

SRG fms.



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SUBJECT: EDM/FL

Following the discussions at the recent SRG meeting concerning lymphocytes and benzo(a)pyrene (BaP) the following is a brief summary and comment upon some of the data available concerning genetic changes and metabolism in lymphocytes in response to BaP.

Adducts

1. Unstimulated (non-dividing) lymphocytes in culture do not show DNA adducts when incubated with BaP. However, when the lymphocytes are stimulated to divide, BaP adducts have been demonstrated. A combination culture of unstimulated lymphocytes plus monocytes with BaP gives the same spectrum of adducts in lymphocytes as the monocytes.
2. Isolated stimulated lymphocytes incubated with BaP gave adducts of one specific metabolite, benzo(a)pyrene diol epoxide I. there was an 8-fold variation in levels between donors.
3. Isolated unstimulated lymphocytes incubated with BaP resulted in DNA adducts there was an 18-fold difference in adduct levels reported depending upon the donor used.

Chromosome Alterations

4. Isolated lymphocyte culture, treated in G1 phase of the cell cycle, tested up to insoluble levels of BaP, micronuclei scored, negative response.
5. Isolated stimulated lymphocytes and BaP in 1 study showed an increased frequency of sister chromatid exchanges as the dose of BaP was increased, but no response in a second study (6).

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7. At low doses (1 to 20 $\mu\text{g ml}^{-1}$ BaP) clastogenic activity to stimulated lymphocytes in a whole blood culture has been demonstrated in both the presence and absence of an exogenous (S9) metabolic activating system.

Metabolism

8. The level of lymphocyte epoxide hydrolase, an enzyme post P450 in the activation of BaP to DNA binding forms, has been demonstrated to exhibit greater variation in unstimulated cells (2 to 7.2 units) than in stimulated dividing lymphocytes (4.4 to 7 units).
9. Red blood cells have the capacity to activate BaP to a species that will cause micronuclei formation.

CONCLUSIONS

Genetic alterations in lymphocytes in response to BaP is reported in some papers but not in others. The natural variation in metabolic potential of cells from different donors may account for this finding and emphasises the requirement to use adequate study populations in such studies. The metabolic activity of other cell types 'in contact' with lymphocytes may also contribute to the genetic alterations that can be measured in lymphocytes in response to BaP.

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