There is **a formal** aspect not satisfied by this review: according to the indications of IJMS (similarly to most journals) novel data cannot be included in a review . This article (classified as Review) is a hybrid as the Authors describe two novel PHP 1a cases clinically and genetically characterized in their institutions both harboring the most common mutation detected so far in PHP 1a patients. Section 3 -Results (as in a research article) includes the detailed description of Patient 1 (3.2.1) and Patient 2 (3.2.2). Then the Authors extend to December 15 2023 the review of the literature on genotype- phenotype correlations in Pseudohypoparathyroidism type 1a (PHP 1a) patients made by Yang till May 31 2021 (ref 8), but instead of considering all the causative pathogenic variants focus on the patients with the most frequent mutation detected so far (GNAS exon 7 c.565_568delGACT). This choice makes the clinical signs associated with this mutation more incisive raising the challenge of personalized follow-up and management of the carrier patients.

The Authors should restructure their manuscript as a research article which describes their new cases with review of the literature .

As regards the content I have the following criticisms:

Replace “mental retardation” with “intellectual disability” throughout the text and in the Figures

The c.565_568delGACT here at focus is named c.2494 2497del-GACT when the Authors describe the results of WES in their patients 1 and 2. Of course a geneticist knows that it is the same mutation with a different mRNA transcript reference, though a clinical geneticist reader may not understand. Please homogenize or give the appropriate coordinates (NM 000516.4 and NM 080425.2), respectively.

It would be interesting to analyze the sequence of GNAS exon 7 for evolutionary conservation, GC content. SINE and LINE elements, tandem repeats, which might concur to the instability and proneness of exon 7 to this most common alteration .

Minor criticism

Page 2 : According to this more recent classification…….as iPPSD2 that includes the previously called PHP type 1a and 1a (1b?)