Editorial
Volume 7:3, 2022

Clinical Gastroenterology Journal

ISSN: 2952-8518 Open Access

Source of Mutagenic Activity in Cancer Pathogenesis

Nicholas Guyer*

Department of Hepatology, School of Science and Technology, USA

Editorial

The progression of carcinogenesis and cancer is significantly accelerated by disruption of genomic integrity, yet the pathways and underlying mechanisms for mutagenic disruption appear to be more varied. Whole genome sequencing improvements have increased our understanding of the ranges of somatic and germline DNA changes (chromosomal deletions, deficiencies in mismatch repair, epigenetic changes, translocations, and rearrangements changes such histone modifications and methylation, which affect the genomic template's transcriptional activity. with ultradeep whole transcriptome sequencing becoming more widespread, there is renewed attention on yet another source of mutagenic activity in cancer pathogenesis, namely aberrant or misregulated RNA editing.

The nucleotide sequence of RNA is changed during the physiological epitranscriptional (also known as cotranscriptional or posttranscriptional) enzymatic process of RNA editing, resulting in an edited sequence that is different from the corresponding genomic template. In mammals, there are two different ways for editing RNA, each of which is controlled by a family of conserved enzymes. Adenosine-to-inosine (A-to-I) RNA editing, in which the changed nucleoside base (inosine) is identified by the translational apparatus as a guanosine, is by far the most common process. This essentially results in an A-to-G mutation. Adenosine deaminases acting on RNA (ADARs), of which there are three members in vertebrates (ADAR1-3) and two of which are catalytically active, mediate the 2 A-to-I RNA editing process (ADAR1 and ADAR2). A-to-I RNA editing takes place physiologically and extensively; >100 million editing sites were found by ultradeep sequencing, the most majority of which were found in noncoding areas, particularly within repeated Alu repeats. However, there are a variety of coding region-changing A-to-I RNA editing targets, such as the mammalian GluR, 5-HT2cR, and potassium channel (Kv1.1) transcripts, whose conserved (physiologic) editing results in functional diversity [1-3]

The second, considerably less common process is cytosine-to-uracil (C-to-U) RNA editing, with Apobec-1-mediated cytosine deamination within the nuclear Apo lipoprotein B messenger being the most well-studied example. The sources of mutational activity in gastric cancer (GC) and in particular whole transcriptome mutational profiles are relatively underexplored. In this issue of Gastroenterology, have surveyed A-to-I RNA editing events in GC with findings that highlight transcriptomic editing as a pathogenic mechanism. One of the important findings supports the findings mentioned to by demonstrating that ADAR1 expression was up-regulated (representing ADAR1 amplification) and ADAR2 expression was down-regulated (reflecting ADAR2 deletion). Significantly worse overall survival was associated with either elevated ADAR1 or lowered ADAR2, and the two together (raised ADAR1 and lowered ADAR2) were additive in predicting lower survival. One of the important findings supports the findings mentioned to by demonstrating that ADAR1 expression was up-regulated (representing ADAR1 amplification) and ADAR2 expression was down-regulated (reflecting ADAR2 deletion). Significantly worse overall survival was associated with either elevated ADAR1 or lowered ADAR2, and the two together (raised ADAR1 and lowered ADAR2) were additive in predicting lower survival.

They used in vitro tumorigenic assays to show that transfection of catalytically active but not dead ADAR1 is protumorigenic and that catalytically active but not dead ADAR2 transfection attenuates tumorigenicity. In addition, they report a novel ADAR2-mediated A-to-I RNA target, podocalyxin-like (PODXL), which encodes a cell surface protein regulating cell adhesion and morphology. These results reveal that PODXL may be a downstream factor in ADAR2-mediated tumour suppression, and the authors imply that changes in PODXL may be responsible for the loss-of-function phenotype associated with ADAR2 deletion. It is important to note that overexpression of PODXL has been reported in individuals with aggressive colorectal and breast cancers; providing more evidence that a functional change in the coding region of PODXL may have negative effects. The ADAR2 site was upstream (i.e., 5') of another, ADAR1-specific PODXL A-to-I RNA editing site that the authors discovered. The synonymous alteration (ACA / ACG, Thr238) produced by this ADAR1-specific RNA editing event begs the question of its functional significance. Given that ADAR1 overexpression on its own was linked to a protumorigenic phenotype, it is likely that this synonymous RNA editing event had an impact on the stability or translation of the PODXL gene. The report also raises the question of whether additional, unidentified RNA editing events caused by ADAR1 overexpression could be driving mutations in the context of GC pathogenesis [4,5]

***Address for Correspondence:** Nicholas Guyer, Department of Hepatology, School of Science and Technology, USA, E-mail: nichgu23@tmh.org*

***Copyright:** © 2022 Guyer N. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.*

Date of Submission: 05 June 2022, Manuscript No. cgj-22-75838; **Editor assigned:** 07 June 2022, PreQC No. P-75838; **Reviewed:** 16 June 2022, QC No. Q-75838; **Revised:** 23 June 2022, Manuscript No. R-75838; **Published:** 30 June 2022, DOI: 10.37421/2952-8518.2022.7.168

Acknowledgement

We thank the anonymous reviewers for their constructive criticisms of the manuscript. The support from ROMA (Research Optimization and recovery in the Manufacturing industry), of the Research Council of Norway is highly appreciated by the authors.

Conflict of Interest

The Author declares there is no conflict of interest associated with this manuscript.

References

1. Barazzoni, Rocco, Gianluca Gortan Cappellari, Maurizio Ragni, and Enzo Nisoli. “Insulin resistance in obesity: an overview of fundamental alterations.” *Clin Gastroenterol J* 23 (2021): 149-157.

2. Palmisano, Brian T., Lin Zhu, and John M. Stafford. “Role of estrogens in the regulation of liver lipid metabolism.” *Clin Gastroenterol J* (2017): 227–256.

3. Kulbay, Merve, Nathan Bernier-Parker, and Jacques Bernier. “The role of the DFF40/CAD endonuclease in genomic stability." *Clin Gastroenterol J* 26 (2021): 9–23.

4. Bertoluci, Marcello Casaccia, and Viviane Zorzanelli Rocha. “Cardiovascular risk assessment in patients with diabetes.” *Clin Gastroenterol J* 9 (2017) 1-13.

5. Drucker, Daniel J. “Diabetes, obesity, metabolism, and SARS-CoV-2 infection: the end of the beginning ” *Clin Gastroenterol J* 3 (2021): 479-498.

How to cite this article: Guyer, Nicholas. "Source of Mutagenic Activity in Cancer Pathogenesis." Clin Gastroenterol J 7 (2022): 168.