Review of: "[Commentary] Insulin Sensitizers as Anti-Aging Agents: Exploring the Role of Albumin and its Implications for Healthy Aging"

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Potential competing interests: No potential competing interests to declare.

Dear all,

I read with interest the commentary entitled “Insulin Sensitizers like Metformin and GLP1 with Degludec as Anti-Aging”.

This commentary aims to shed light on the complex physiological role of human albumin. What emerged was that albumin expression is upregulated by insulin which represses the activity of the transcription factor Foxo1. In turn, human albumin interacts with insulin, preventing its aggregation, suggesting that albumin could help regulate the stability and activity of insulin. Interestingly, it has been reported that T2DM can lead to decreased serum albumin levels and that insulin is clinically necessary to prevent hypoalbuminemia.

Besides, it has been reported that unmodified albumin acts as an anti-aging protein, even if its mechanism of action remain to be clarified.

Finally, human albumin binds metformin, semaglutide and deglutec influencing both their pharmacokinetics and pharmacodynamics.

Overall these data are very interesting, but I believe that the commentary should be further implemented to better clarify the possible physiological role of albumin.

For instance, it is possible to hypothesize that albumin modifications (i.e. oxidation, glycation) could impair its ability to bind fatty acids or insulin, thus disregulating free fatty acid metabolism, insulin stability or its physiological lifetime?

What we know about the interaction mode of insulin sensitizers with albumin? These molecules can compete for the binding of fatty acid or insulin? Could these molecules act as competitors for the binding of fatty acids or insulin to albumin, compromising their physiological function over time?

Regards