Reviewer’s report

Title: Similar effects of active and passive maternal tobacco smoke exposure on in utero mutagenesis

Version: 1 Date: 6 April 2005

Reviewer: Kirsti Husgafvel-Pursiainen

Reviewer’s report:

General

This is a clearly written paper on a topic that is both timely and interesting. It is truly important to provide further understanding of the mechanisms by which tobacco smoke, both active smoking and involuntary exposure, is associated with adverse effects in utero. In this context, genotoxicity, including somatic as well as germline effects, is of special interest as it is likely to play a role in teratogenesis, and other causes of adverse pregnancy outcome; exposure to mutagens/genotoxicants in utero may also be related to cancer in childhood or even later in life. Published data on HPRT mutations in newborns (cord blood) to mothers exposed actively or involuntarily to tobacco smoke are indeed sparse and partially inconsistent. In fact, this also appears to be the case to some extent for HPRT mutation data from adults smokers or involuntary smokers.

The author has managed to compile meta-analysis and a concise summary of published data, added with some own data (partially under further study). He in an in-depth way brings up and analyzes the two sides of the existing data, i.e. the HPRT mutation frequency and the types of mutations, in particular the exon 2/3 deletions characteristic to illegitimate VDJ recombination. The tables included help the reader to follow the patterns and the trends seen in the data. In my view, the conclusion the paper reaches, i.e. elevated occurrence of HPRT mutations/exon 2/3 deletions in association to all three categories of tobacco smoke exposure (smokers, quitters, and involuntary smokers) is sound and represent an interesting finding. Such information, hopefully added with new data from independent further studies, is very important and will give support, for instance, for preventive measures and legislative actions to be taken/currently under consideration for protecting pregnant women from tobacco smoke exposure from the earliest possible stage of the pregnancy.

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

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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)

- In the introduction, the author may wish to include some references to more recent reviews on genotoxicity and adverse health effects of smoking and involuntary smoking in adults and in utero (e.g. IARC monograph vol 83, 2004).

- Since the review and pooled analysis is focused on results from 3-4 currently available studies on HPRT mutations in neonates/cord blood (altogether some 100-150 mutations), it would be good to bring up this fact more clearly in the discussion. As a whole, such data are still rather limited and may be prone to some bias due to as yet unidentified factors in e.g. mutation detection methods, study design or controlling confounding. In this context, it would be good to shortly mention other
exposures, occupational or environmental, that may be associated with elevated HPRT mutation frequency/exon 2/3 deletions.

Discretionary Revisions (which the author can choose to ignore)

**Which journal?:** Appropriate or potentially appropriate for BMC Medicine: an article of outstanding merit and interest in its field

**What next?:** Accept for publication in BMC Medicine after minor essential revisions

**Quality of written English:** Acceptable

**Statistical review:** No

**Declaration of competing interests:**

I declare that I have no competing interests.