4. V. R. Eshleman, G. A. Parks, *Science* **285**, 531 (1999).
5. C. Huber, G. Wächtershäuser, *Science* **276**, 245 (1997).
6. G. Renaud, *Surf. Sci. Rep.* **32**, 1 (1998).
7. L. Giordano, J. Goniakowski, J. Suzanne, *Phys. Rev. Lett.* **81**, 1271 (1998).
8. K. C. Hass, W. F. Schneider, A. Curioni, W. Andreoni, *Science* **282**, 265 (1998).
9. X.-G. Wang, A. Chaka, M. Scheffler, *Phys. Rev. Lett.* **84**, 3650 (2000).
10. P. Liu, T. Kendelewicz, G. E. Brown Jr., G. A. Parks, *Surf. Sci.* **412–413**, 287 (1998).
11. P. Liu *et al.*, *Surf. Sci.* **417**, 53 (1998).
12. P. J. Eng *et al.*, *Science* **288**, 1029 (2000).
13. J. A. Kelber *et al.*, *Surf. Sci.* **446**, 76 (2000).
14. P. Fenter *et al.*, *Geochim. Cosmochim. Acta* **64**, 1221 (2000).
15. P. Fenter *et al.*, *J. Phys. Chem. B* **105**, 8112 (2001).
16. P. Fenter *et al.*, *Geochim. Cosmochim. Acta* **64**, 3663 (2000).
17. P. van Cappellen, L. Charlet, W. Stumm, P. Wersin, *Geochim. Cosmochim. Acta* **57**, 3505 (1993).
18. P. A. O'Day, *Rev. Geophys.* **37**, 249 (1999).
19. S. C. B. Myneni, T. K. Tokunaga, G. E. Brown Jr., *Science* **278**, 1106 (1997).
20. A. M. Schieidegger, G. M. Lamble, D. L. Sparks, *J. Colloid Interface Sci.* **186**, 118 (1997).
21. R. J. Hunter, *Foundations of Colloid Science*, vol. 1 (Oxford Univ. Press, Oxford, 1995).
22. J. A. Davis, D. B. Kent, *Rev. Mineral.* **23**, 177 (1990).
23. T. Hiemstra, P. Venema, W. H. Van Riemsdijk, *J. Colloid Interface Sci.* **184**, 660 (1996).
24. P. Fenter *et al.*, *J. Colloid Interface Sci.* **225**, 154 (2000).
25. L. Cheng *et al.*, *Phys. Rev. Lett.*, in press.
26. A. S. Templeton *et al.*, *Proc. Natl. Acad. Sci. U.S.A.*, in press.
27. M. A. Nugent, S. L. Brantley, C. G. Pantano, P. A. Maurice, *Nature* **395**, 588 (1998).
28. K. J. Davis, P. M. Dove, J. J. De Yoreo, *Science* **290**, 1134 (2000).
29. The author thanks G. A. Parks for useful discussions and C. A. Doyle for help in preparing the figure.

PERSPECTIVES: PROTEIN SYNTHESIS

Discriminating Right from Wrong

Michael Ibba

Ribosomes are the protein synthesis factories of the cell that translate the codons of mRNA into the corresponding polypeptide sequence. After initiation, protein synthesis proceeds by delivery of aminoacyltransfer RNAs (aa-tRNAs), each carrying the correct amino acid, to the ribosome's A-site. The delivery vehicle is a ubiquitous protein called elongation factor Tu (EF-Tu, also known as EF-1a), which is thought to be a nonspecific carrier as it binds to all 20 of the canonical aa-tRNAs. Although numerous quality-control checkpoints exist within the translation machinery, EF-Tu is not believed to be among them. This view is set to change with the work of LaRiviere *et al.* (*1*) appearing on page 165 of this issue. These investigators show that EF-Tu directly contributes to the accuracy of protein synthesis by binding to aa-tRNAs over a remarkably wide range of affinities.

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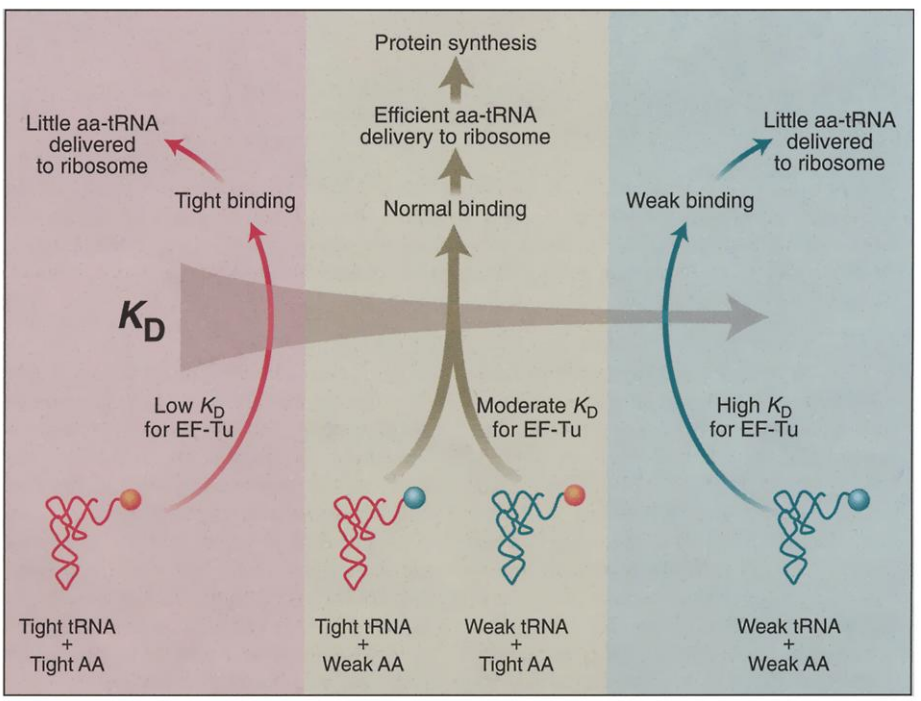
Protein synthesis is a highly accurate process: Usually only 1 in every 10,000 codons in mRNA is decoded incorrectly (*2*). The accuracy of protein synthesis is believed to depend principally on the fidelity of both aa-tRNA synthesis and the interaction between mRNA codons and their tRNA anticodons (*3*). In addition, other components of the translation machinery may contribute to quality control in particular cases. For example, some organisms synthesize Asn-tRNA^{Asn} and Gln-tRNA^{Gln} through the mischarged intermediates Asp-tRNA^{Asn} and Glu-tRNA^{Gln}. These intermediates do not lead to the misinterpretation of Asn and Gln codons as Asp and Glu because they are specifically rejected by EF-Tu (*4*, *5*), as is the rare aa-tRNA carrying the so-called 21st amino acid selenocysteine (*6*). Although the structure of EF-Tu bound to an aa-tRNA indicates how specificity can be achieved for elongator versus initiator aa-tRNAs (*7*), the means by which particular elongator aa-tRNAs may be discriminated before delivery to the ribosomal A-site is less clear. This led LaRiviere *et al.* to investigate in more detail the affinity of EF-Tu for a wide variety of aa-tRNA species.

One of the challenges in studying substrate recognition by EF-Tu is the synthesis of a sufficiently wide variety of aa-tRNAs encompassing both tRNAs charged with the correct amino acids and those mischarged with the wrong amino acids. The difficulty lies in the generation of mischarged tRNAs, whose cellular synthesis is normally minimized by the intrinsic quality control exerted by aminoacyl–tRNA synthetases. LaRiviere *et al.* exploited existing knowledge about tRNA recognition by both EF-Tu and aminoacyl–tRNA synthetases to carefully introduce a number



Binding weakness to strength. Thermodynamic compensation during binding and discrimination of aminoacyl tRNAs (aa-tRNAs) by elongation factor Tu (EF-Tu). The functional groups comprising aa-tRNA, the aminoacyl (AA) and tRNA moieties, are recognized individually when they bind to EF-Tu. An aa-tRNA that contains two tightly binding moieties (red) has a low dissociation constant (K_D) for EF-Tu, whereas one that has two weakly binding moieties (blue) has a high K_D for EF-Tu. In both cases, the affinity for EF-Tu, whether high or low, is beyond the range for optimal delivery of the aa-tRNA to the ribosomal A-site. Combinations of a tight and a weak binding moiety in an aa-tRNA optimize the affinity of that aa-tRNA for EF-Tu, resulting in its subsequent delivery to the ribosome.

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of mutations into four different tRNAs that normally specify four distinct amino acids. These changes allowed each of the tRNAs to be charged with both their own particular amino acid and the other three amino acids. At the same time, care was taken to ensure that the changes introduced into the tRNAs did not disturb their interactions with EF-Tu. The investigators ended up with 16 aa-tRNAs, of which 12 were mischarged species.

When the affinities (dissociation constants) of the 16 aa-tRNAs for EF-Tu were determined, the results were surprising, to say the least. Although correctly charged aa-tRNAs all bound to EF-Tu within a 10-fold range of affinities, the complete data set encompassed a 5000-fold difference in binding. The significance of this range of affinities is illustrated by the fact that uncharged $tRNA^{Phe}$ only binds to EF-Tu 1000 times less tightly than the corresponding charged species Phe-$tRNA^{Phe}$ (*8*). Closer examination of the behavior of particular mischarged aa-tRNAs suggests how EF-Tu might exploit these large differences in substrate binding to ensure the fidelity of protein synthesis. Although some mischarged aa-tRNAs bind to EF-Tu with less affinity than their correctly charged counterparts, surprisingly, some bind considerably more tightly. At first sight, a strong affinity for EF-Tu does not seem to be the best way to prevent delivery of a mischarged aa-tRNA to the ribosome. But, as LaRiviere *et al.* explain, both very tight and very weak binding could compromise the efficient delivery of an aa-tRNA to the ribosomal A-site (see the figure). Previous studies indirectly suggest that mischarged aa-tRNAs that bind tightly to EF-Tu would be less abundant in the cell, thus confining discrimination by EF-Tu to weakly binding mischarged species.

Perhaps the most immediate question raised by the LaRiviere *et al.* data is how EF-Tu manages to discriminate the 20 correctly charged aa-tRNA isoforms in the cell from the 380 mischarged species. This problem of molecular recognition is compounded by the fact that the 380 mischarged species simply represent different combinations of the same tRNA and amino acid moieties present in the 20 correctly charged aa-tRNAs. The answer suggested by LaRiviere *et al.* is that EF-Tu uses a form of "combinatorial" recognition. After they analyzed the individual contributions of the amino acid and tRNA moieties to the overall binding energy, it became clear that the two parts of an aa-tRNA could be broadly divided into "tight" and "weak" EF-Tu binders. The key point with regard to recognition is that the combination of a tight and weak partner in a correctly charged aa-tRNA results in the groups thermodynamically compensating for each other, enabling effective binding of the aa-tRNA to EF-Tu (see the figure). On the other hand, mischarged aa-tRNAs generally seem to contain two groups that are either both tight binders or both weak binders. Thus, mischarged aa-tRNAs bind to EF-Tu too ineffectively for subsequent delivery to the ribosome. The data do yield a few exceptions to this rule, but these should be clarified once this approach is expanded to include more aa-tRNAs. Sampling of other aa-tRNAs should also help in the interpretation of tight and weak binding events in terms of known structures of EF-Tu, particularly for the recognition of the tRNA moiety (*7*, *9*).

The LaRiviere *et al.* study provides compelling evidence that EF-Tu can differentiate correctly charged from mischarged aa-tRNAs. Together with earlier findings showing that EF-Tu associates with other components of the translation machinery (*10*), possibly promoting aa-tRNA delivery to the ribosome, the LaRiviere work makes it clear that describing EF-Tu as a nonspecific carrier is incorrect. Whatever the final mechanistic details, it now appears that EF-Tu is a critical component of the stringent quality-control machinery that ensures the accurate translation of mRNA into protein.

References

1. F. J. LaRiviere, A. D. Wolfson, O. C. Uhlenbeck, *Science* **294**, 165 (2001).
2. C. G. Kurland, *Annu. Rev. Genet.* **26**, 29 (1992).
3. M. Ibba, D. Söll, *Science* **286**, 1893 (1999).
4. H. D. Becker, D. Kern, *Proc. Natl. Acad. Sci. U.S.A.* **95**, 12832 (1998).
5. M. Stanzel, A. Schön, M. Sprinzl, *Eur. J. Biochem.* **219**, 435 (1994).
6. J. Rudinger *et al.*, *EMBO J.* **15**, 650 (1996).
7. P. Nissen *et al.*, *Science* **270**, 1464 (1995).
8. F. Janiak *et al.*, *Biochemistry* **29**, 4268 (1990).
9. P. Nissen *et al.*, *Structure Fold. Des.* **7**, 143 (1999).
10. B. S. Negrutskii *et al.*, *J. Biol. Chem.* **274**, 4545 (1999).

PERSPECTIVES: PLANETARY SCIENCE

Jupiter and Its Moons

David J. Stevenson

We live in an exciting time for people who care about the origin of planets. New planets and planetary systems are discovered regularly (*1*) and can be compared with our own solar system. In our solar system, the Galilean moons that orbit Jupiter form a planetary system that is also coming into focus, thanks to the remarkable success of the Galileo mission (*2*).

How did these planetary bodies form? We do not yet have a fully satisfying answer to this question, but a story is emerging that differs from the formation of the solar planets and from the formation of Earth's moon. In this multiplicity of origins, the Galilean moons emerge as a last gasp in the formation of Jupiter. Their formation may have postdated the accumulation of nearly all of Jupiter's mass and took place over a period of millions of years—surprisingly long for bodies that orbit their parent once every few days.

Galileo discovered the four moons that bear his name (*3*) in January 1610. In those days, one could publish rapidly (*4*). Already in March 1610, Galileo wrote in *Sidereus Nuncius* that "I should disclose and publish to the world the occasion of discovering four Planets never seen from the beginning of the world up to our own times. I summon all astronomers to apply themselves to examine and determine their periodic times." Galileo understood the cosmological importance of his discovery, which provided key evidence in support of the Copernican system and showed that not all heavenly bodies revolve around Earth. However, appreciation of what the Galilean satellites might tell us about planet formation took much longer and is still ongoing.

There are many similarities between the Jovian system and our solar system. Both systems are extremely regular. Bodies orbit in a nearly common plane—Jupiter's equatorial plane for the Galilean satellites and the Sun's ecliptic plane for the solar system. In both cases, bodies orbit in a prograde sense (anticlockwise when viewed from above), with orbits spaced in approximate geometric progression. The total mass of Jupiter's satellites is about the same as that of Mars and probably about 1% of the heavy-element mass (everything except hydrogen and helium) inside Jupiter. This is a similar ratio to the heavy-element distribution in our solar system, where the Sun contains around 10 Jupiter masses and the planetary system tens of Earth masses of heavy elements.

Yet there are also striking differences. The solar system is spread out relative to the size of the Sun, with even the Sun-hugging

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