

# Review of: "Why We Stop Synthesizing Essential Amino Acids: The Extracellular Protein Hypothesis"

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**Potential competing interests:** No potential competing interests to declare.

The manuscript by Esumi presents an interesting hypothesis on how the essentiality of amino acids developed over the lineages. The Extracellular Protein Hypothesis (EPH) seems to be one explanation. In fact, humans seem to balance the deficiency of essential amino acids in different cellular compartments, extracellular and intracellular, revealing a different composition of amino acids. It is plausible that during evolution, mammalian cells gained the capacity to ingest food and lost the ability to produce essential amino acids.

In my opinion, the most critical point of the manuscript is the lack of experimental data. However, if this paper is intended to be a review, the presented data from the literature might be enough. Moreover, I consider the Abstract a bit confusing. I would directly explain the main two hypotheses. In addition, the paper has many repetitions. I would strengthen it in some passages.

However, I strongly encourage Esumi, in view of all constructive criticism, to finalize the paper for peer review.

Best regards, Annette Kaiser