Reviewer's report

Title: Agrarian diet and diseases of affluence - Do evolutionary novel dietary lectins cause leptin resistance?

Version: 4 Date: 24 October 2005

Reviewer: Rob M. van Dam

Reviewer's report:

General

The authors have addressed the raised issues and the manuscript has improved substantially.

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

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

- In the section 'Global epidemiologic pattern' it is suggested that the variation in coronary heart disease is puzzling, but this only seems to be true for some of the geographic variation. Although some variation in CHD rates may be puzzling, for example differences in dietary intakes of fatty acids are likely to contribute to differences between Poland and Spain and lifestyle factors have been identified that could explain variation in CHD over time in the US (Hu FB, et al. N Engl J Med. 2000 Aug 24;343(8):530-7).

- The section 'Molecular Evolution of Leptin' mostly refers to the leptin gene. Because the hypothesis concerns the possible effects of lectins on the leptin receptor, perhaps it would be more appropriate to refer to the leptin receptor gene.

- In the section 'Implications of the hypothesis' the final part starting with the sentence 'If dietary lectins could inhibit leptin binding, then leptin..' seems to include information on 'testing the hypothesis'.

- The sentence 'If dietary lectins could inhibit leptin binding, then leptin binding affinity should be lower in leptin resistant humans on an agrarian diet.' should specify to which group the leptin resistant humans on an agrarian diet are compared, i.e. lower than whom? Lower than leptin resistant humans on a non-agrarian diet? The following sentence on the association with obesity and fasting does not directly seem to provide evidence for an effect of an agrarian diet.

Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions

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

**Quality of written English:** Acceptable

**Statistical review:** No

**Declaration of competing interests:**

I declare that I have no competing interests.