

**ESPS Manuscript NO: 4371**

The manuscript has been improved according to the suggestions of the reviews:

1. The format has been updated, including lengthening the abstract.
2. Revision has been made according to the suggestions of the reviewers.

(1) Both reviewers requested the addition of figures to help clarify some of the regulatory pathways that affect HuR expression. We have added these. Figure 1 illustrates the mechanisms that regulate expression of HuR mRNA levels, while Figure 2 depicts many of the mechanisms that regulate HuR protein levels.

Reviewer 00646291 also requested the following revisions:

(2) “The introduction would be more attractive to the reader if the long one paragraph was broken down to three.”

We have done so.

(3) “It would make better sense if the Regulation of HuR mRNA Expression preceded the Expression Patterns during Development, Aging, and Cellular Senescence.”

We agree and have altered the order of these sections as requested.

(4) “The section II (Pathological Overexpression of HuR, Regulation by MicroRNAs, and Disease) mainly focuses on cancer, and other diseases in which HuR

has been reported to play significant roles such as cardiovascular, neurological, and muscular diseases are not presented. These diseases should be introduced or the title of the section should change to cancer instead of disease."

We agree. We focused primarily on cancer since the study of tumor cells has provided a very useful model to identify new mechanisms (mostly miRNAs) involved in regulating HuR levels. Therefore, we have changed the last word of this section from "Disease" to "Cancer". In a new section added on future directions (see next point), we briefly bring up other diseases and suggest that our knowledge of HuR regulatory mechanisms gained from cell studies may now be extended to organismal studies.

(5) "The introduction of a section with future directions of research would be useful and would improve the quality of the review."

We have added this material and have rolled it into the last section that is now titled, "Summary and Future Directions."

3. References and typesetting were corrected.

Thank you again for publishing our manuscript in the World Journal of Biological Chemistry.

Sincerely,

A handwritten signature in cursive script that reads "Beth S. Lee". The ink is dark and the signature is fluid, with the first letters of each name being capitalized and prominent.

Beth S. LEE, PhD

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