

disordered phase) around 90–100 °C. In contrast, our work indicates that the stacking of these sheets (higher order self-assembly achieved by water removal) results in: (1) the complete suppression of the melting transition with the purple-membrane lattice remaining ordered; and (2) the absence of protein denaturation up to 140 °C. We believe that the high temperature stability at 140 °C is related to the retention of the two-dimensional ordered lattice which under hydrated conditions melts away around 70 °C. In other words the inter-protein interactions coming from the two-dimensional ordered lattice appear to prevent the protein denaturation.

C. R. Safinya

Materials and Physics Departments,
University of California, Santa Barbara,
California 93106, USA

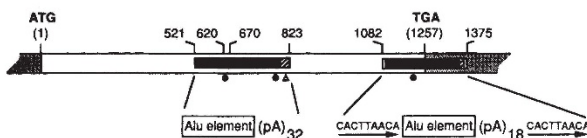
K. J. Rothschild

Physics Department and the Molecular
Biophysics Laboratory,
Boston University, Boston,
Massachusetts 02215, USA

- Shen, Y., Safinya, C. R., Liang, K. S., Ruppert, A. F. & Rothschild, K. J. *Nature* **366**, 48–50 (1993).
- Hampp, N. *Nature* **366**, 12 (1993).
- Mullaney, P. F. *Nature* **210**, 953 (1966).
- Klibanov, A. M. *Trends biochem. Sci.* **14**, 141–144 (1989).
- Fitzpatrick, P. A., Steinmetz, A. C. U., Ringe, D. & Klibanov, A. M. *Proc. natn. Acad. Sci. U.S.A.* **90**, 8653–8657 (1993).

Alu sequences in RMSA-1 protein?

SIR — Yeo *et al.*¹ report a previously undescribed chromosomal protein that “regulates mitotic spindle assembly”. The protein, termed RMSA-1, was identified as the antigen recognized by autoimmune serum from a patient with discoid lupus erythematosus. The antibodies in this serum bound to a protein of 47,000 (47K) on immunoblots of protein isolated from human, mouse, monkey and chicken cells. The serum was used to isolate a single human complementary DNA clone from a lambda zap cDNA expression library. The authors searched various sequence databases with the sequence of the putative RMSA-1 cDNA, but do not report the results of these searches in their paper.



The RMSA-1 open reading frame and untranslated regions. The open reading frame is shown as a large white box; 5' and 3' untranslated regions are grey; Alu elements are represented by black boxes; poly(A) tails by hatched boxes and these are shown in more detail underneath. The white boxes flanking the second Alu element are 9-bp target-site duplications (inset). The filled circles and the triangle are the putative p34^{cdc2} kinase sites and nuclear localization signal, respectively.

We searched the RMSA-1 DNA and protein sequences against the US National Center for Biotechnology Information's non-redundant nucleotide and protein sequence databases using the BLAST network service. Surprisingly, we found that the 418-codon open reading frame reported in this paper contains two Alu sequences (see figure). The presence of these Alu elements is absolutely unambiguous, whether protein or DNA sequence is used as query in the database search. The first Alu element runs from codons 173 to 278 of the putative RMSA-1 open reading frame, whereas the second begins at codon 364 and extends 112 nucleotides past the translational stop codon. The two Alu elements align with more than 70 per cent nucleotide identity with putatively active Alu elements², both contain characteristic poly(A) tails, and the second Alu element is flanked by a typical target site duplication. Of particular note, all three consensus p34^{cdc2} phosphorylation sites identified by Yeo *et al.* are contained within these Alu regions. Also, the poly-L-lysine sequence reported by the authors as a potential nuclear localization signal is encoded in the poly(A) tail of the first Alu element, which would contribute significantly to a predicted *pI* of greater than 10, rather than a *pI* of 6.33, as stated by Yeo *et al.*

Several issues are raised in the light of our observations. The presence of two translated Alu elements (accounting for 34 per cent of the encoded protein) calls into question whether the cloned cDNA encodes the 47K protein recognized on immunoblots, or whether, for example, it represents the messenger RNA of an expressed pseudogene. In fact, given the co-migration of a crossreacting 47K species on immunoblots of proteins from humans, mice and chickens (and the fact that Alu elements are not present in the last two organisms), it seems unlikely that these Alu elements would be represented in the true 47K product. Furthermore, Yeo *et al.* used antisense RNA expression of the entire cloned cDNA (which includes both elements and a third Alu element downstream of the open reading frame) for functional studies. Given the very large number of Alu insertions within introns, untranslated regions and possibly, in rare cases, coding sequences of human genes^{3,4}, the results of such experiments are difficult to interpret. Of course, should it be the case that translated Alu elements exist in the functional 47K human protein, this would represent the first report of its kind and would have important evolutionary implications⁴.

In our opinion, this example supports the view that

peer review of papers containing DNA or protein sequence data should involve direct evaluation by experts in sequence analysis. This would require direct access of sequence information at the time of review, together with the submitted manuscript, to allow searches to be repeated or performed by a sequence specialist before acceptance for publication.

Stuart Tugendreich

Quinghua Feng

Jenya Kroll

Dorothy D. Sears

Jef D. Boeke

Philip Hieter*

Department of Molecular Biology
and Genetics,

The Johns Hopkins University

School of Medicine,

725 N Wolfe Street, Baltimore,

Maryland 21205, USA

*To whom correspondence should be addressed.

YEO *ET AL.* REPLY — We agree that Alu elements are present in the RMSA-1 cDNA sequence that we reported¹. Tugendreich *et al.* suggest that one possible explanation is that we may have cloned an expressed pseudogene. However, we have reviewed our published and unpublished data and firmly believe this not to be the case. We are currently carrying out confirmatory, direct experiments to establish that the RMSA-1 coding sequence contains Alu elements.

Jing-Ping Yeo

Frank Alderuccio

Ban-Hock Toh

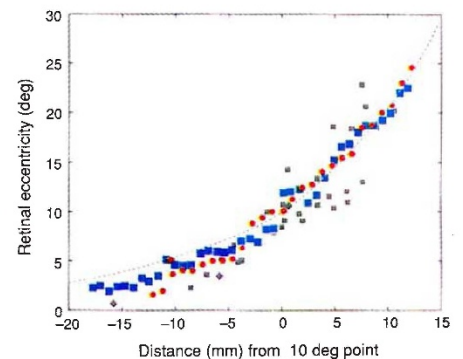
Department of Pathology and Immunology,

Monash University Medical School,

Prahran, Victoria 3181, Australia

- Yeo, J.-P., Alderuccio, F. & Toh, B.-H. *Nature* **367**, 288–291 (1994).
- Matera, A. G., Hellmann, U. Schmid, C. *Molec. cell. Biol.* **10**, 5424–5432 (1990).
- Claverie, J.-M. *Genomics* **12**: 838–841 (1992).
- Makalowski, W., Mitchell, G. Labuda, D. *Trends Genet.* **10**, 188–193 (1994).

Erratum



In the Scientific Correspondence by Stephen A. Engel *et al.* of 16 June (“fMRI of human visual cortex”) the labelling of the graph axes were inadvertently omitted from Fig. 2. The correct figure is shown above.