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# PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastrointestinal Surgery

**Manuscript NO:** 60149

**Title:** Research progress on O-GlcNAcylation in the occurrence, development, and treatment of colorectal cancer

**Reviewer's code:** 00503405
**Position:** Editorial Board
**Academic degree:** MD, PhD
**Professional title:** Senior Lecturer, Senior Scientist
**Reviewer's Country/Territory:** Hungary
**Author's Country/Territory:** China

**Manuscript submission date:** 2020-10-17
**Reviewer chosen by:** Jin-Lei Wang
**Reviewer accepted review:** 2020-11-21 09:12
**Reviewer performed review:** 2020-11-23 12:04
**Review time:** 2 Days and 2 Hours

| | |
|---|---|
| **Scientific quality** | [ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good<br>[Y] Grade D: Fair [ ] Grade E: Do not publish |
| **Language quality** | [ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing<br>[ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection |
| **Conclusion** | [ ] Accept (High priority) [ ] Accept (General priority)<br>[ ] Minor revision [Y] Major revision [ ] Rejection |
| **Re-review** | [ ] Yes [Y] No |
| **Peer-reviewer statements** | Peer-Review: [Y] Anonymous [ ] Onymous<br>Conflicts-of-Interest: [ ] Yes [Y] No |

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**SPECIFIC COMMENTS TO AUTHORS**

In this review artivcle of Liu and Peng, the authors aimed to summarize current knowledge about the role of O-GlcNAcylation in the process of colorectal carcinogenesis. The topic is of great clinical importance, and the manuscript is brief and comprehensive regarding the cellular/immunological functions of O-GlcNAcylation in CRC. Some point hwever need revision: - it should be strictly separated that what kind of CRCs are altered by the different molecular targets of acetylation (i.e. genetically determined CRcs, like APC mutation, Lynch syndrome etc., or sporadical CRCs etc.) - I suggest to include 2 more figures. One should summarize the main points of acetylaion effects in the process of CRC -genesis, the other should summarize the possible therapeutic targets, for a better undersatnding of this complex topic. After major revision I suggest to accept the manuscript for publication in WJG.

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**Reviewer's code:** 05458182
**Position:** Peer Reviewer
**Academic degree:** MD
**Professional title:** Deputy Director
**Reviewer's Country/Territory:** Russia
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| | |
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| **Scientific quality** | [ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good<br>[ ] Grade D: Fair [ ] Grade E: Do not publish |
| **Language quality** | [ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing<br>[ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection |
| **Conclusion** | [ ] Accept (High priority) [Y] Accept (General priority)<br>[ ] Minor revision [ ] Major revision [ ] Rejection |
| **Re-review** | [ ] Yes [Y] No |
| **Peer-reviewer statements** | Peer-Review: [Y] Anonymous [ ] Onymous<br>Conflicts-of-Interest: [ ] Yes [Y] No |

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**SPECIFIC COMMENTS TO AUTHORS**

The title reflects the main subject of the manuscript. The abstract summarizes and reflects the work described in the manuscript. The key words reflect the focus of the manuscript. The manuscript adequately describes the background, present status and significance of the study. The manuscript describes methods, experiments and data analysis in adequate detail. The manuscript interprets the findings adequately and appropriately, highlighting the key points concisely, clearly and logically. The figure and tables have a good quality and appropriately illustrative of the paper contents. The manuscript meets the requirements of use of SI units. The manuscript cites appropriately the latest, important and authoritative references. The manuscript is well organized and presented. The style, language and grammar are accurate and appropriate. The author prepares the manuscript according to the appropriate research (PRISMA 2009 Checklist) methods and reporting. The manuscript met the requirements of ethics. The manuscript is a review of the literature dedicated O-GlcNAcylation. It highlights physiological effects of O-GlcNAcylation, its role in CRC cell cycle, stress of CRC cells and therapy for CRC. O-GlcNAcylation refers to a single N-acetylglucosamine with O-glycoside bond to a protein serine or threonine hydroxyl oxygen atom to modify the protein in the nucleus and cytoplasm. Authors proposed that the change of O-GlcNAcylation is a marker of CRC, and the inactivation of functional molecules involved in O-GlcNAcylation hinders the biosynthesis of normal glycosylation structures, thus promoting the progression and metastasis of CRC. As we know, O-GlcNAcylation is a dynamic protein modification process. In this review O-GlcNAcylation presented as one of the important process involved in tumorigenesis and the development of malignant biological phenotypes. The manuscript notes that the change of O-GlcNAcylation is related to cell development, mitosis, proliferation and

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survival, and tumor metastasis. Abnormal changes of O-GlcNAcylation may lead to tumor transformation of CRC cells. O-GlcNAcylation can dynamically regulate intracellular metabolism and signaling pathways, thus enhancing the resistance of CRC cells to various stimuli from the environment and itself. The generally elevated O-GlcNAcylation level in CRC was considered to be a key factor in the occurrence and development of CRC. The manuscript has shown that nucleotide sugar analogs, tumor-specific carbohydrate vaccine, SIRT1 longevity gene, dendritic cells as targets, and NOTCH gene can be use as diagnostic markers and therapeutic targets of CRC. Many studies have shown that O-GlcNAcylation and O-linked N-acetylglucosamine transferase (OGT) may be potential targets for treating cancer. Authors suggest using determination of OGT and O-GlcNAcylation in urine or blood for the diagnosis or evaluation of treatment response. Special attention of the authors was paid to Tn antigen. As known, it may be a useful diagnostic marker because it is rarely found in normal tissues, but it is widely expressed in various adenocarcinoma and some malignant hematopoietic cells. Tn antigen increased in the tumor metastasis region and tumor including. CRC. It also suggests that the occurrence of intracellular Tn and sTn may be an early event of CRC. Manuscript describe the dendritic cells (DCs) that have recently become an interesting method to induce antitumor immunity as a target. Targeting DCs with glycan-modified tumor antigens can improve the tumor-specific T cell response and long-term tumor regression. Some studies have shown that changes in O-GlcNAcylation during tumorigenesis can help to deceive the immune system. Authors suppose that the individualized carbohydrate code of the tumor may destroy the immune state of the tumor by changing the O-GlcNAcylation of CRC, and become the target of interference of glycan checkpoint. Alternatively, these new checkpoint blockers can be combined with DC-targeted vaccination strategies to achieve the best success of future immunotherapy regimens.

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