

## EDITORIAL

### *It's an RNA World After All!*

The central dogma with respect to the flow of genetic information was originally put forward in the late 1960s by Francis Crick and Leslie Orgel. In its simplest form it states that DNA carries the genetic information and that it is copied both to itself and to RNA, which is then decoded to synthesise proteins. While a few courageous souls might be willing to challenge the underlying truth of this (particularly with respect to the prokaryotes), the central dogma has continuously evolved and adapted in order to incorporate the hitherto unsuspected importance of RNA in regulating gene expression.

The discovery of retroviruses in the 1970s demonstrated that RNA, like DNA, could act as the template for its own replication, and subsequently as an information storage molecule. This finding demonstrated that, contrary to the dogma, the information flow between DNA and RNA was bi-directional. Presumably because this bi-directional flow was restricted to a number of viruses, RNA was, however, persistently thought of as little more than DNA's information delivery boy. Attitudes began to change in the early 1980s with the observation that some RNA species possessed a range of protein independent catalytic abilities (e.g. ribozymes). RNA's ability to act as an information storage molecule and its newly characterised catalytic capacities led to the 'RNA World' hypothesis which had, at least in part, been suggested by Crick and Orgel in 1968. This hypothesis implied that RNA evolved earlier than DNA from the primordial soup and that its catalytic activities supported its capacity to self replicate. While a discussion on this 'chicken or the egg' argument is far beyond the scope of this issue, it serves to illustrate the potential diversity of functions that RNA could play in regulating gene expression.

Another assumption under increasing scrutiny is that the expression of genetic information is primarily regulated at

the transcriptional step. While the central role of transcriptional regulation is undeniable, this assumption ignores the essential roles RNA plays in gene expression by way of a plethora of post-transcriptional regulation mechanisms, most of which are not completely understood. The thrust of this Showcase on RNA Biology is to explore some of the RNA species (e.g. non-coding RNA, miRNA, siRNA, mRNA) and the various processes (e.g. mRNA-targeting and alternative splicing, translation, pre-mRNA processing and mRNA stability) that drastically increase the number of pathways through which gene expression is post-transcriptionally regulated.

The first three articles describe various aspects of mRNA metabolism which strongly emphasise the roles that the 5' UTR and particularly the 3' UTR have in regulating gene expression. Ross Smith and Jillian Dunphy describe the *cis*-acting elements and *trans*-acting factors that regulate mRNA trafficking in order to translate mRNAs at specific subcellular locations thereby localising the proteins that they encode. Thomas Preiss describes global and mRNA-specific translational control mechanisms, while Mythily Sachchithanathan, Robert Medcalf and I discuss the capacity of the 3' UTR, via various *cis*-elements and *trans*-acting factors, to influence gene expression by regulating AU-rich mediated decay and pre-mRNA 3' processing. Finally, John Mattick explores the world of non-coding, micro and small interfering RNA. He points out that the vast majority of the genomes of complex organisms are transcribed largely into non-coding RNA and argues that the intronic and other non-coding RNAs represent an essential second tier of gene regulation.

It can no longer be assumed that regulated gene expression results only from altered rates of transcription. Instead, the more global scenario is that gene expression, development and differentiation are regulated by various combinations of transcriptional and post-transcriptional events.

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#### Cover Illustration

Ribbon drawing of the first two RNA recognition motif domains of HuD mRNA-stabilising protein bound to an AU-rich RNA element.

*This figure was prepared by Traci Hall (NIEHS, NIH, USA) with PyMol (<http://www.pymol.org>).*

#### Stem Cells

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In April, Showcase on Research will be on **Lipid Signalling** – Guest Editor: Stuart Pitson