Reviewer's report

Title: Hyperglycemia regulates thioredoxin-ROS activity through induction of thioredoxin-interacting protein (TXNIP) in metastatic breast cancer-derived cells MDA-MD-231

Version: 1 Date: 1 March 2007

Reviewer: Junji Yodoi

Reviewer's report:

General
1. The author said in this paper, almost of all experiment as shown in “Duplicate”. It is necessary to do experiment in “Triplicate” for statistic science. Therefore, the author should remove statistic bar and/or explain why they didn’t all the experiment at least 3times per each.

2. The author should show how much cells to use the experiment for treatment with glucose, Phloretin and SB203580.

3. In Figure3 (A), the author doesn’t write the length of stimulation time clearly. In Figure4 (A), the author should insert not only bar chart but also histogram in FACS data. That makes more clearly to understand TXNIP is induced by high-glucose stimulation.

4. The authors showed some important clues that TXNIP is induced by high-glucose stimulation accompany with increased ROS activity and decreased TRX activity. But the authors didn’t refer to the TRX and ROS activity under the stimulation of Phloretin. The author should also show TRX activity and ROS activity under the stimulation of Phloretin. In addition, the authors did the experiment that p38 inhibitor decrease ROS activity and increase TRX activity under high-glucose condition. However the author conclude hyperglycemia-induced TXNIP elevation is associated with decreased TRX activity resulting in increasing levels of ROS in MDA-MD-231 cells, the author doesn’t show TXNIP expression under stimulation of p38 inhibitor on hyperglycemia(Figure4). The author should refer to that point.

5. It has been already known that TXNIP is induced by high-glucose stimulation(1,2). The authors said the new point of their research is that they show for the first time to the metabolic condition of hyperglycemia affects the level of both TXNIP RNA and protein in breast-cancer derived cells MDA-MD-231. If so, the author should discuss/suggest how work TXNIP between Diabetes and Cancer. The authors also should discuss following references.


Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)
What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions