Reviewer's report

Title: The mitochondrial DNA T16189C polymorphism and HIV-associated cardiomyopathy

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Reviewer: Paul Brink

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Hypothesis being examined: Association of a mitochondrial polymorphism, T16189C, with persons with HIV and dilated cardiomyopathy (DCM) compared to a control group with HV but without DCM.

In assessing article two issues comes to the fore for me:
(1) The a priori reason for doing the study (support for the hypothesis)
(2) the study design and reasons for selecting the specific study design

There is also some other minor issues one being very important, namely, a major mismatch between articles referred to and actual listed references.

On the first count (mismatch between articles referred to and actual listed references): I count +/- 14 references in the text, but 34 in the reference list. Thus 20 references are not referred to in text at all and one is not sure what they are doing in the list. Furthermore, the references are poorly formatted (some no journal name, some no year, sometimes same author is first author on more than one reference but one cannot figure out in text which article is referred to etc.)

(1) A priori reason for doing the study / support for the hypothesis

The study is done in an Africa population where DCM has been historically reported to be high. HIV prevalence is, I recall, also very high. So, are we really dealing with a separate entity of DCM developing in persons with HIV or could it be just co-incidental? This point needs to be addressed. Furthermore, the study quoted in support of the existence of HIV-associated cardiomyopathy as an entity profiles an HIV-affected person with certain characteristics (nutritional status, economic status, etc.). So, we can we make across board assumptions? I see that CD4 and viral counts appear in table 1. This could help somewhat in profiling (surrogate), but needs to be discussed. We do not know to which extent in the current study experimental & control group reflect a similarly select group as in reference Twagirumukiza 2007.

Support for DCM being genetic is reports of clustering within families from studies northern hemisphere.

(Xxxx Scrap How does HIV & CMO. Does HIV add (more risk/ less risk) xxx.)

The study design and reasons for selecting the specific study design
Reports of family clustering of DCM suggesting “genetics” at play is used as motivation for the study. Of course, these are studies from the northern hemisphere. I am not aware of similar studies in Africa. Finding families segregating DCM has indeed been responsible for finding genes playing a causal role in DCM, albeit rare. However, this opened up new avenues for exploring mechanisms of DCM. Is there any special reason for not exploring this powerful option, for example, affected sib pair studies? As alluded to above, both HIV+ individuals as well as DCM being prevalent one should be able to address the question familial clustering of both conditions.

Groups being compared: “controls were drawn from people of black African ancestry” This sound right for America, but for Africa? Set apart from whom? Furthermore, is the underlying assumption that Africa (whole? Sub-Sahara?) form a genetically homogeneous population? Has Africa not had its bottlenecks, its population migrations, etc, all of which would affect allele frequencies in certain geographical areas. Also, I believe that S.A now have a huge immigrant population from all over Africa. How would this have affected the study?

Other issues:

Problem with references already mentioned

Statement: pg 8, line 2: “It is remarkable that the original study of Khogali et al has not been replicated by other researchers”

Why is it so “remarkable”? Was the challenge of confirming or refuting finding not taken up? Was similar studies done with a different outcome. The reader does not know.

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