**Reviewer's report**

**Title:** HMG-CoA reductase inhibition aborts functional differentiation and triggers apoptosis in cultured primary human monocytes: a potential mechanism of statin-mediated vasculoprotection

**Authors:**

Dr Joannis E Vamvakopoulos (joannis.vamvakopoulos@helsinki.fi)
Colin Green (s.jenks@ic.ac.uk)

**Version:** 1  Date: 27 May 2003

**Reviewer:** Jörg Kreuzer

**Level of interest:** A paper whose findings are important to those with closely related research interests

**Advice on publication:** Other (see below)

This small study investigates the effect of HMG CoA reductase inhibition on differentiation and apoptosis of human monocytes. This is not an entirely new aspect of statin research, however deserves additional attention, as the data so far are not entirely conclusive.

In the present report it is described that only in monocytes but not in lymphocytes, mevastatin lead to apoptosis. Furthermore the authors report inhibition of differentiation of monocytes as indicated by IL-1b release. The findings are sound, the experiments are conducted very thoroughly and the data are presented accordingly. The manuscript is well written and the conclusion is interesting.

**Major points:**

I am little bit concerned about the way differentiation is assessed. Rather than exclusively relying on IL-1 release the authors should also use differentiation specific surface antigens of monocytes to assess the cell phenotype.

Also I am nor quite clear about the data presented in the last paragraph of the result section and the corresponding part of the discussion in the last paragraph of the discussion section. As far as I can see the authors have no data for either of their explanations for the lack of mevalonate to completely inhibit the effect of mevastatin.

What happens when differentiated monocytes, i.e. macrophages, are treated in the same experimental setting as monocytes? Do they also show apoptosis? These additional experiments would strengthen the author's hypothesis considerably.

**Minor point:** Cerivastatin is not a hydrophilic statin

**Competing interests:**

None declared.