MOLECULAR AND NEUROLOGICAL CHARACTERIZATION OF THREE SAUDI FAMILIES WITH LIPOID PROTEINOSIS.

This report describes the clinicopathological features of three Saudi families with lipoid proteinosis and identifies two novel mutations in family 1 and 2 and a previously described 1163 bp deletion in family 3.

Major Compulsory Revisions

Genetic results: Family 1;The stop codon created by the two base deletion (AA) occurs not in the next codon, but in the second codon downstream (….GCATAA…).

Family 2; Exon 7 is also present in ECM1c, a transcript which has an extra exon 5a within intron 5 and known to be expressed in the basal layer of the epidermis of human skin (Mongiat M., et al., J Biol Chem. 2003, 278:17491-17499).

Discussion: Particular attention should be paid to the correct referencing of publications:

1) The human ECM1 gene was identified independently by two research groups: ref. 11 and Johnson MR et al., Matrix Biol. 1997, 16: 289-292.


3) ECM1 is known to interact with several proteins in the extracellular matrix of the human skin: perlecan, collagen IV, lam 332, fibulin1C/D, fibulin-3,PLSCR1 and MMP-9. Either they are referenced individually or one refers to a review article (cfr. Sercu S., et al., The importance of the extracellular matrix protein1 (ECM1) as basement membrane protein in maintaining skin function. Textbook of Aging Skin (eds. MA.Farage; K.W.Miller, H.I.Maibach) p.77-91, Springer-Verlag Berlin,Heidelberg 2010.

4) Identification of the ECM1 c transcript by the research group of Dr. R.Iozzo should be referred to (see above).


Minor Essential Revisions

Clinical description: It is always important information for future readers to have a
detailed dermatologic description. Therefore, could you for example specify the localization of the pigmentation, which joints are affected etc.….

Table-1: change II-5 in II-6 ? (Sub ID).

Fig 1: missing labels a, b and c.
Fig 1: Family-3 ; II-1 is F (circle) and II-3 is M (square).
Fig.3: (d) : arrow is missing in the photograph.

Discretionary Revisions
Genetic Results: Family 2; add to the text that the ECM1 chromatograms of patients I-1 and II-4 are not shown, or otherwise add the chromatograms to figure 1.

Family 3; change sentence into: ……from the transcripts ECM1a/c and ECM1b …… and …. related by a founder effect…….

Minor issues not for publication
Background:….. neurologic and neuroradiologic characteristics (features)…..

Results: …. two novel mutations in family 1 ……

Conclusions: …… less common than….

Methods: …. delete point in Declaration of Helsinki

Conclusion: … less common than ….

Figure legends: fig. 1: …… intron 8

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.