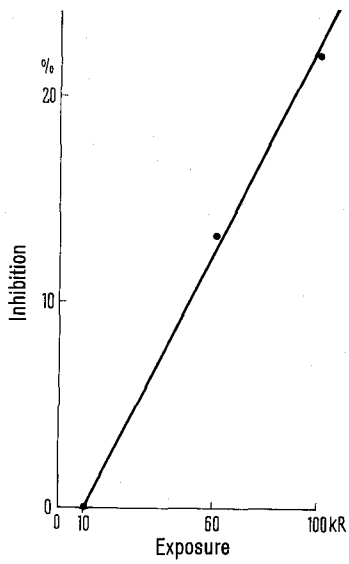
Radiosensitivity of ATP: L-Methionine S-Adenosyltransferase

Irradiation effects on nucleic acid metabolism has often been suggested to be the basis of cellular radiosensitivity. CREASY and STOCKEN[1] found 50 to 80% inhibition of the high energy phosphate synthesis in rat or cat nuclei following the administration of 25 R X-irradiation. HANCOCK and GOLDBERG[2] found that yeast cytidylate kinase to be 60% inactivated following exposure to 10 KR under their experimental conditions. GORDON[3] has shown that only a 10 R difference in X-irradiation of a mung seed homogenate resulted in 20% inhibition of the conversion of indolacetaldehyde to indolacetic acid. This appears to be the one extreme. On the other extreme, MITCHELL et al.[4] have found that 500 KR are required for a 20% inhibition of arginine decarboxylase activity of *E. coli* extracts, although these latter enzymes are not directly involved in nucleic acid metabolism. Enzyme radiosensitivity may differ vastly from a) organism to organism for the same enzyme; b) enzyme to enzyme in the same organism depending on the class of enzymatic reaction and c) experiment to experiment for any given energy depending on the experimental conditions utilized in preparation, irradiation and assay. Furthermore, extrapolations from in vitro results to the in vivo situation often result in inaccurate conclusions. Nevertheless, keeping these difficulties in mind, it seems that investigation of radiosensitivity of a spectrum of a general class of enzymes may lead to some understanding of pertinent radiological mechanisms.

The S-methyl function of L-methionine is activated by the enzyme ATP:L-methionine S-adenosyl transferase through the following reaction: adenosine triphosphate + L-methionine → S-adenosyl-L-methionine + pyrophosphate + monophosphate.



Inhibition of ammonium sulfate preparation by X-irradiation.

Mouse liver has been shown to possess S-adenosyltransferase activity[5] with biochemical properties similar to those described by CANTONI[6,7] for rabbit and pig. Since methylation is involved in RNA metabolism and requires S-adenosyl L-methionine, we found it of interest to study the radiosensitivity of S-adenosyltransferase. The S-adenosyltransferase preparation was made from female C57BL/10J mouse liver and assayed following the procedures of CANTONI[6,7]. The reaction mixture contained 100 μmoles ATP, 100 μmoles reduced glutathione, 100 μmoles *tris* buffer pH 7.6, 300 μmoles $MgCl_2$ and enzymes, e.g. 3 mg of a 30–50% ammonium sulfate protein fraction obtained from 10,000 × *g* supernatant of fresh homogenate of mouse liver. The enzyme preparations were maintained at 4 °C during all procedures prior to assay at 40 °C. Irradiation was done with a Maxitron GE 250, using 250 Kv, 30 ma and 0.25 mm alluminum filter. The dose rate was 1200 R/min at a target distance of 10 inches.

An exposure to total doses of 10, 60 and 100 KR did not depress the enzyme activity assayed as 10,000 × *g* supernatant derived from irradiated a) whole animals, b) whole liver or c) the 10,000 × *g* supernatant itself. However, the ammonium sulfate enzyme preparation was affected by 60 and 100 KR. The results in the Figure show that the ammonium sulfate preparation is inhibited by approximately 13 and 22% at 60 and 100 KR exposures, respectively. The dose response appears to be linear beyond 10 KR total doses, but shows a definite threshold level up to 10 KR.

In summary, this study has shown S-adenosyltransferase to be resistant to X-irradiation up to the 10 KR level and therefore it appears to be less radiosensitive than yeast cytidylate kinase prepared in a similar fashion[2]. It is concluded that mouse liver S-adenosyltransferase in vitro is not a radiosensitive enzyme and thus could be categorized as 'very resistant' in comparison with some other enzymes.

Zusammenfassung. In vitro-Nachweis, dass S-Adenosyltransferase der Mäuseleber gegen Röntgenstrahlen bis zu 10 kR Stärke widerstandsfähig ist und weniger empfindlich als Citidylat-Kinase.

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Die langsamen positiven Potentiale im Säuger-ERG Elektroretinogramm

In einer vergleichenden Studie über einige wichtige Familien der Säugetiere wurde das Elektroretinogramm (ERG) unter besonderer Berücksichtigung der langsamen positiven Wellen untersucht[1]. Dabei standen zwei Erscheinungen im Vordergrund: 1. die sogenannte c-Welle («sekundäre positive Erhebung» der älteren Nomenklatur)

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