

Review of: "[Perspective] Exploring the Synergistic Approach of Dual GLP-1 Agonist with Degludec Basal Insulin for Type 1 Diabetes Treatment for Albumin-InsulinProducing Cells Expression"

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Potential competing interests: No potential competing interests to declare.

This manuscript addressed the recently published paper in *NEJM* by Dr. Paresh Dandona (Semaglutide in Early Type 1 Diabetes, *N Engl J Med* 2023; 389:958-959) and raised their interpretation, commentary, and perspective for the roles of GLP-1RA in type 1 diabetes. They emphasized the importance of beta cell protection/regeneration, the reprogramming of liver cells into insulin-producing cells and extending GLP-1RA half-life by albumin-modification. The authors also planned a further clinical trial to explore the full potential of this synergistic approach in type 1 diabetes treatment. There are several concerns as seen below.

1. The *NEJM* paper is not synergistic purpose, but gradually replace insulin by Semaglutide. In my opinion, it's crucial for the large clinical trials to confirm the results and discriminate the patients who can eliminate their insulin demand or not.
2. The manuscript proposed many interpretations which de-focus the main theory. It would be better to focus on why type 1 diabetes is difficult to be cured and how GLP-1R agonists can overcome these difficulties?
3. The reprogramming of liver cells to insulin-releasing cells is interesting, however, the expression and corresponding role of GLP-1R in this process is controversial in reported studies.
4. In the second paragraph of perspective part, the sections of reprogramming of liver cells and the derivative modification of Rhein-C12-GLP-1 are not closely related.