Internal Examiners Corrections

Title

The title has been changed to more accurately describe the study.

Acknowledgements

Melissa has been changed to Nerissa

Abbreviations

The G2 allele description has been changed to note that it is a deletion, in keeping with the rest of the text.

Introduction

P4 Figure 1.1 – Now Fig 2.1 P5. A detailed description, modified slightly from the original text, has been added. The figure has been enlarged, as suggested.

The figure and table legends have been expanded, to allow for a more thorough description of the data within.

P4. Last sentence, now P6. Las sentence before section 2.3. The sentence has been changed from "This suggests that while there is genetic heterogeneity between different ethnic groups for certain loci, while other loci are risk factors for SLE regardless of ethnicity" to "This suggests that while there is genetic heterogeneity between different ethnic groups with respect to certain loci, other loci are risk factors for SLE regardless of ethnicity.", as suggested.

P5. 2nd sentence, now P7 1st line.: SLE is more common in… The suggestion was to reference the statement. The reference at the end of the sentence, following the sentence in question, is the reference. The reference covers both sentences, and it would be redundant to have the same reference for both sentences. Hence, the reference will be left at the end of the second sentence only.

P5 Section 1.5, now P7. 2nd line in section 2.5. The reference "Africa, 2014" should read "Statistics South Africa, 2014". It has been corrected.

P6. Table 1.1, now P7. End of section2.4. Is laborious to look through. The table has been moved to an appendix.

P9. (Including Fig 1.3). The link between SLE and *APOL1* was questioned, and noted to be vague in the introduction. The possible link between SLE, Lupus Nephritis and APOL1 has been expanded in section 2.6.4.

P10. Fig 1.5, now p12 fig 2.5. The insertion allele has been clarified as the wild type allele throughout the manuscript.

P11. 2nd last sentence, now P13, section 2.6.4 2nd last sentence: The population studied by Lin et al. was made clear. The sample size of Kasembeli is small, but this is used here to highlight the dearth of

data on APOL1 in the black population with lupus, and hence helps justify this study. Both reference dates are noted at the end of the sentence.

Subjects and Methods

P15. Fig 2.2, now figure 3.2 P17. The PCR conditions have been kept as a figure, and not changed to a table format, as changing this does not increase the readability of the manuscript.

More information for the restriction endonucleases has been added on P17 1st and 2nd paragraphs respectively.

P 17., now P19 Fig 3.4. The PCR conditions have been kept as a figure, and not changed to a table format, as changing this does not increase the readability of the manuscript.

Section 2.6, now section 3.6 P19&20. A new table has been inserted to assist with the understanding of the genotyping of APOL1, and the functional significance has been explained, with a reference. (Fig 3.2).

Results

P18., now P22.The table size has been decreased, to make it fit into one page. However, the legend could not fit, and had to be carried over to the following page.

P21. Figure 3.1, now P23. Fig 4.1 has been retained, as it adds background to the study, while figure 3.2/4.2 has been removed.

P22. Now P24. The ladder and amplicon sizes have been added. The figure legend has been bolstered.

P24. Now table 4.2 P27. This table highlights the effect of the novel alleles on the data, and hence is important to the understanding of the limitations of this study. An explanation of table 4.2 has been added before the table to highlight the impact on the data the novel deletions have.

P25. Table 3.3, now table 4.3 P27 highlights a fundamental issue… The legend has been expanded to clarify the issues raised here, and to help with the analysis of the table.

The point the examiner makes regarding SLE and LN does make sense. However, by definition Lupus nephritis (LN) cannot occur outside of the setting of the SLE. If a renal biopsy is shown to be due to LN, then the patient has SLE, even if there are no other clinical or serological signs of SLE. (It should be noted that the only caveat to this is that the ANA must be positive, if not then the diagnosis must be questioned). Inasmuch, the two phenotypes are linked, and mentioning LN implies that SLE is present. Therefore, the change suggested has not been implemented.

P28., now on P.28-30. The significant values have been highlighted with grey, to assist in reading of the data tables.

Discussion

P31. Table 4.1 now P32 table 5.1 – The typo has been corrected to 165.

References

The references have been reformatted as suggested by the examiner.

Appendices

A copy of the patient information sheet and patient consent sheet has been added to the appendices.

External Examiners Corrections

Misleading title: It was essentially a study looking at the frequency of APOL variants in LN.

The title has been changed to more accurately describe the study performed.

Lack of a summary/abstract.

An abstract has been added. (Page 1)

If that was the theme, the literature could have been more focussed.

The title was misleading, and has been changed to more accurately describe the study. As such, the title and theme now link and the literature review now makes more sense.

It is not stated how these patients were recruited, over what period of time and why these patients were chosen.

The methodology was altered to outline clearly why and how the patients were recruited, over what time frame and what the inclusion and exclusion criteria were. (Page 15)

Were the controls matched for race, age gender?

As the controls were taken from the literature, they were not matched for age or gender. They were matched for race. This is highlighted in table 4.1 and subsequent legend on Page 22.

Results are presented in tables and figures with little interpretation.

Interpretation of the figures and tables in the body of the results has been expanded throughout the manuscript.

Table 1.1 is confusing. While we are informed about the Control group in the text, the table fails to explain what the other 3 groups are. While LN is clearly identifiable, it takes a while to figure out that the all 3 are derived from the SLE group. By definition also, eGFR < than 60 and LN are forms of CKD. Surely all patients with CKD, eGFR less than 60 and LN have renal disease. Yet the table seems to indicate that only 72.9% of patients CKD have renal disease.

Table 1.1 does not exist. But this point is valid for tables 4.1 (Page 22), and 8.1. (Page 55) It is a serious oversight, and has been rectified.

In the Discussion the author states “The study ….to describe the clinical presentation of SLE in African patients…” It was never designed to do that!

This study was not designed to describe the clinical presentation of SLE. This was a poor choice of wording. However, the recording of patient demographics, SLICC score, and serology allows for a description of this studies patient characteristics compared to international data. As such, the sentence has been changed to read “This study provides data that describes some of the clinical characteristics of SLE patients of African origin.” (Page 31)