Computer Analysis of Hairpins at Transcription Termination Sites in Procaryote Genomes

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Regulation mechanisms of transcription termination in procaryotes are not clearly understood. *Escherichia coli* is known to have two transcription termination systems: 'rho-independent' and 'rho-dependent' terminations. Rho-dependent termination requires the involvement of the rho protein, but this does not seem to be a universal mechanism in procaryotes since no rho homologs have been found in some of the completely sequenced genomes. The rho-independent termination is thought to involve the formation of an RNA hairpin in the nascent transcript that causes the polymerase to pause in elongation.

We attempted to identify RNA hairpins by calculating free energy values from these sequences. The free energy of 3'-flanking region of ORFs were systematically computed in the complete genome sequences of *Haemophilus influenzae* Rd [1], *Mycoplasma genitalium* [2], *Mycoplasma pneumoniae* [3], *Synechocystis* PCC6803 [4], *Methanococcus jannaschii* [5] and *Escherichia coli* K-12 [6], using "RNAfold" [7], a program for RNA structure prediction. These values were used to characterize the use of hairpin formation for transcription termination in these species. As a control, the sequence of *Saccharomyces cerevisiae* [8, 9], the only completely sequenced eucaryotic genome, was also analyzed by the same method.

Escherichia coli K-12 and Haemophilus influenzae Rd had a sharp drop in free energy at 30bp downstream of the stop codon, accounting for the abundance of hairpin-forming genes. However, no obvious drop at the same position was observed for Mycoplasma genitalium, Mycoplasma pneumoniae, Synechocystis PCC6803 and Methanococcus jannaschii, implying that those species rely on hairpin formation less often for terminating transcription. Since no rho-factor gene has been reported in these species, it is unlikely for them to have a 'rho-dependent' termination system. These observations lead us to suspect the existence of alternative mechanisms for transcription termination.

Acknowledgments

This work was supported in part by a Grant-in-Aid for Scientific Research on Priority Areas 'Genome Science' from The Ministry of Education, Science, Sports and Culture in Japan.



Figure 1: Free energy of 3'-flanking region of complete genomes

References

- Fleischmann, D., Adams, M. D., White, O., Clayton, R. A., Kirkness, E. F., Kerlavage, A. R., Bult, C. J., Tomb, J. F., Dougherty, B. A., Merrick, J. M. and et al. (1995) Science, 269(5223), 496-512.
- [2] Fraser, C. M., Gocayne, J. D., White, O., Adams, M. D., Clayton, R. A., Fleischmann, R. D., Bult, C. J., Kerlavage, A. R., Sutton, G., Kelley, J. M. and et al. (1995) Science, 270(5235), 397–403.
- [3] Himmelreich, R., Hilbert, H., Plagens, H., Pirkl, E., Li, B. C. and Herrmann, R. (1996) Nucleic Acids Res, 24(22), 4420–4449.
- [4] Kaneko, T., Sato, S., Kotani, H., Tanaka, A., Asamizu, E., Nakamura, Y., Miyajima, N., Hirosawa, M., Sugiura, M., Sasamoto, S., and et al. (1996) DNA Res, 3(3), 109–136.
- [5] Bult, C. J., White, O., Olsen, G. J., Zhou, L., Fleischmann, R. D., Sutton, G. G., Blake, J. A., FitzGerald, L. M., Clayton, R. A., and et al. (1996) Science, 273(5278), 1058–1073.
- [6] Blattner, F. R., Plunkett, G., 3rd, Bloch, C. A., Perna, N. T., Burland, V., Riley, M., and et al. (1997) Science, 277(5331), 1453–1474.
- [7] Schuster, P., Fontana, W., Stadler, P. F., Hofacker, I.L., and et.al. (1994) Proc R Soc Lond B Biol Sci, 255(1344), 279–284.
- [8] Goffeau, A., et.al. (1997) Nature, 387(6632 Suppl), 5–105.
- [9] Goffeau, A., Barrell, B. G., Bussey, H., Davis, R. W., Dujon, B., Feldmann, H., Galibert, F., Hoheisel, J. D., Jacq, C., Johnston, M., Louis, E. J., Mewes, H. W., Murakami, Y., Philippsen, P., Tettelin, H. and Oliver, S. G. (1996) Science, 274(5287), 546, 563-567.