Reviewer's report

Title: Homozygosity and Risk of Childhood Death due to Invasive Bacterial Disease

Version: 2 Date: 27 March 2009

Reviewer: Jakob Mueller

Reviewer's report:

Major comments

The manuscript describes convincingly an association between locus-specific homozygosity and risk to childhood death due to invasive bacterial disease. Sample size and data analysis is sound and the text is concise. This study on humans complements the studies on heterozygosity-fitness correlations in many animal species. It further contributes to the current debate about the mechanisms of genetic fitness correlations by contrasting inbreeding effects against locus-specific effects. It would be interesting to name and discuss the associated region in more detail.

Minor essential revisions:

1) The standardised observed homozygosity as used in this study seems to be directly complementary to standardised heterozygosity as described by Coltman et al. 1999. It is therefore not a new measure. Moreover, if standardisation was based on the total sample, then there is a typo in the methods section.

2) Basic characteristics of the used microsatellites should be given, e.g. heterozygosity range. In addition: Were they in Hardy-Weinberg equilibrium? Had the associated microsatellites an exceptional number of alleles?

3) It would increase the intelligibility if some concrete population attributable risk values are discussed in the text.

4) For the discussion it would be interesting to have some estimates about consanguineous marriages in the Kenyan population.

5) In general, references are missing in the discussion section.

6) The reference section needs some revision.

7) The adjustment for geographical location is not explained in the methods section.

8) Table 1 is redundant to table 2.

9) Are the whiskers in fig.1 SEs? One could also think to plot the distributions of SOHs in cases and controls and test for skewness.
10) The legend of fig. 2 needs some revision.

**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.