Editorial:

APOPTOSIS IN TOXICOLOGICAL RESEARCH

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Toxicological research on apoptosis addresses the questions if and by which mechanisms certain chemicals induce apoptosis and to which degree this contributes to adverse effects. Recent studies have shown that benzene upregulates pro-apoptotic genes in the bone marrow, uranium induces apoptosis in lung epithelial cells and fluoride causes apoptosis in osteoblasts. The elucidation of these mechanisms is highly important, but unfortunately knowledge of their in vivo relevance remains scarce. For example it would be interesting to know if long term excessive fluoride causes skeletal disease because of apoptosis induction. Or does benzene induced apoptosis in bone marrow contribute to its carcinogenic effect by inducing replacement proliferation? Although much has been published addressing apoptosis in vitro it remains important to learn whether this translates in vivo or rather represents a specific situation that only occurs under specific in vitro conditions. The table summarizes the conclusions of recently published articles on apoptosis in toxicological research.

Table 1: Studies on apoptosis

<table>
<thead>
<tr>
<th>Key message</th>
<th>Reference</th>
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<td>Brevetoxins are known to induce neurotoxicity by interaction with sodium channels. However, they also induce apoptosis in Jurkat cells, as evidenced by caspase activation and PARP clearance.</td>
<td>Murrell and Gibson, 2009</td>
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<td>Arsenic induces apoptosis in a human hepatocyte cell line through the mitochondrial pathway dependent on the generation of reactive oxygen species.</td>
<td>Wang et al., 2009</td>
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<td>Propyl gallate, which is used in processed food and cosmetics induced apoptosis in Hela cells by depletion of intracellular glutathione levels and generation of oxidative stress.</td>
<td>Han et al., 2009</td>
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<td>Benzene transcriptionally upregulates caspase 4 and caspase 12 in mouse bone marrow cells. However, no apoptosis is induced in absence of functional P53.</td>
<td>Yi et al., 2009</td>
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<td>Lactational exposure to the phytoestrogen coumestrol caused apoptosis in the ovaries of rats.</td>
<td>Moon et al., 2009</td>
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<td>Uranium induces apoptosis in lung epithelial cells by activation of caspase 3 and 8.</td>
<td>Periyakaruppan et al., 2009</td>
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<td>Long term excessive fluoride intake may cause skeletal disease. This study shows that fluoride induces apoptosis in osteoblasts in vitro.</td>
<td>Yan et al., 2009</td>
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<td>Fluoride treatment of rat exocrine pancreas cells causes autophagy. This study describes the turning point, when cells switch from autophagy to apoptosis.</td>
<td>Ito et al., 2009</td>
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<td>Calmidazolium causes apoptosis by Ca** release from the endoplasmic reticulum in a protein kinase C dependent manner.</td>
<td>Liao et al., 2009</td>
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REFERENCES

Han YH, Moon HJ, You BR, Park WH. The anti-apoptotic effects of caspase inhibitors on propyl gallate-treated HeLa cells in relation to reactive oxygen species and glutathione levels. Arch Toxicol 2009;83:825-33.


