

I thank the three reviewers for their critiques and suggestions to improve the manuscript. Below is my response with the changes made in the manuscript highlighted in red.

For the Editor:

1. The 4th point made by the editor in his comments concerning Table 1 (and perhaps now Table 2) is the formatting. Note that the tables were made by the Microsoft Word Insert Table tool and my copies look OK. I have added a pdf file of the manuscript with the resubmission where the table formatting also looks fine. Could it be that opening my word file on the internet produces a distortion in the tables?

2. I changed the Author Contributions section to reflect the nature of the paper, i.e., there is no original recent data presented.

Reviewer 1

Manuscript Number	20584
Manuscript Title	Discovery and characterization of the first non-coding RNA that regulates gene expression, micF RNA: a historical perspective
Review Time	2015-07-20 22:24

Comments To Authors

In this review, authors provided the interesting knowledge on the original discovery and characterization of the first non-coding RNA gene and its transcript. The initial discovery of micF RNA in prokaryotes was performed in the 1980s, which occurred over 5 years before the discovery of the first eukaryotic regulatory miRNA. The author is one of the main scientists, which presented the concept and initial experimental evidence that RNA can regulate gene expression. This review manuscript is well-written and the topic of this review seems to be significant.

Authors just need to check some errors, including; - In page 8, line 5 from bottom, revise “~ at 550C and 370C.” to “at 55°C and 37°C.” - In page 20, line 11 in Table 1, revise “Bines RNA” to “binds RNA”.

Additionally, authors need to check the format of the references (many references need format correction).

Author Response to reviewer 1 (in red):

1. In page 8, line 5 from bottom, revise “~ at 550C and 370C.” to “at 55°C and 37°C.”

Note, corrected to: "annealing at 55°C and 37°C."

2. In page 20, line 11 in Table 1 revise “Bines RNA” to “binds RNA”.

Note, in Table 1 my copy shows "binds RNA".

3.need to to check the format of the references (many references need format correction).

References have been corrected. Thank you.

Reviewer 2

Manuscript Number	20584
Manuscript Title	Discovery and characterization of the first non-coding RNA that regulates gene expression, micF RNA: a historical perspective
Review Time	2015-07-27 19:56

This manuscript described the history of the discovery of a regulatory RNA- micF RNA. The author of this manuscript and his collaborators made a significant contribution in this field. However, in table 1, the author cited 2 references (should be reference 32 and 33, not reference 31), more related references in which some pioneer discoveries on functional non-coding small RNAs were described should be cited as well, such as: Stark, B. C., Kole, R., Bowman, E. J. & Altman, S. Ribonuclease P: an enzyme with an essential RNA component. Proc. Natl Acad. Sci. USA 75, 3717–3721 (1978).

Comments
To
Authors

Jonathan Rosen*, Thomas Ryder, Hisako Ohtsubo & Eiichi Ohtsubo. Role of RNA transcripts in replication incompatibility and copy number control in antibiotic resistance plasmid derivatives. *Nature* 290, 794 - 797 (30 April 1981); doi:10.1038/290794a0. Zieve, G. W. Two groups of small stable RNAs. *Cell* 25, 296–297 (1981). Lerner, M. R. & Steitz, J. A. Snurps and scyrps. *Cell* 25, 298–300 (1981). Saito, H. & Richardson, C. C. (1981) *Cell* 27, 533-542. Busch, H., Reddy, R., Rothblum, L. & Choi, Y. C. SnRNAs, SnRNPs, and RNA processing. *Annu. Rev. Biochem.* 5, 617–654 (1982). Lewin, R. Surprising discovery with a small RNA. *Science* 218, 777–778 (1982). Walter, P. & Blobel, G. Signal recognition particle contains a 7S RNA essential for protein translocation across the endoplasmic reticulum. *Nature* 299, 691–698 (1982). Reed RE, Baer MF, Guerrier-Takada C, Donis-Keller H, Altman S. Nucleotide sequence of the gene encoding the RNA subunit (M1 RNA) of ribonuclease P from *Escherichia coli*. *Cell* 1982; 30 (2): 627-36. Kruger, K. et al. Self-splicing RNA: autoexcision and autocyclization of the ribosomal RNA intervening sequence of *Tetrahymena*. *Cell* 31, 147–157 (1982). Simons, R. W. & Kleckner, N. (1983) *Cell* 34, 683-691. Guerrier-Takada, C., Gardiner, K., Marsh, T., Pace, N. & Altman, S. The RNA moiety of ribonuclease P is the catalytic subunit of the

enzyme. Cell 35, 849–857 (1983). In 1961, Jacob and Monod proposed the operon and repressor model of protein synthesis and regulation {Jacob, F. & Monod, J. Genetic regulatory mechanisms in the synthesis of proteins. J. Mol. Biol. 3, 318–356 (1961)}, and after several years of research in the field of molecular biology, we were clear that mRNA, tRNA, and rRNA were involved in protein synthesis. Afterward, some non-coding small RNAs were noticed and studied by several researchers in the world. The author of this manuscript ignored some pioneer contributions made by other researchers, therefore, I recommend the author to add more related references to give readers a brief but thorough view of the history of non-coding small RNA research. There was a grammatical error in the text: “Dorman and co-workers hypothesized that Stp induces a conformational change in micF RNA that makes it is susceptible to degradation by nucleases[56]”

Author Response (in red):

1. "....more related references in which some pioneer discoveries on functional non-coding small RNAs were described should be cited as well".

All of the the additional non-coding functions and most of the

references suggested by reviewer 2 were added. Please see revised manuscript p.5 lines 11-17 from bottom and p. 9 lines 20-28 from bottom highlighted in red and the addition of Table 2.

Kindly note concerning the reviewer's comments: I did not mean the paper to be a comprehensive history of discovery of RNA functions but to be focused specifically on the initial discoveries of RNA as a regulator.

Reviewer 3

Reviewed by 00484021

Manuscript Number	20584
Manuscript Title	Discovery and characterization of the first non-coding RNA that regulates gene expression, micF RNA: a historical perspective
Review Time	2015-08-13 02:28

Comments To Authors	In the manuscript titled "Discovery and characterization of the first non-coding RNA that regulates gene expression, micF RNA: a historical perspective", Nicholas Delihis provides a fascinating review of the early work done with non-coding RNAs in prokaryotes. He focuses in particular on the micF RNA, which he helped characterize and provides insight into the early work on non-coding RNAs which have since become a major area of research. The manuscript is well written and concise in its focus on micF and background/context necessary to understand the early work.
Classification	

There were no changes recommended by Reviewer 3

