

Editorial

Editorial on the Special Issue: Regulation by Non-Coding RNAs

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Abstract: This Special Issue of *IJMS* is devoted to regulation by non-coding RNAs and contains both original research and review articles. An attempt is made to provide an up-to-date analysis of this very fast moving field and cover regulatory roles of both microRNAs and long non-coding RNAs. Multifaceted functions of these RNAs in normal cellular processes, as well as in disease progression, are highlighted.

Keywords: non-coding RNAs (ncRNAs); microRNAs (miRNAs); long ncRNAs (lncRNAs); Alu sequences; ncRNAs and human disease processes; regulation of ncRNA expression; ncRNAs and cell differentiation

These are exciting times for RNA molecular biologists, especially those concentrating on eukaryotic non-coding RNAs (ncRNAs)! New RNAs are constantly being found, e.g., thousands of large circular RNAs have recently been identified in human cells, some of which are shown to act as regulators that bind and sequester microRNAs [1]. The continuous discovery of new RNAs provides a rich environment for future RNA research and affords the possibility of many new functions being discovered.

This Special Issue of *IJMS* [2] contains both original research and review articles, and is devoted to regulation by ncRNAs. Multifaceted roles of these RNAs in normal cellular functions, as well as in disease processes, are highlighted. To mention a few, long ncRNAs (lncRNAs) and microRNAs (miRNAs) are both intimately involved in hematopoietic differentiation [3]. ncRNAs play a role in the adaptive immune response [4] and in diseases such as muscular dystrophies [5] and cancers [6–14]. Another paper discusses roles of lncRNAs in the pathogenesis of haematological malignancies [15]. The budding field of miRNAs and possible lncRNAs functions in cardiovascular disease is presented [16], as well as miRNA functions in abdominal aortic aneurysm [17]. In addition, it was

shown that miRNAs regulate the expression of the Huntington gene *HTT* [18]; mutations in *HTT* cause Huntington's disease. There is also a review on the 3' non-coding region of mRNAs, which discusses alterations in 3' UTRs sequences of mRNAs that may contribute to the development of various diseases in humans [19]. The fascinating viral immune system in prokaryotes, the RNA-based CRISPR complex is presented [20], and on "the other-side of the coin", the intricate mechanism of evasion of host RNA-directed DNA methylation of single-stranded DNA viruses by the land plants [21]. The intimate genomic association of transposable elements and their remnants with ncRNA genes is also presented, and how lncRNA Alu-containing transcripts can participate in disease formation when mutated, such as the formation of brainstem cell atrophy that leads to death [22]. Highlighted also are the Alu-lncRNAs/Alu-mRNA interactions that inhibit mRNA expression. In addition, one paper is devoted to computational methods in comparative genomics in light of the availability of new sequencing technologies [23]. Another paper surveys the current knowledge on regulation of miRNAs, principles of target recognition, and highlights new and novel non-canonical functions [24], whereas a separate paper also discusses techniques for the prediction of microRNA targets [25]. However this Issue includes numerous other highly informative papers describing the interesting roles of miRNAs and lncRNAs in various biological processes and the regulation of these ncRNAs [26–46]. In all, there are 44 papers, which attest to the large amount of interest and research activity in ncRNA molecular biology.

Conclusions

We indeed hope the readers will enjoy this Special Issue of *IJMS* and an attempt to present up-to-date findings in the rapidly moving and exciting field of non-coding RNA molecular biology and involvement of RNA in disease development.

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Conflicts of Interest

The author declares no conflict of interest.

References

1. Hansen, T.B.; Jensen, T.I.; Clausen, B.H.; Bramsen, J.B.; Finsen, B.; Damgaard, C.K.; Kjems, J. Natural RNA circles function as efficient microRNA sponges. *Nature* **2013**, *495*, 384–388.
2. Regulation by non-coding RNAs. Available online: http://www.mdpi.com/journal/ijms/special_issues/regulation-by-non-coding-rnas (accessed on 23 September 2013).
3. Morceau, F.; Chateauvieux, S.; Gaigneaux, A.; Dicato, M.; Diederich, M. Long and short non-coding RNAs as regulators of hematopoietic differentiation. *Int. J. Mol. Sci.* **2013**, *14*, 14744–14770.

4. Curtale, G.; Citarella, F. Dynamic nature of noncoding RNA regulation of adaptive immune response. *Int. J. Mol. Sci.* **2013**, *14*, 17347–17377.
5. Erriquez, D.; Perini, G.; Ferlini, A. non-coding RNAs in muscle dystrophies. *Int. J. Mol. Sci.* **2013**, *14*, 19681–19704.
6. Hauptman, N.; Glavač, D. Long non-coding RNA in cancer. *Int. J. Mol. Sci.* **2013**, *14*, 4655–4669.
7. Calore, F.; Lovat, F.; Garofalo, M. Non-coding RNAs and cancer. *Int. J. Mol. Sci.* **2013**, *14*, 17085–17110.
8. Deng, G.; Sui, G. Noncoding RNA in oncogenesis: A new era of identifying key players. *Int. J. Mol. Sci.* **2013**, *14*, 18319–18349.
9. Lung, R.W.; Tong, J.H.; To, K.F. Emerging roles of small epstein-barr virus derived non-coding RNAs in epithelial malignancy. *Int. J. Mol. Sci.* **2013**, *14*, 17378–17409.
10. Li, X.; Zhang, Z.; Yu, M.; Li, L.; Du, G.; Xiao, W.; Yang, H. Involvement of miR-20a in promoting gastric cancer progression by targeting early growth response 2 (EGR2). *Int. J. Mol. Sci.* **2013**, *14*, 16226–16239.
11. Schwarzenbacher, D.; Balic, M.; Pichler, M. The role of microRNAs in breast cancer stem cells. *Int. J. Mol. Sci.* **2013**, *14*, 14712–14723.
12. Lee, C.H.; Kuo, W.H.; Lin, C.; Oyang, Y.J.; Huang, H.C.; Juan, H.F. MicroRNA-regulated protein-protein interaction networks and their functions in breast cancer. *Int. J. Mol. Sci.* **2013**, *14*, 11560–11606.
13. Nishizawa, T.; Suzuki, S. The role of microRNA in gastric malignancy. *Int. J. Mol. Sci.* **2013**, *14*, 9487–9496.
14. Hannafon, B.N.; Ding, W.Q. Intercellular communication by exosome-derived microRNAs in cancer. *Int. J. Mol. Sci.* **2013**, *14*, 14240–14269.
15. Garitano-Trojaola, A.; Agirre, X.; Prósper, F.; Fortes, P. Long non-coding RNAs in haematological malignancies. *Int. J. Mol. Sci.* **2013**, *14*, 15386–15422.
16. Iaconetti, C.; Gareri, C.; Polimeni, A.; Indolfi, C. Non-coding RNAs: The “Dark Matter” of cardiovascular pathophysiology. *Int. J. Mol. Sci.* **2013**, *14*, 19987–20018.
17. Maegdefessel, L.; Spin, J.M.; Adam, M.; Raaz, U.; Toh, R.; Nakagami, F.; Tsao, P.S. Micromanaging abdominal aortic aneurysms. *Int. J. Mol. Sci.* **2013**, *14*, 14374–14394.
18. Kozlowska, E.; Krzyzosiak, W.J.; Koscińska, E. Regulation of huntingtin gene expression by miRNA-137, -214, -148a, and their respective isomiRs. *Int. J. Mol. Sci.* **2013**, *14*, 16999–167016.
19. Michalova, E.; Vojtesek, B.; Hrstka, R. Impaired Pre-mRNA processing and altered architecture of 3' untranslated regions contribute to the development of human disorders. *Int. J. Mol. Sci.* **2013**, *14*, 15681–15694.
20. Richter, H.; Randau, L.; Plagens A. Exploiting CRISPR/Cas: Interference mechanisms and applications. *Int. J. Mol. Sci.* **2013**, *14*, 14518–14531.
21. Pooggin, M.M. How can plant DNA viruses evade siRNA-directed DNA methylation and silencing? *Int. J. Mol. Sci.* **2013**, *14*, 15233–15259.
22. Hadjijargyrou, M.; Delias, N. The intertwining of transposable elements and non-coding RNAs *Int. J. Mol. Sci.* **2013**, *14*, 13307–13328.

23. Bussotti, G.; Notredame, C.; Enright, A.J. Detecting and comparing non-coding RNAs in the high-throughput era. *Int. J. Mol. Sci.* **2013**, *14*, 15423–15458.
24. Doxakis, E. Principles of miRNA-target regulation in metazoan models. *Int. J. Mol. Sci.* **2013**, *14*, 16280–16302.
25. Zheng, H.; Fu, R.; Wang, J.T.; Liu, Q.; Chen, H.; Jiang, S.W. Advances in the techniques for the prediction of microRNA targets. *Int. J. Mol. Sci.* **2013**, *14*, 8179–8187.
26. Shuang, T.; Shi, C.; Chang, S.; Wang, M.; Bai, C.H. Downregulation of miR-17~92 expression increase paclitaxel sensitivity in human ovarian carcinoma SKOV3-TR30 cells via BIM instead of PTEN. *Int. J. Mol. Sci.* **2013**, *14*, 3802–3816.
27. Ruan, H.; Liu, S.; Li, F.; Li, X.; Fan, C. Prevention of tendon adhesions by ERK2 small interfering RNAs. *Int. J. Mol. Sci.* **2013**, *14*, 4361–4371.
28. Ma, J.; Yu, S.; Wang, F.; Bai, L.; Xiao, J.; Jiang, Y.; Chen, L.; Wang, J.; Jiang, A.; Li, M.; et al. MicroRNA transcriptomes relate intermuscular adipose tissue to metabolic risk. *Int. J. Mol. Sci.* **2013**, *14*, 8611–8624.
29. Eskildsen, T.V.; Jeppesen, P.L.; Schneider, M.; Nossent, A.Y.; Sandberg, M.B.; Hansen, P.B.; Jensen, C.H.; Hansen, M.L.; Marcussen, N.; Rasmussen, L.M.; et al. Angiotensin II regulates microRNA-132/-212 in hypertensive rats and humans. *Int. J. Mol. Sci.* **2013**, *14*, 11190–11207.
30. Nagata, Y.; Shimizu, E.; Hibio, N.; Ui-Tei, K. fluctuation of global gene expression by endogenous miRNA response to the introduction of an exogenous miRNA. *Int. J. Mol. Sci.* **2013**, *14*, 11171–11189.
31. Thomas, M.; Lange-Grünweller, K.; Hartmann, D.; Golde, L.; Schlereth, J.; Streng, D.; Aigner, A.; Grünweller, A.; Hartmann, R.K. Analysis of transcriptional regulation of the human miR-17–92 cluster; evidence for involvement of Pim-1. *Int. J. Mol. Sci.* **2013**, *14*, 12273–12296.
32. Hou, J.; Zhao, D. MicroRNA regulation in renal pathophysiology. *Int. J. Mol. Sci.* **2013**, *14*, 13078–13092.
33. Kang, S.M.; Choi, J.W.; Hong, S.H.; Lee, H.J. Up-regulation of microRNA* strands by their target transcripts. *Int. J. Mol. Sci.* **2013**, *14*, 13231–13240.
34. Battista, M.; Musto, A.; Navarra, A.; Minopoli, G.; Russo, T.; Parisi, S. miR-125b Regulates the early steps of ESC differentiation through Dies1 in a TGF-independent manner. *Int. J. Mol. Sci.* **2013**, *14*, 13482–13496.
35. Kushibiki, T.; Hirasawa, T.; Okawa, S.; Ishihara, M. Regulation of miRNA expression by low-level laser therapy (LLLT) and photodynamic therapy (PDT). *Int. J. Mol. Sci.* **2013**, *14*, 13542–13558.
36. Lin, L.L.; Wu, C.C.; Huang, H.C.; Chen, H.J.; Hsieh, H.L.; Juan, H.F. Identification of microRNA 395a in 24-epibrassinolide-regulated root growth of *Arabidopsis thaliana* using microRNA arrays. *Int. J. Mol. Sci.* **2013**, *14*, 14270–14286.
37. Rosa, A.; Brivanlou, A.H. Regulatory non-coding RNAs in pluripotent stem cells. *Int. J. Mol. Sci.* **2013**, *14*, 14346–14373.
38. Zhang, C.; Li, G.; Wang J.; Zhu, S.; Li, H. Cascading *cis*-cleavage on transcript from trans-acting siRNA-producing locus 3. *Int. J. Mol. Sci.* **2013**, *14*, 14689–14699.
39. Pacilli, A.; Ceccarelli, C.; Treré, D.; Montanaro, L. SnoRNA U50 levels are regulated by cell proliferation and rRNA transcription. *Int. J. Mol. Sci.* **2013**, *14*, 14923–14935.

40. Nicolás, F.E.; Ruiz-Vázquez, R.M. Functional diversity of RNAi-associated sRNAs in fungi. *Int. J. Mol. Sci.* **2013**, *14*, 15348–15360.
41. Gomes, A.Q.; Nolasco, S.; Soares, H. Non-coding RNAs: Multi-tasking molecules in the cell. *Int. J. Mol. Sci.* **2013**, *14*, 16010–16039.
42. Mayr, F.; Heinemann, U. Mechanisms of Lin28-mediated miRNA and mRNA regulation—A structural and functional perspective. *Int. J. Mol. Sci.* **2013**, *14*, 16532–16553.
43. Hecker, M.; Thamilarasan, M.; Koczan, D.; Schröder, I.; Flechtnner, K.; Freiesleben, S.; Füllen, G.; Thiesen, H.J.; Zettl, U.K. MicroRNA expression changes during interferon-beta treatment in the peripheral blood of multiple sclerosis patients. *Int. J. Mol. Sci.* **2013**, *14*, 16087–16110.
44. Yu, S.; Zhang, R.; Zhu, C.; Cheng, J.; Wang, H.; Wu, J. MicroRNA-143 downregulates interleukin-13 receptor alpha1 in human mast cells. *Int. J. Mol. Sci.* **2013**, *14*, 16958–16969.
45. Stoller, M.L.; Chang, H.C.; Fekete, D.M. Bicistronic gene transfer tools for delivery of miRNAs and protein coding sequences. *Int. J. Mol. Sci.* **2013**, *14*, 18239–18255.
46. Li, J.; Xuan, Z.; Liu, C. Long non-coding RNAs and complex human diseases. *Int. J. Mol. Sci.* **2013**, *14*, 18790–18808.

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