Reviewer’s report

Title: Endogenous melatonin and oxidatively damaged guanine in DNA

Version: 5 Date: 3 September 2009

Reviewer: Ryszard Olinski

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Below is my review of the revised manuscript (Z. Davanipour et al. “Endogenous melatonin and oxidatively damaged guanine in DNA”). I also confirm that I have assessed all the reviewer’s reports

Using reliably HPLC/MS/MS methodology for urinary 8-oxodG and 8-oxoGua determination the authors have found that increased levels of 8-oxodG may have a link with lower melatonin production.

There are no firm evidences concerning a link between melatonin production and the DNA damage. Therefore, a new finding described in the manuscript is potentially desirable. However, several shortcomings make the proposed manuscript hard to accept in the present form:

i/ To describe oxidative damage to DNA authors analysed solely urinary excretion rate of 8-oxodG and 8-oxoGua. However to tell something about cancer risk the excretion rate (which presumably represents repair processes) should be combined with measurements of the modification in cellular DNA (in surrogate tissue like lymphocytes) to study the question of rates of repair versus rates of damage. As a matter of fact only comparison of these two parameters can tell something about a meaning of the DNA damage in certain condition. For example an agent which increases the adducts level in urine might be regarded as harmful because it increases DNA damage but might in fact be profitable if it stimulated DNA repair and therefore decreases background cellular level of oxidative damage to DNA. Therefore, the final conclusion that “low levels of endogenous melatonin production (…) may lead to higher levels of oxidatively damaged guanine in DNA, thereby increasing the risk of developing cancer” (p.3) is largely over interpretation of the presented results.

ii/ It is inappropriate to use nmol of 8-oxodG and 8-oxoGua/litre to express the levels (see also rev #3). Authors should used nmol/mmol of creatinine instead (anyway they determined creatinine values – see Laboratory assays, p.7). Only in this case it will be possible to compare and discuss the authors result in the context of prior literature, as requested in rev #1.

iii/ is there some relationship between family members concerning 8-oxodG and 8-oxoGua?

There is nothing in Discussion chapter which explain why the authors choose family pairs (see also rev #1)

iv/ there is no evidences concerning involvement of NER in 8-oxodG presence in
urine. Therefore, the statement “these data indicate that (...) older women may tend to repair such damage via the NER pathway” is rather irrelevant.(see also rev #3 and 4)