Journal club

EUKARYOTIC ANTISENSE AHEAD OF ITS TIME

I was an undergraduate student in the laboratory of Stu Heywood at the University of Connecticut–Storrs in the mid-1970s. His laboratory studied embryonic chick muscles. Beginning the summer between my sophomore and junior years, as a wide-eyed and impressionable budding scientist (who, for reasons unknown at the time, looked forward to every precipitation that required mouth-pipetting 25 ml of ethanol), I was truly in awe of what was already known about the steps of eukaryotic protein synthesis and of the types of experiments that could uncover new effectors of mRNA translation. Stu called one such effector ‘translational control RNA’ (tcRNA) in a paper (Bester *et al.*) that was published after I left for the University of Wisconsin–Madison to start graduate school. It turns out that what Stu ended up calling tcRNA102, as it is 102 nucleotides, is probably the

“
tcRNA102 ...
is probably the
first antisense
regulatory
RNA identified
in a higher
eukaryote
”

first antisense regulatory RNA identified in a higher eukaryote. tcRNA102 had imperfect complementarity to the 5′ untranslated region (UTR) of the myosin heavy chain (MHC) mRNA, was a constituent of isolated MHC mRNP particles, and stoichiometrically inhibited the translation of mRNAs with which it associated.

According to PubMed, Stu’s last paper was published in 1989, and neither he nor anyone subsequently has figured out how tcRNA102 inhibits the translation of the MHC mRNA. With the development of the genetically and developmentally tractable model organism *Caenorhabditis elegans*, seminal studies by Victor Ambros and Gary Ruvkun — which were published almost 20 years after Stu’s initial report of tcRNA102 — uncovered *lin-4*, the first microRNA. *lin-4* is also imperfectly complementary to a UTR — that of *lin-14* mRNA — albeit to the 3′ UTR. Although Stu never brought the story of tcRNA102 to full bloom before retiring, and his findings have largely faded from memory and are rarely

discussed, Stu’s passion for science lives on in the many students and postdocs who he trained, including me.

Lynne E. Maquat

Department of Biochemistry
and Biophysics, School of Medicine and
Dentistry, and Center for RNA Biology,
University of Rochester, Rochester, New
York 14642, USA

lynne_maquat@urmc.rochester.edu

The author declares no competing interests

ORIGINAL ARTICLES Bester, A. J., Kennedy, D. S. & Heywood, S. M. Two classes of translational control RNA: their role in the regulation of protein synthesis. *Proc. Natl Acad. Sci. USA* **72**, 1523–1527 (1975) | Heywood, S. M. tcRNA as a naturally occurring antisense RNA in eukaryotes. *Nucleic Acids Res.* **14**, 6771–6772 (1986) | Heywood, S. M. & Kennedy, D. S. Purification of myosin translational control RNA and its interaction with myosin messenger RNA. *Biochemistry* **15**, 3314–3319 (1976) | Heywood, S. M., Kennedy, D. S. & Bester, A. J. Studies concerning the mechanism by which translational-control RNA regulates protein synthesis in embryonic muscle. *Eur. J. Biochem.* **58**, 587–593 (1975) | Lee, R. C., Feinbaum, R. L. & Ambros, V. The *C. elegans* heterochronic gene *lin-4* encodes small RNAs with antisense complementarity to *lin-14*. *Cell* **75**, 843–854 (1993) | McCarthy, T. L. *et al.* Characterization of translational-control ribonucleic acid isolated from embryonic chick muscle. *Biochemistry* **22**, 935–941 (1983) | Wightman, B., Ha, I. & Ruvkun, G. Posttranscriptional regulation of the heterochronic gene *lin-14* by *lin-4* mediates temporal pattern formation in *C. elegans*. *Cell* **75**, 855–862 (1993)