Reviewer’s report

Title: Insulin translates unfavourable lifestyle into obesity

Version: 0 Date: 04 Oct 2018

Reviewer: Christian Benedict

Reviewer's report:

1. Please briefly discuss the side effects of diazoxide and octreotide. Are some of the weight maintenance effects of these drugs related to their side effects?

2. I wonder whether the authors could add a paragraph about the brain as therapeutic target in the treatment of systemic hyperinsulinemia and body weight. For instance, some hope has been tied to the use of intranasal insulin in the treatment of systemic hyperinsulinemia and obesity.

3. Are there genetic interventions available to manipulate the gene expression of insulin in humans?

4. Insulin sensitivity and glucose tolerance are often worse in the evening than in the morning in healthy people (eg., 22751690), hinting that snacking late into the night may be worse for people than eating earlier in the day, and therewith predispose people to weight (re)gain. Please discuss these findings in your ms.

5. It might be worth mentioning that insulin fulfils many important physiological functions.

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