Editorial

Post-transcriptional gene regulation via RNA control

One of the key assumptions of the genetic operator model proposed by Jacob and Monod [1] was the need for a short-lived ‘messenger’ template for protein synthesis likely made of RNA. The thesis here was that should protein regulation be primarily determined at the level of gene transcription, all intermediate templates needed for protein synthesis had to be rapidly degraded. If this were not the case, switching off transcription would not be able to switch off the synthesis of the resulting protein [1,2]. Shortly after the publication of the genetic operator model, the identity of such short-lived intermediate substance was confirmed as messenger RNA (mRNA) [3,4].

Since such beginnings in prokaryotic systems which contemplated a rather ordinary role of RNA as a passive intermediary in the business of gene expression, we have now moved on to place RNA at the very centre of the eukaryotic circuitry involved in gene expression control.

This issue of Briefings in Functional Genomics celebrates the rise of RNA regulation presenting a collection of articles discussing modern topics in the area of RNA control, focusing on events affecting RNA quality and quantity that occur during or after transcription, termed co-transcriptional and post-transcriptional regulatory processes, respectively.

The selection of contributors to this issue was largely based on key presentations made during the meeting ‘Gene expression and RNA processing’ which took place in Oct 2011 at the Iguazu Falls, one of the seven nature wonders of the world located at the border between Argentina and Brazil. After the meeting, authors from across the RNA field were asked to contribute the latest ideas and concepts in their respective areas of research, which span very broadly all the way from the mechanisms of alternative splicing to the roles of mRNA stability, microRNA (miRNA) regulation, and translational and post-translational control in animal and plant systems.

In the first contribution to this issue, Baralle and co-workers [5] provide a thoughtful discussion of the process of RNA splicing describing the strengths and weaknesses of a wide spectrum of methods currently available in splicing research; by focusing on efforts that use single-gene approaches versus those looking at global patterns of splicing, they provide valuable notions regarding the use of each experimental approach and set out the scene for what is to come in the experimental analysis of RNA splicing. In a second article, Yanovsky and co-workers [6] take the discussion directly to the biological relevance of post-transcriptional regulation focusing on the roles played by alternative splicing in the operation of circadian networks. Their work makes it clear that environmental cues such as temperature and photoperiod can change the alternative splicing of ‘core’ circadian controller genes and also affect splicing patterns across the transcriptome leading to the idea that the workings of circadian networks rely on post-transcriptional as well as on transcriptional regulatory processes.

The theme of RNA regulation is further developed in the subsequent contribution by Palacios [7] who focuses on a cellular surveillance system able to detect premature (nonsense) stop codons in mRNAs, termed nonsense-mediated RNA decay (NMD). Interestingly, the article emphasizes the importance of NMD in the regulation of normal gene expression through action on mRNA targets bearing NMD-inducing features highlighting the roles played by NMD on RNA regulation during cell division, animal development and human disease.

The article by Palatnik and co-workers [8] introduces the topic of small RNA regulation, with a focus on the biogenesis of miRNAs comparing and contrasting the ways by which miRNAs are generated from their longer biochemical precursors in plants and animals. The topic of miRNA regulation is then taken to the context of animal and human biology in the article by Freeman and Espinosa [9]
who discuss how inputs from miRNA- and RNA-binding proteins (RBPs) mold the RNA programmes controlled by the tumor-suppressor transcription factor p53 so as to adapt them to specific cellular and environmental parameters.

From matters of RNA processing and stability, the discussion then moves on to the influence of particular cis-regulatory mRNA sequences and trans-acting factor on the process of protein translation. In this regard, the contribution by Szostak and Gebauer [10] describes how RBPs can influence gene outputs via controlling different aspects of the translation cycle of mRNAs bearing specific sequence and structural motifs in their untranslated regions suggesting that the understanding of RBP translation-control functions is likely to expand significantly in the near future possibly leading to new therapeutic opportunities to combat disease based on the artificial modulation of gene-specific translation patterns.

The series concludes with an insightful discussion by Srebrow and co-workers [11] who touch on the links between RNA processing and post-translational modifications focusing on the role of the small ubiquitin-related modifier (SUMO) conjugation on factors controlling alternative splicing. Furthermore, the authors go on to describe the unexpected roles played by canonical splicing regulators on the process of protein sumoylation stressing the highly integrated nature of the molecular systems responsible for gene expression control.

Therefore, the collection of articles in this special issue of *Briefings in Functional Genomics* should provide fertile grounds to reflect about the underlying mechanisms and biological significance of post-transcriptional gene regulation in plant and animal systems, highlighting the central role played by RNA control in the molecular networks controlling genetic outputs.

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### References


