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Selective degradation of oxidized RNA

Statement of the Problem: Oxidation is probably the most common type of damage that occurs in cellular RNA. Oxidized RNA may be dysfunctional and is implicated in the pathogenesis of age-related human diseases. Cellular mechanisms controlling oxidized RNA have begun to be revealed. Currently, many ribonucleases and RNA-binding proteins have been shown to reduce oxidized RNA and to protect cells under oxidative stress. Although information about how these factors work is still very limited, we suggest mechanisms that can be used to minimize oxidized RNA in bacteria and human cells.

Methodology & Theoretical Orientation: RNA oxidation levels are determined by chromatographic separation of nucleosides and detection of 8-oxoG levels. Cell viability was determined by growth rate. Functions of ribonucleases and other proteins were studied by examining mutants lacking genes encoding these proteins, or over-expressing the genes.

Findings: Many ribonucleases and other proteins were found important for maintaining cell viability under oxidative stress. We have also identified proteins that specifically bind oxidized RNA at high affinity. In mutants lacking these activities, oxidized RNA accumulates. Over-expression of these activities reduces oxidized RNA and rescue cells under oxidative stress. Normalized RNA oxidation levels reduce overtime after pulse oxidative challenge.

Conclusion & Significance: The results demonstrate mechanisms for selective removal of oxidized RNA in bacteria and cultured human cells. Selective reduction of RNA oxidation depends on the activities of ribonucleases, suggesting that RNA degradation plays a major role in this process. The finding of specific proteins with high affinity to oxidized RNA implies that oxidized RNA is recognized by these proteins, targeting the RNA to effective degradation or repair. The findings demonstrate an important mechanism for maintaining RNA quality for normal function of the cell, and for prevention of related human diseases.

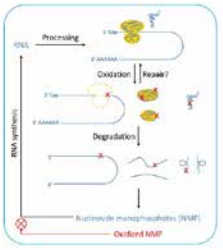

Fig. 1 Molecular mechanisms for reducing oxidized RNA in cells. RNA may become nonfunctional once it is oxidized. At the early stage after oxidation modification, the RNA may possibly be reverted to normal, functional RNA by repair activities. Oxidized RNA is also subjected to degradation, which is responsible to irreversibly eliminate probably the majority of oxidized RNA. The oxidized nucleotides resulted from degradation are blocked from transcription, reducing the formation of oxidized RNA by synthesis. RNA molecules are shown as blue lines. Oxidized residues in RNA are marked by a red 'X'.

Biography

Zhongwei Li has his expertise in RNA Biology and related biomedical problems. He studies applied biochemical, molecular and genomics approaches to understand how RNA is processed and degraded in various organisms, and to elucidate the role and significance of ribonucleases. He teaches Biomedical Science courses for Under-graduate medical program and Graduate programs. His research primarily focuses on RNA damage control and prevention of human diseases. His goals are to develop RNA damage biomarkers and identifying protective genes to cope with degenerative disorders. In addition, he is studying bacteria aiming to develop treatment of infectious diseases, including identification of bacterial genes involved in infection, different pathways for bacterial RNA metabolism, and methods for quick diagnosis of bacteria in clinical settings. More recently, he has taken the responsibility of faculty affairs administration to help the college grow after obtaining full LCME accreditation.

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