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**MUT/07/20**

**COMMITTEE ON MUTAGENICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT. (COM)**

**Aneuploidy: Action both oncogenically and as a tumour suppressor. (Weaver BAA et al, Cancer Cell, 11, 25-36, 2007)**

Introduction

1. Members will wish to comment on the appended paper which was noted by a member of ACP at a recent meeting. The COM were asked to comment on the paper.
2. The authors report that cells and animals that are heterozygous for CENtromere-associated Protein *E* (CENP-E <sup>+/-</sup>) become aneuploid due to random malsegregation of one or a few chromosomes at high rates in the absence of DNA damage. CENP-E is an essential, mitosis-specific, cell-cycle-regulated motor that accumulates primarily in late G2 and is used in mitosis and is degraded at the end of mitosis. It appears to maintain chromosome interactions with microtubules and also has dual functions in mitotic checkpoint signalling.
3. The authors report that reduced CENP-E in heterozygotes can promote spontaneous tumourigenesis in mice but can also lead to inhibition of spontaneous liver tumour formation in the same mice. In a small experiment a group of 25 homozygous CENP-E mice and 13 mice heterozygous for CENP-E were given a single dose on PND 3-5 of 7,12-DMBA. It was reported that 40% of homozygous mice developed lung tumours as opposed to 31% of heterozygous mice. The lung tumours in heterozygous mice were of a smaller size. This provides some limited evidence that aneuploidy may reduce the response to carcinogens.

Advice from COM

4. The default risk assessment approach has to date been that chemically induced *in vivo* aneugenicity is considered to be a hazardous property even if there are no particular biological effects reported in standard animal toxicology tests (such as impaired fertility or promotion of tumourigenesis). Would the new data reported in the appended paper alter this view?
5. Do members have any additional comments on this paper?

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