



SDI FINAL EVALUATION FORM 1.1

PART 1:

Journal Name:	International Journal of Biochemistry Research & Review
Manuscript Number:	Ms_IJBCRR_24489
Title of the Manuscript:	Disruption of disulfide bonds of insulin receptor as a cause of insulin resistance
Type of Article	Commentaries and Opinions

PART 2:

FINAL EVALUATOR'S comments on revised paper (if any)	Authors' response to final evaluator's comments
The author addressed some of my previous concerns but some major ones still require attention as suggested below - Some affirmations need to be substantiated with relevant publication in the field in the body of the paper (e.g. "Disruption of the insulin- ligand -initiated receptor signal transduction is currently the cause espoused"). In other circumstances, it is not clear if the statements are part of the author's opinion or hypothesis. For clarity and connection to the proposed hypothesis, some issues should be addressed and substantiated with the literature (e.g. Subheadings for Physiological and abnormal energy metabolism, carbohydrate metabolism x fat metabolism and insulin receptor disulfide bonds, DM2 and change in the energy metabolism) Would the proposed hypothesis better stated as follows (using your own statements expressed in the conclusions of the paper)? "The insulin receptor can effect conformational, auto- phosphorylation and signal transduction functions when it is in tetrameric holo-enzyme form. For this, the disulfide bond formation is an essential pre-requisite. Under physiological conditions of carbohydrate metabolism as a source of energy, disulfide bond formation occurs normally. But when energy metabolism switches to β-oxidation of fats, disruption of disulfide bond formation of the insulin receptor occurs, leading to insulin resistance in DM2." Typos ~~heteromear~~ For insulin signal transduction to occur downstream, the insulin <u>receptor</u> Hyperglycemia, in presence <u>the of</u> high levels... It's two dimensional β,β- complexes than the receptor <u>without. insulin (9)</u>Though The proposed:- Hypothesis is resumed and the insulin sensitivity is restored.. <u>etc</u> <u>Abstract - Theories or hypotheses?</u> References style and typos must be revised More updated citations.	1) It is the author's opinion reflecting the general consensus on the issue. The sentence is restructured, as follows, as the same appears not to have been taken kindly. 'Defect in Insulin signalling pathway is considered as a possible cause". 2) The introduction, the hypothesis and the conclusion parts of the paper belong to the author's statements which have sound backing of facts of the literature. A brief review of the relevant literature part is from the literature. Hope now the reviewer has clarity of what is what. 3 Citations sought by the reviewer. a) A review on the insulin receptor, its structure, function and signalling is added as a reference under the sub heading "insulin receptor" b) A reference to carbohydrate vs fat metabolism, especially, their interplay in DM2 is known ever since the Randles hypothesis was published in the Lancet, way back in 1963. Hence no reference to the metabolisms is considered necessary. However, a reference to the role of L.C.F.A in causing insulin resistance has included in the paper. c) It is a basic fact that since cells can not utilize glucose in DM2, the cells turn to beta oxidation of fats for their energy needs. So reference sought on energy metabolic changes is considered not necessary.. d) Reference to disulfide bond is added. e) Reference to PDI sub -heading is also added. 4) Typos pointed out are corrected as suggested 5) The correction as hypothesis in the abstract is effected 6) What conclusion can be expected to a hypothesis? Still on the insistence of a reviewer and the editor, the same was added towards the end of the paper. The author does not consider it necessary to make any changes. 7) Suggestions on references noted. 8) The author thanks the reviewer for his untiring efforts in improving the paper.