COVER SHEET

Destination(s) and Dates for

Lerici, Italy

Which Trip Report Being Submitted: October 21 - 29, 1990

Name of Traveler:

Gary A. Sega

Joint Trip Report ☐ Yes

☐ No

If so, Name of Other Traveler(s):

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ORNL

FOREIGN TRIP REPORT

DATE: November 6, 1990

SUBJECT: Report of Foreign travel of Gary A. Sega,
Research Staff, Biology Division

TO: Alvin W. Trivelpiece

FROM: Gary A. Sega

PURPOSE: To attend and participate as an invited speaker at an
International Symposium on Trends in Biological
Dosimetry held in Lerici, Italy, Oct. 23-27, 1990.

SITES
VISITED: Oct. 23-27, 1990, Lerici (La Spezia), Italy

ABSTRACT: The traveler participated in a International Symposium on
Trends in Biological Dosimetry and presented an invited
paper entitled, "Adducts in sperm protamine and DNA vs.
mutation frequency". The purpose of the Symposium was
to examine the applicability of new methods to study
quantitatively the effects of xenobiotic agents (radiation and
chemicals) on molecular, cellular and organ systems, with
special emphasis on human biological dosimetry. The
general areas covered at the meeting included studies on
parent compounds and metabolites; protein adducts; DNA
adducts; gene mutations; cytogenetic end-points and
reproductive methods.

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My purpose in attending the International Symposium on Trends in Biological Dosimetry, which was held in Lerici, Italy from Oct. 23 to 27, 1990, was to present our studies of the molecular mechanisms that give rise to mutations in mammalian germ cells. I felt that our work was especially germane to the Symposium because we are one of the few groups working with a system in which a DIRECT connection can be made between the biological effects of chemical agents (i.e., genetic effects) and chemical dosimetry studies that determine the actual dose received by the biologically affected cells, their DNA and protein.

This Symposium was conceived as a result of several previous meetings. One, held in Munich in 1982, addressed Cytometric Approaches to Biological Dosimetry and was organized by W. G. Eisert (Gesellschaft für Strahlen- und Umweltforschung, GSF, Germany) and M. L. Mendelsohn (Lawrence Livermore National Laboratory, USA). Two others were organized by the International Agency for Research on Cancer and the Finnish Institute of Occupational Health, and were held in Espoo, Finland, in 1983 and 1987. All of the presentations made at the present Symposium will be published as a book by John Wiley & Sons, Inc.

Dosimetry expresses measurable amounts of exposure. The term is also used to describe the quantity of an active agent delivered to a target material within a biological system. Among the various types of dosimetry, biological dosimetry relies on selective, quantitative biological responses to measured dosages. It is particularly valuable in situations where physical or chemical dosage is unknown, where dose is difficult to standardize, and where individual biological susceptibility is likely to vary. Some aspect of this broad description of "dosimetry" was generally the focus of each paper presented at the Symposium. In all, there were some 50 platform presentations given at the meeting, and a like number of posters were presented.

A large number of the presentations looked at effects of chemicals or radiation in cell types that were not likely to be the important targets for biological effects such as cancer or heritable mutation induction. However, the biological damage in these cells could be useful as an indirect estimator of total exposure.

Our results were of particular interest to those participants working in the area of mammalian germ cell mutagenesis. In mammals, variability in the genetic sensitivity of different germ-cell stages to mutagens could be the result of how much chemical reaches the different stages, what molecular targets may be affected in the different stages and whether or not repair of lesions occurs. In the mouse, several chemical mutagens have been found that cause their greatest genetic damage in late-spermatid and early-spermatozoa stages and that also bind very strongly to the protamine in these stages. Chemicals which are less genetically damaging to these stages have been found to have much less affinity for protamine. Furthermore, we have found that the level of chemical binding to DNA in late-spermatid and early-spermatozoa stages is not correlated with the

level of induced genetic damage, although DNA breakage in these sensitive stages does increase. We have proposed that this DNA damage is the indirect result of chemical binding to sulfhydryl groups in protamine which prevents normal chromatin condensation within the sperm nucleus which can eventually break the DNA.

Clearly not all mutagenic chemicals act by the mechanism we focused on at the Symposium, and other molecular targets are likely to be important in other germ-cell stages. However, our chemical dosimetry experiments with mouse germ cells that show high levels of binding of some chemicals to sperm protamine, but not to DNA in genetically sensitive germ-cell stages give a new perspective in our understanding of mutational processes in mammalian germ cells. I was delighted to be able to present our findings before an international scientific audience, many of whom heard about our work for the first time at this Symposium.

While at the Symposium I was able to contact Dr. R.A. Baan from the Netherlands. He is working on detection of DNA damage induced by radiation and genotoxic chemicals by use of immunochemical and biochemical methods. In particular, we discussed our slightly different approaches for measuring DNA damage in spermiogenic stages exposed to ionizing radiation and the different results we each have obtained.

Significant discussions and plans for collaboration were also carried out with Drs. M. Spano from Rome, Italy and D. Evenson from the US. These two investigators are using flow cytometric techniques to study reproductive toxicology. We hope to be able to collaborate in studies where these techniques can be used to detect mutagen-altered protamines in germ cells.

One of the main objectives in my research in the Biology Division at ORNL is to develop an understanding of the molecular mechanisms that give rise to mutations in mammalian germ cells. A corollary of this objective is to learn more about the effects that chemicals have in somatic cells in the induction of cancers. This meeting afforded me the opportunity to learn more about how various cellular systems within the mammal respond to exposures from radiation and chemicals and how some chemicals may be either toxified or de-toxified within a living organism.

I feel that attendance at this Symposium gave me a better appreciation of the myriad effects that take place within a mammal after chemical- or radiation exposure. I also feel that reporting our molecular dosimetry work with mammalian germ cells gave other investigators food for thought in that they may be a little more inclined to consider targets other than DNA to be important in mutagenesis and carcinogenesis. The positive comments that I received about our work should reflect favorably on DOE, as well as the Biology Division and ORNL.

APPENDIX

Itinerary

Oct. 21-22, 1990	Travel from Oak Ridge, Tennessee, to Lerici, Italy
Oct. 23-27, 1990	Participated in International Symposium in Trends in Biological Dosimetry, Lerici, Italy
Oct. 28-29, 1990	Returned to Oak Ridge, Tennessee

Persons contacted to a Significant Extent

Dr. R.A. Baan, TNO Medical Biological Laboratory, Rijswijk, The Netherlands

Dr. M Spano, ENEA Casaccia, Rome, Italy

Dr. D.P. Evenson, South Dakota State University, Brookings, South Dakota

Literature Acquired

Book of Abstracts

END

DATE FILMED

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