Structural diversity of frameshifting signals : reprogramming the programmed

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Stellingen behorende bij het proefschrift:
“ Structural Diversity of Frameshifting Signals: Reprogramming the Programmed”

1. Since a simple stem-loop structure can be an efficient frameshifting signal, the mechanical model of frameshifting, in which the tRNA in the P-site is bent towards the A-site by the presence of a pseudoknot but not by a hairpin, should be re-examined. [Namy, O., *et al.*, 2006, *Nature*, **441**, 244-247; Yu, C.-H., *et al.*, 2011, *Nucleic Acids Res.*, **39**, 8952-8959; this thesis]

2. To understand the relation between the length and composition of loop 2 and the length of stem 1 in frameshifting pseudoknots, efforts have to be made to get an atomic-level structure of a frameshifting pseudoknot with a stem 1 of more than 6 base pairs. [Giedroc, D.P. and Cornish P.V., 2009, *Virus Res.*, **139**, 193-208; Napthine, S., *et al.*, 1999, *J. Mol. Biol.*, **288**, 305-320; this thesis]

3. It is very unlikely that a mutant of the Murine Hepatitis virus frameshifting pseudoknot with a relatively unstable structure as compared to the wild-type one can induce 90% of frameshifting. Therefore, frameshift efficiencies quantified by dual-luciferase reporter systems in cultured cells should be accompanied by protein product analysis [Plant, E.P., *et al.*, 2010, *J. Virol.*, **84**, 4330-4340; Tholstrup, J., *et al.*, 2011, *Nucleic Acids Res.*, doi:10.1093/nar/gkr686]

4. The structural similarity between functionally distinct RNA elements in riboswitches and frameshifting signals implies an evolutionary linkage between these widespread regulatory RNA elements. [Chapter 6, This thesis]

5. The controversial effects caused by upstream RNA sequences or polypeptides suggest frameshifting can not be simply monitored by chopped sequences. [Matsufuji, S., *et al.*, 1995, *Cell*, 80, 51-60; Kurian, L., *et al.*, 2011, *Nature*, **477**, 490-494]

6. It is intriguing that -1 frameshifting signals function as mRNA destabilizing signals in eukaryotic cells while eukaryotic RNA viruses rely on -1 frameshifting for their life cycle and infectivity. [Belew, A.T. *et al.*, 2011, *Nucleic Acids Res.*, **39**, 2799-2808]

7. Using avian “minimal” IBV frameshifting pseudoknot to fish out “human” RNA binding protein, Annexin A2, may have no biological relevance. [Kwak, H., *et al.*, 2011, *PLoS One*, **6**, e24067]

8. The effects on gene expression seen by the introduction of potential G-quadruplex forming sequences can also be explained by changes in the secondary structure of the entire translation initiation region. [Wieland, M. and Hartig, J.S., 2007, *Chem. Biol.*, **14**, 757-763; Wieland, M. and Hartig, J.S., 2009, *Nat. Protoc.*, **4**, 1632-1640; de Smit, M.H. and van Duin, J., 1994, *J. Mol. Biol.*, **244**, 144-150]

9. We make mutants to get to know something. However, these mutants tell us that, most of the time, we know nothing.

10. Good health goes above a good thesis?

Leiden, 22 December, 2011 Chien-Hung Yu