Reviewer's report

Title: Abnormal glucose tolerance and insulin resistance in polycystic ovary syndrome amongst the Taiwanese population- not correlated with insulin receptor substrate-1 Gly972Arg/Ala513Pro polymorphism

Version: 1 Date: 11 January 2006

Reviewer: Robert P Kauffman

Reviewer's report:

General

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. Paper should be shortened. In the background section, the entire second paragraph should either be deleted or shortened into one or two summary sentences. The same recommendation applies to the next paragraph beginning, "Therefore, polymorphisms... This is not a review article on IRS-1 polymorphisms. You subject matter is well focused and the background should reflect this. Also, I suggest that the entire first paragraph in the "PCR and Restriction fragmented length..." section be deleted. If the reader is interested, he/she can check the Hitman reference.

2. A sentence or two in the introduction explaining the genetic background of Hoklo and Hakka populations would be helpful to the non-Taiwanese readers. (Move this from the discussion.)

3. In the Methods section, you do not use the 1990 NIH or 2003 ASRM/ESHRE Rotterdam definition for PCOS. Since the LH/FSH ratio has been discounted as a diagnostic criteria for PCOS (because of the pulsatile secretion of gonadotropins), you will need to justify its inclusion as a diagnostic criterion. Why use a ratio of <2 rather than <3?

4. Specifically define what the "specific criteria for PCOS on ultrasound" actually was. Did you use the Rotterdam conference suggestion?

5. How did you select you (total) testosterone and SHBG discriminatory values? Are these cutoff values derived from a Taiwanese population?

6. How many subjects did you screen to come up with your study population? Can I assume that you ruled out other causes of hyperandrogenism (i.e., 21-hydroxylase deficiency) before enrolling patients into either study group?

7. Are the plus/minus values standard deviations or standard errors?

8. I would move the ranges following the mean and SD/SE values to a table. I think the mean and SD or SE surface in the text.

9. The mean BMIs and ages belong in the RESULTS.

10. I assume you measured "total" testosterone. Please state this fact the first time that you mention that "testosterone" was measured. Also, please note that the laboratory values are serum levels.

11. Were all serum values drawn from the fasting state? Obviously, insulin levels were drawn fasting, but please distinguish if prolactin was drawn fasting. Were all labs drawn in the early follicular phase?

12. Please note the glucose load for the OGTT (? 75g).

13. After looking at Table I, it is obvious that you used more than chi-square in your statistical analysis. Table I looks like either the Student's t-test for independent samples or the Mann-Whitney test was used. Chi-square is for categorical variables. Were the continuous variables studied by a
14. In the RESULTS, I recommend that you compare each insulin sensitivity index using ANCOVA (assuming your data follow a normal distribution) with BMI as the independent variable and PCOS/non-PCOS as the covariables. Insulin sensitivity is directly affected by BMI, and hence, the dependent variables (insulin sensitivity indices) should be adjusted for BMI. Show results as figures in your paper. (Note: I am not a professional statistician, so you might want to review your data with a "real" statistician.)

15. I feel that the percentage of subjects above and below the discretionary values is extraneous information, and I would delete it. What I believe you want to relate the reader is the comparison between the two study groups. If you want to show the linear distribution of the results, this can be done by a linear regression graph (if ANCOVA figures are used, that will accomplish the same thing.)

16. The incidence of AGT seems high in your patient population. Please address this issue in your DISCUSSION section.

17. On page 11, delete the sentence "We first analyzed....above." It is repetitive. The same suggestion in the next paragraph for "We further investigated...section."

18. Because of your relatively small study population, do you think that any of your results could be explained by a beta-error? Please comment on this. Also, could your small population explain that absence of finding an IRS-1 mutation?

19. In the CONCLUSION, delete part of the first sentence (from "Comparing...to 513[32]). It is unnecessarily repetitive.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. "The level of insulin resistance" is better characterized as "insulin sensitivity indices"

2. Put the formulae for the glucose/insulin ratio and HOMA-IR as footnotes in Table I.

3. In Table I, if the P value is <0.05, please state the precise number (i.e., <0.01, 0.0055, etc.)

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Discretionary Revisions (which the author can choose to ignore)

1. Who manufactured your assays kits?

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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

Quality of written English: Needs some language corrections before being published

Statistical review: Yes

Declaration of competing interests:

I declare that I have no competing interests.