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Human relevance of follicular thyroid tumors in rodents caused by non-genotoxic substances

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1 Human relevance of follicular thyroid tumors in 2 rodents caused by non-genotoxic substances

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5

6 Abstract

7 Chronic stimulation of the thyroid gland of rodents by TSH leads to thyroid follicular
8 hyperplasia and subsequently to thyroid follicular adenomas and carcinomas.

9 However, the interpretations of rodent thyroid tumors are contradictory. The U.S. Food
10 and Drug Administration (FDA) concluded that findings with drugs that lead to
11 increased levels of thyroid-stimulating hormone (TSH) in rats are not relevant to
12 humans, whereas the U.S. Environmental Protection Agency (US EPA) concluded that
13 chemicals that produce rodent thyroid tumors may pose a carcinogenic hazard for
14 humans although the thyroid of rodents appears to be more sensitive to a
15 carcinogenic stimulus than that of humans. Meanwhile, based on the CLP Criteria of
16 the European Chemicals Agency (ECHA), rodent thyroid tumors caused by the
17 induction of uridine-diphosphate-glucuronosyl transferases (UDGT) were assessed as
18 not relevant to humans.

19 To clarify these discrepant positions, the function and regulation of the thyroid gland
20 are described and the types of thyroid tumors and the causes of their development in
21 humans and animals are examined. Based on these data and the evidence that so far,
22 except radiation, no chemical is known to increase the incidence of thyroid tumors in
23 humans, it is concluded that rodent thyroid tumors resulting from continuous
24 stimulation of the thyroid gland by increased TSH levels are not relevant to humans.

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