulatory networks, FEAR (Cdc14 early anaphase release network) and MEN (mitotic exit network), in early and late anaphase, respectively. The Amon group showed that the FEAR network is sufficient for rDNA and telomere segregation. Strunnikov and co-workers confirmed previous findings that, in FEAR mutants, the MEN-mediated release of Cdc14 later in anaphase could compensate for the absence of Cdc14 in early anaphase — by the delayed targeting of condensin to rDNA.

So how does Cdc14 target condensin to rDNA? Amon and colleagues gained insight through their observations that the condensin subunit Ycs4 is sumoylated in a Cdc14-dependent manner during anaphase. Overexpression of Cdc14 correlated with the induction of Ycs4 sumoylation and the subsequent targeting of condensin to rDNA. However, whether the sumoylation and condensin targeting events are causally related is unknown at present. In addition, the exact protein target of Cdc14 remains to be identified, and what makes rDNA the primary target of condensin also needs to be clarified.

The newly discovered dual function of Cdc14 provides an important temporal link between chromosome segregation and exit from mitosis. In addition, Uhlmann and colleagues propose a two-step model for chromosome segregation, whereby cohesin cleavage is followed by Cdc14-mediated chromosome segregation. This model provides a mechanistic basis for the temporal pattern of the segregation of the complex yeast genome, whereby rDNA and telomeres segregate late during mitosis.

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References and links

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