case in deuterium-rich metorites, whose D/H ratios vary within less than 100 μm by more than 400%. How can a hydrothermal mechanism yield such results?

It is tempting to believe that the enormous isotopic heterogeneity in altered silicates predates the formation of the meteorites and thus was produced in the gas phase. This question must be addressed through laboratory experiments by measuring the alteration rate of amorphous silicates and by studying the far-infrared spectra of young stellar objects to search for the presence of clay minerals in circumstellar disks (*16*).

The use of the D/H ratio demonstrates a clear connection between the solar system and interstellar water. The search for its origin on Earth requires collaboration between different disciplines and represents an unique opportunity to reconcile astronomical and geochemical records.

References and Notes

1. C. Lecuyer *et al.*, *Chem. Geol.* **145**, 249 (1998).
2. J. Geiss, G. Gloecker, *Space Sci. Rev.* **84**, 239 (1998).
3. J. Halbout *et al.*, *Geochim. Cosmochim. Acta* **54**, 1453 (1990).
4. F. Robert *et al.*, *Space Sciences Series of the International Space Science Institute* (Kluwer Academic, Dordrecht, Netherlands, 2000), vol. 92, pp. 201–234.
5. E. Deloule, F. Robert, *Geochim. Cosmochim. Acta* **59**, 4695 (1995).
6. T. C. Texeira *et al.*, *Astrophys. J.* **347**, L19 (1999).
7. P. D. Brown, T. J. Millar, *Mon. Not. R. Astron. Soc.* **237**, 661 (1989).
8. L. d'Hendecourt, talk given at the conference on Deuterium in the Universe, Observatoire de Meudon, France, 25 to 27 June 2001; see wwwusr.obspm.fr/unicom/deuterium.
9. D. Bockelé-Morvan *et al.*, *Icarus* **193**, 147 (1998).
10. A. Drouart *et al.*, *Icarus* **140**, 129 (1999).
11. A. Morbidelli *et al.*, *Meteoritics Planet. Sci.* **35**, 1309 (2000).
12. Y. Aikawa, E. Herbst, *Astrophys. J.* **526**, 314 (1999).
13. A. E. Glassgold *et al.*, in *Protostars and Planet IV*, V. Mannings *et al.*, Eds. (Arizona Univ. Press, Tucson, AZ, 2000), pp. 429–450.
14. E. Deloule *et al.*, *Geochim. Cosmochim. Acta.* **62**, 3367 (1998).
15. L. Leshin, *Geophys. Res. Lett.* **27**, 2017 (2000).
16. K. Malfait *et al.*, *Astron. Astrophys.* **345**, 181 (1999).

17. I acknowledge stimulating discussions with J. Aléon, N. Dauphas, E. Deloule, L. Leshin, B. Marty, J. Eiler, Y. Aikawa, D. Bockelé-Morvan, L. d'Hendecourt, E. Herbst, F. Hersan, D. Gautier, T. Owen, and T. Millar at recent conferences.

PERSPECTIVES: PROTEIN SYNTHESIS

Believe It or Not—Translation in the Nucleus

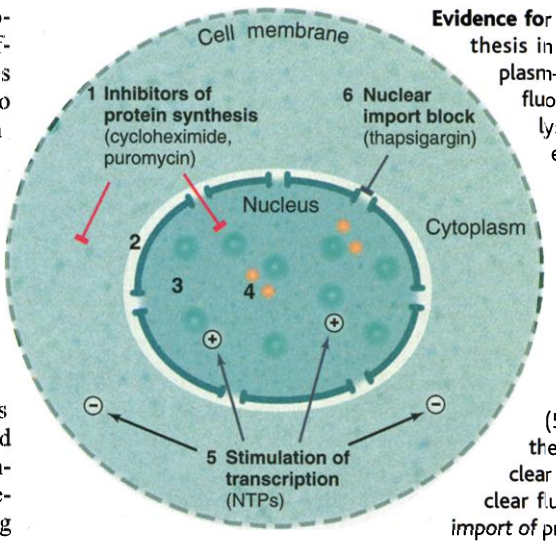
Matthias W. Hentze

The nucleus is the principal defining feature of eukaryotic cells. The genetic material of the cell is stored in the nucleus and is transcribed into mRNAs, which are then processed and exported to the cytoplasm. So the orthodoxy goes, once in the cytoplasm mRNAs are "read" by rotund factories called ribosomes and are translated into proteins. That transcription and translation take place in two different cellular compartments distinguishes eukaryotic cells from bacteria, which do not have a nucleus. This spatial separation protects cells from the deleterious effects of making faulty proteins, which could happen if incompletely processed mRNAs were to be translated in the nucleus. This "separatist" view is now challenged by Iborra *et al.* (*1*), who report on page 1139 of this issue that mRNA translation also takes place in the nucleus.

The concept of nuclear translation is not entirely new. Earlier studies showed that a small fraction of amino acids are incorporated into polypeptides in the nucleus. However, many attributed this finding to cytoplasmic contamination (*2*). More recently, structures with the biochemical and pharmacological characteristics of polyribosomes have been described in the nuclei of the slime mould *Dictyostelium* (*3*). This work, however, did not indicate whether these structures were unambiguously localized in the nucleus or whether they carried out protein synthesis. Although these earlier reports of nuclear translation were greeted with skepticism, it is now accepted that most components of the translation machinery are present in the nucleus. For example, the two ribosomal subunits are assembled in the nucleolus, translation initiation and elongation factors reside in the nucleus, and even the addition of amino acids to transfer RNAs (tRNAs) by aminoacyl–tRNA synthetases can take place in the nucleus (*4*–*6*). But the question is, can these separate components unite and orchestrate protein synthesis in the nucleus?

The author is in the Gene Expression Programme, European Molecular Biology Laboratory, Meyerhofstrasse 1, D-69117 Heidelberg, Germany. E-mail: hentze@embl-heidelberg.de

In their study, Iborra *et al.* adopted a strategy that would enable them to visualize nuclear protein synthesis. They pinpointed nuclear sites of translation by labeling permeabilized mammalian cells or purified nuclei with fluorescent lysine. The accumulation of nuclear fluorescence was time dependent and sensitive to inhibitors of eukaryotic protein synthesis (cycloheximide and puromycin), but not to the bacterial translation inhibitor chloramphenicol (see the figure). The authors estimate that nuclear translation accounts for about 10 to 15% of protein synthesis in the cell.



Evidence for nuclear translation. (1) New protein synthesis in the nucleus (green dots) and the cytoplasm—as indicated by nuclear and cytoplasmic fluorescence after incorporation of fluorescent lysine—is equally sensitive to inhibitors of eukaryotic translation. (2) Isolated nuclei show no detectable extranuclear or perinuclear fluorescence, indicating that proteins made in the cytoplasm are not being imported into the nucleus. (3) Purified nuclei display undiminished intranuclear fluorescence. (4) Nuclear translation sites are not randomly distributed, but overlap with sites of gene transcription as indicated by immunogold labeling (yellow dots). (5) Stimulation of transcription by increasing the concentration of nucleotides enhances nuclear but not cytoplasmic fluorescence. (6) Nuclear fluorescence is not affected by blocking the import of proteins into the nucleus by thapsigargin.

Iborra and colleagues put forward several arguments in support of their claim that the nuclear fluorescence they observed truly represents protein synthesis in the nucleus and does not result from the import of proteins made in the cytoplasm (see the figure). First, they performed their experiments under conditions that allowed the incorporation of only a few amino acids into the proteins being synthesized.

This minimized the number of completed proteins available for transport into the nucleus. Second, they were not able to detect any extranuclear or perinuclear fluorescence in purified nuclei. Third, purified nuclei were just as efficient at making new proteins as the nuclei of permeabilized cells, suggesting that proteins were not being imported from the cytoplasm. Fourth, electron microscopy revealed that nuclear translation sites (marked by biotin-lysine) were not randomly distributed throughout the nucleus but rather overlapped with transcription sites (marked by Br-UTP). Interestingly, these translation sites also overlapped with the distribution of the translation initiation factor eIF4E, the ribosomal protein L7 and, perhaps most intriguingly, the β subunit of the proteasome (which degrades proteins). Fluorescence in the nucleus increased when the proteasome was inhibited, suggesting that most newly made nuclear proteins are normally degraded. Fifth, stimulating transcription by increasing nucleotide concentrations doubled the amount of nuclear fluorescence without affecting cytoplasmic fluorescence. Together with the colocalization experiments, this finding suggests that transcription and translation in the nucleus may be coupled.

In principle, exclusion of a single vital component of the translation apparatus from the nucleus of a living cell should result in translation being restricted to the cytoplasm. How can we be sure that no such cytoplasmic translation factor leaked into the nucleus during cell permeabilization or nuclear isolation? To address this concern, the authors pretreated cells with thapsigargin—which inhibits the import of proteins into the nucleus and diffusion of proteins through nuclear pores—and then permeabilized them in the presence of the drug. This treatment effectively prevented a 40-kD fluorescein-dextran marker molecule from entering the nucleus, but did not affect nuclear translation. Although one cannot completely exclude the possibility that translation factors leaked into the nucleus, the results of this experiment are reassuring. There is no doubt that Iborra and colleagues have mounted a case of unprecedented strength in support of nuclear translation.

The Iborra *et al.* paper is sure to spur intense discussion between "believers" and "converts" on the one hand, and "nonbelievers" on the other. Doubtless, nonbelievers will demand to see nuclear translation in intact cells rather than in permeabilized cells or purified nuclei. As was the case with local translation at synapses in the central nervous system, we need more evidence to confirm that local translation products are not transported. The persuasive power of electron micrographs illustrating puromycin-sensitive nuclear ribosomes at work will win some converts. Harnessing the power of genetics and RNA interference to produce mutants that carry out either nuclear or cytoplasmic translation but not both would garner additional converts.

Few readers will fail to be fascinated by what nuclear translation can tell us about, for example, the origin of eukaryotic cells (*7*). Perhaps nuclear translation serves the same purpose as the purported restriction of translation to the cytoplasm does: namely, to prevent synthesis of faulty proteins. Nuclear translation provides the cell with an additional opportunity to assess the integrity of mRNAs before they are exported to the cytoplasm. If detected in the nucleus, "faulty" mRNAs may be subjected to intranuclear degradation or altered splicing (to avoid the production of mRNAs with premature stop codons). Such processes complement the more conventional pathway that degrades mRNAs with premature stop codons after translation by ribosomes in the cytoplasm (*8–10*). How will mRNAs that need to decode UGA stop codons for selenoprotein synthesis pass the nuclear translation test? Are proteins produced by nuclear translation functional, or are they all destined for degradation by the proteasome? What is the interplay between nuclear translation and export of mature mRNAs out of the nucleus? A recent study reports that premature translation termination codons induce the accumulation of unspliced precursor mRNAs at the site of transcription (*11*). Is this discovery a smoking gun, highlighting a consequence of linking nuclear transcription and translation? For players and spectators alike, future research on translation, whether in the nucleus or the cytoplasm, is likely to be full of suspense and surprises.

References

1. F. J. Iborra, D. A. Jackson, P. R. Cook, *Science* **293**, 1139 (2001).
2. J. A. Goidl, W. R. Allen, *Trends Biochem. Sci.* **3**, N225 (1978).
3. G. Mangiarotti, *Biochemistry* **38**, 3996 (1999).
4. E. Lund, J. E. Dahlberg, *Science* **282**, 2082 (1998).
5. G. J. Arts *et al.*, *EMBO J.* **17**, 7430 (1998).
6. J. Dostie, F. Lejbkowicz, N. Sonenberg, *J. Cell Biol.* **148**, 239 (2000).
7. J. A. Lake, M. C. Rivera, *Proc. Natl. Acad. Sci. U.S.A.* **91**, 2880 (1994).
8. M. W. Hentze, A. E. Kulozik, *Cell* **96**, 307 (1999).
9. S. Li, M. F. Wilkinson, *Immunity* **8**, 135 (1998).
10. L. E. Maquat, G. G. Carmichael, *Cell* **104**, 173 (2001).
11. O. Mühlemann *et al.*, *Mol. Cell*, in press.

PERSPECTIVES: SOLAR ENERGY

Solar Cells by Self-Assembly?

Jenny Nelson

In the quest for solar cells that are flexible, ultrathin, and cost-efficient, molecular solids are emerging as strong contenders. Soluble light-emitting molecular solids are already used in display applications. Solar cells made from such materials could benefit from low-tech, large-volume production techniques, greatly reducing their production cost relative to crystalline photovoltaic materials.

But molecular-solid–based devices have long suffered from low efficiencies. On p. 1119 of this issue, Schmidt-Mende *et al.* (*1*) report a photovoltaic device made from a crystalline dye and a liquid crystal that partially overcomes these problems. The very simple device converts visible photons to electrons with impressive efficiency.

The realization of an efficient organic solar cell remains a major scientific challenge. In crystalline, inorganic solar cells, the different electron affinities of the semiconductor layers create a permanent electric field, which causes the photovoltaic effect. Electron-hole pairs generated by absorbed photons are easily separated by the field.

An organic solar cell can be made to a similar design by sandwiching the organic semiconductor between two different metal contacts. However, the intermolecular forces are weaker in a molecular solid, and there is a higher degree of disorder. A photogenerated electron-hole pair (exciton) is therefore bound much more strongly and cannot normally be split by the electric fields available in the simple device. Only excitons generated within a few nanometers of the metal contact can be split, but hundreds of nanometers of material are needed to absorb most of the light.

Organic photovoltaic cells made in this way therefore achieve tiny power conversion efficiencies and low incident-photon–to–current or quantum efficiencies (QE). A good QE does not guarantee good photovoltaic energy conversion, but it is a prerequisite. Inorganic photovoltaic devices routinely achieve QEs approaching 100%; the QEs of the organic devices described so far were below 1%.

A solution was found in 1995, when several groups independently showed that QE

The author is in the Centre for Electronic Materials and Devices, Physics Department, Imperial College, London SW7 2BZ, UK. E-mail: jenny.nelson@ic.ac.uk