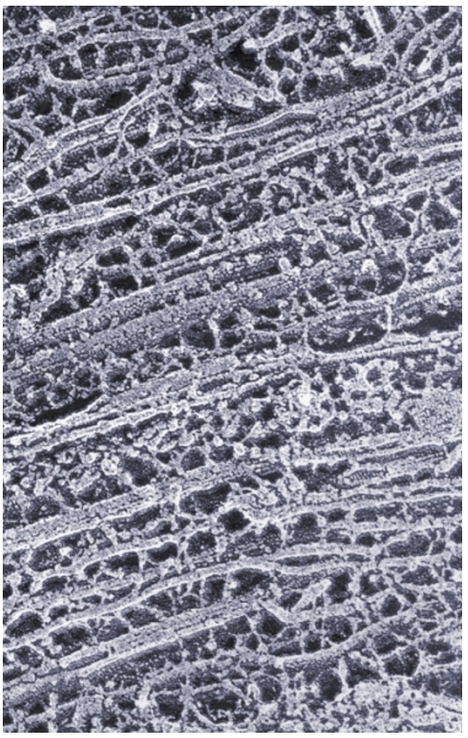


**References and links**

**ORIGINAL RESEARCH PAPER** Terada, S., Kinjo, M. & Hirokawa, N. Oligomeric tubulin in large transporting complex is transported via kinesin in squid giant axons. *Cell* **103**, 141–155 (2000)

**FURTHER READING** Hirokawa, N. The mechanisms of fast and slow transport in neurons: identification and characterization of the new kinesin superfamily motors. *Curr. Opin. Neurobiol.* **7**, 605–614 (1997)


**mispaired DNA bases; presumably the observed conformational changes occur only in response to binding a mismatch.**

**Why are these papers so significant? The human cousins of bacterial MutS — MSH2 and MSH6 — are mutated in hereditary nonpolyposis colorectal cancer (HNPCC). Not only can these mutations be mapped to the new MutS structures but, according to Obmolova *et al.*, "the crystal structures … provide a molecular framework for understanding HNPCC mutations".**

*Alison Mitchell*


**References and links**

**ORIGINAL RESEARCH PAPERS** Obmolova, G. *et al.* Crystal structures of mismatch repair protein MutS and its complex with a substrate DNA. *Nature* **407**, 703–710 (2000) | Lamers, M. H. *et al.* The crystal structure of DNA mismatch repair protein MutS binding to a G•T mismatch. *Nature* **407**, 711–717 (2000)

**FURTHER READING** Kolodner, R. D. Guarding against mutation. *Nature* **407**, 687–689 (2000)


RNA PROCESSING

# Control freak

The yeast *Saccharomyces cerevisiae* likes to be in control, especially when it comes to gene expression. We already knew that transcription, splicing, messenger RNA export, mRNA stability, mRNA translation and post-translational modification are regulated processes. Tollervey and colleagues now report in *Cell* that degradation of unspliced pre-mRNAs occurs in the nucleus in a regulated manner, providing yet another regulatory mechanism for gene expression.

Using several mutants defective in mRNA processing, Tollervey and co-workers found that unspliced pre-mRNAs are degraded in the nucleus in a 3′ to 5′ direction by a large protein complex containing several exoribonucleases (the exosome), or in a 5′ to 3′ direction by the exonuclease Rat1p. This is, in fact, similar to what is known to happen in the cytosol, where mRNAs are degraded either 3′ to 5′ by the exosome or 5′ to 3′ by the cytosolic exonuclease Xrn1p. But contrary to what happens in the cytosol, exosome-mediated degradation is predominant in the nucleus.

Nuclear degradation of pre-mRNA seems to compete with splicing. It is increased in the presence of glucose — yeast's favourite food — indicating that it is a physiological regulatory pathway for gene expression. The 3′ to 5′ Rat1p-dependent pathway is probably inhibited by the cap structure of the pre-mRNA, providing another level of control.

Degradation of inaccurately spliced pre-mRNAs has also been observed in mammalian cells, and there again, the activity seems to be nuclear. An obvious experiment will be to test whether homologues of the genes identified in yeast have the same function in mammalian cells.

*Raluca Gagescu*


**References and links**

**ORIGINAL RESEARCH PAPER** Bousquet–Antonelli C., Presutti, C. & Tollervey, D. Identification of a regulated pathway for nuclear pre-mRNA turnover. *Cell* **102**, 765–775 (2000)

**FURTHER READING** Mitchell, P. & Tollervey, D. Musing on the structural organization of the exosome complex. *Nature Struct. Biol.* **7**, 843–846 (2000)


# IN BRIEF

TRANSCRIPTION

## Dynamic association of capping enzymes with transcribing RNA polymerase II.

Schroeder, C. *et al. Genes Dev.* **14**, 2435–2440 (2000)

## Different phosphorylated forms of RNA polymerase II and associated mRNA processing factors during transcription.

Komarnitsky, P., Cho, E.-J. & Buratowski, S. *Genes Dev.* **14**, 2452–2460 (2000)

RNA polymerase II is a molecular platform to which many messenger RNA-processing factors bind during transcription. Are such factors associated simultaneously with RNA pol II, or do they interact in a transient and sequential manner? Using mRNA-capping enzymes, both papers indicate that RNA-processing enzymes associate dynamically with differently modified forms of the polymerase at different stages of the transcriptional cycle.

CELL POLARITY

## Plasma membrane compartmentalization in yeast by messenger RNA transport and a septin diffusion barrier.

Takizawa, P. A. *et al. Science* **290**, 341–344 (2000)

*Saccharomyces cerevisiae* restricts the cellular distribution of the transcription factor Ash1p by transporting its messenger RNA into the forming bud. Takizawa *et al.* now present a list of other mRNAs that also localize to the bud, and the transport mechanism for at least one of them — which encodes a transmembrane protein — is the same as for *ASH1* mRNA. The protein is then retained in the bud by a diffusion barrier involving septins that is functionally similar to tight junctions in epithelial cells.

CELL SIGNALLING

## RasGRP is essential for mouse thymocyte differentiation and TCR signalling.

Dower, N. A. *et al. Nature Immunol.* **1**, 317–321 (2000)

## Control of pre-T cell proliferation and differentiation by the GTPase Rac-1.

Gomez, M. *et al. Nature Immunol.* **1**, 317–321 (2000)

These papers describe the actions of two small GTPases, Ras and Rac, in T-cell responses. The first sheds light on how RasGRP, a Ras activator that's directly sensitive to diacylglycerol, mediates responses that had previously been assumed to be a result of the archetypal diacylglycerol-sensitive enzyme — protein kinase C. The second uses Rac mutants that can control actin dynamics, but not other downstream targets of Rac such as mitogen-activated protein kinases, to show that changes in actin dynamics are sufficient to drive some stages of T-cell differentiation.