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October 31, 1984

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VISIT BY CONGRESSMAN GORE

Robert C. Odle, Jr., Assistant Secretary for Congressional, Intergovernmental, and Public Affairs, CP-1, Headquarters (7B-138/FORSTL)

Congressman Albert Gore, Jr., visited the Biology Division of the Oak Ridge National Laboratory on October 30, 1984.

The visit, which lasted only about 30 minutes, was limited to a tour of the mammalian genetics section and discussions with Drs. W. L. and Liane Russell, highly recognized geneticists.

The Congressman requested a briefing on the importance and status of genetics research. The Russells provided the attached summary of the status as it exists at ORNL, and their short discussion related to the summary. Mr. Gore inquired with regard to funding for biological research at ORNL and was advised of the drastic reduction of staffing levels which has occurred over the past four years. The Russells allowed they had been quite favorably treated by DOE and that the problem appeared to be overall reduced federal funding for biological research.

In departing, Mr. Gore indicated he planned to try and improve that situation.

Joseph A. Lenhard
Assistant Manager for Energy
Research and Development

Attachment

cc w/attachment:
C. W. Edington, ER-70, HQ (GTN)
J. W. Range, M-4, ORO

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bcc: Manager's Congressional File

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THE MAMMALIAN GENETICS AND REPRODUCTION SECTION, BIOLOGY DIVISION, ORNL

Mission of the ORNL Mammalian Genetics program:

to study the risk from heritable genetic damages that might be caused by chemical or physical agents. In contrast to somatic effects (e.g., cancer), genetic effects can persist for generations and may affect any of a variety of functions in any body system at any age.

Why mammalian germline studies are needed

- Short-term tests (in non-mammalian systems or in mammalian somatic cells) can identify potential genetic hazard, but cannot be used to estimate actual risk of heritable effects
- The mammalian germline is highly complex, containing many co-existing germ-cell stages (different in the two sexes) that exhibit radically different sensitivities to a given mutagen; the sensitivity profiles may vary with the mutagen and with genetic endpoint
- Certain mammalian germ-cell stages appear to have highly developed repair systems
- The pathway between entry of the potential mutagen into the body and the transmission of a genetic alteration is long and highly complex
- There are examples of poor correlation between results of certain short-term tests and mammalian germline (MG) tests
- A body of MG data must be built up for chemicals that are representative of different classes and modes of action, (a) to determine whether there are patterns of effects that may be used to predict the action of as yet untested chemicals (b) to determine which short-term tests might be the best indicators of genetic hazard
- Overall assessment of genetic risk for substances to which human populations may be exposed (e.g., ethylene oxide, cyclamates) requires quantitative assessment of all genetic endpoints

The Mammalian Genetics program of the ORNL Biology Division is a unique resource; no other one like it exists in the USA

- The physical facility, which can house about 300,000 mice at a time, has operated without major disease for over 30 years. Animals needed for all experiments are bred on the premises
- Over a thousand different stocks of mice are maintained that have unique uses for various experimental purposes
- Valuable genetic material is being preserved for posterity by embryo freezing. Embryo freezing was first developed and perfected in the ORNL Biology Division
- The scientific and technical staff represent a number of disciplines that must interact for a well-rounded program (see below)

Studies being coordinated in the Mammalian Genetics program

- All the major genetic endpoints are being addressed (gene mutations, chromosome aberrations, nondisjunction)
- Quantitative measures of indices of mutational change are correlated with measures of physical effects (e.g., skeletal anomalies, infertility) caused by such types of mutational changes. Some of the latter provide models for inherited disorders.

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- Studies of direct damages (e.g., differential killing of different types of germ-cells) provide information needed to interpret results of heritable-effects studies
- Measurements of molecular dose directly in the target tissues (reproductive organs) are related to information on administered exposure and to level of genetic effect
- Analysis of the type of DNA alteration caused by a chemical is related to the type and amount of genetic effect produced. This also provides important information on intracellular repair
- Detailed genetic analyses of mutations allow correlation of type of genetic change with type of mutagen
- Capabilities for data analysis have been perfected, including computer analyses
- Among support technologies is cytogenetics, including electron microscope studies. Expertise available in the remainder of The Biology Division can also be readily tapped.

Some achievements of The Mammalian Genetics Section

- Quantification of genetic hazards of radiation. Virtually all permissible dose limits, world-wide, are based on the work of the Section. (Among findings: a dose-rate effect [repair], absence of a threshold dose rate in males, humped dose-effect curve, great importance of germ-cell stage and sex.)
- Characterization of radiation effects in embryonic and fetal development. (Among findings: demonstration of critical periods, all-or-none effects in cleavage stages.) The widely used "14-day rule" to avoid radiation-exposure of women during an as-yet-unsuspected pregnancy is based on these findings.
- Development of most of the whole-mammal mutagenesis tests now used the world over. A useful prescreen (mouse spot test) was also developed
- Demonstration of repair capacity of the spermatogonial stem cell, the most important cell type (in the male) with regard to genetic risk
- Demonstration that the fertilized egg can repair genetic damage contributed by the sperm
- Discovery of a supermutagen (ENU) which makes it possible to
  (a) explore the biological factors affecting mutagenicity of chemicals
  (b) produce specific types of mutations useful in basic studies
  (c) produce mutations that model human genetic disorders, allowing laboratory studies of such conditions
- Discovery that the Y chromosome is male determining in mammals (the sex-determining mechanism being different from that in other genetic model organisms)
- Discovery that only one X chromosome of mammalian females is active and that inactivity can extend into attached non-X-chromosome material

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