Reviewer 1

Comment 1: The writers say “Therefore, prenatal genetic counseling and testing are necessary to preventing the hereditary transmission of this skin disease” Are they referring to preimplantation genetic diagnosis or testing of the embryo for abortion if they are affected? Is this course of action advised for skin disorders?

Reply: Thank you for your question. The main clinical manifestations of HED is the triad of abnormal hair development, palmoplantar keratosis, and nail dysplasia. Sensorineural deafness, cataracts, oral mucosal leukoplakia, mental retardation, impaired immune system, skeletal malformations, and pestle finger have also been reported in HED patients. If a patient is found to be conceiving an embryo with a disease-causing gene through prenatal genetic testing, they may have the right to decide whether they want the child or not. The symptoms reported in the family did not seriously affect the health of the patients, but this does not exclude that symptoms are serious in other families. Thus, prenatal genetic counseling and testing is necessary. Also, we revised the presentation of the paper to make it more logical.

Comment 2: Please refer to variants at both nucleotide level and gene level. Add NM accession number for the cDNA. Please show alignments and conservation of amino acid affected by the variant by comparing one species from each vertebrate class.

Reply: Thank you for your comment. We have revised the manuscript accordingly.

Comment 3: Minor comments Please change word “mutation” to variant. Please use three letter codes for amino acids, Glu instead of E and so on. Instead of writing “family diagram is shown in figure 1A”, describe your work and give the citation to figure in paranthesis (Figure 1A). On page 5, please correct CB6 to GJB6.

Reply: Thank you for your suggestions. We have revised the manuscript accordingly.

Reviewer 2

Comment 1: There is an article “Hidrotic ectodermal dysplasia: study of a large Chinese pedigree” By K Rajagopalan, C H Tay in 1977. Do confirm if it is the same family and extension. Further, for a Chinese pedigree, this article may deserve a mention if it is different.

Reply: Thank you for your comment. We have carefully read the mentioned article and confirmed that it is not the same pedigree. The Chinese pedigree we reported on originated from Ganzhou, Jiangxi, China, while the Chinese pedigree reported in the article referred to by you immigrated from Hunan, China to Malaysia. There are similarities and differences between the pedigree we reported on and the pedigree in

the other article. Rajagopalan and Tay (1977) discovered that scalp alopeica was more extensive in female members, while keratoderma of the palms and soles was more notable in male members. However, we did not find these patterns for the pedigree we reported on.

Comment 2: The family tree can mention which was affected member and what dysplastic component was present in them.

Reply: Thank you for your advice. According to your suggestions, we have added a table to the manuscript detailing the clinical manifestations and severity for each patient.