A COMPARISON OF THE CYTOLOGICAL EFFECTS PRODUCED BY
IONIZING RADIATIONS OF DIFFERENT LET

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A COMPARISON OF THE CYTOLOGICAL EFFECTS PRODUCED BY
IONIZING RADIATIONS OF DIFFERENT LET

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Abstract

Rat eyes were irradiated with a single dose of 1000, 850, 700, or 550 rads of X-radiation or 225, 200, 175, 150, or 125 rads of fission neutron radiation. Some eyes are being examined periodically for cataracts; others were tested by wounding the lens at 3, 14, or 28 days after irradiation. At 10 months after irradiation, the 1000-rad-X cataracts were a bit more advanced than the 225-rad-n group; this suggests an RBE of about 4. Wounding the lens initiated a "wave" of DNA synthesis followed by a "wave" of mitotic activity. Radiation partially suppressed the response to wounding. The magnitude of the response was inversely related to the X-ray dose; the magnitude increased with increased time between irradiation and wounding. We are accumulating data to compare neutron and X-irradiated epithelia. Equal percentages of abnormal mitoses were observed after wounding at 3 days after 1000 rad-X or 222 rad-n; this suggests an RBE of 4.4. X-irradiated cells recovered continually during the first 28 days after irradiation. Neutron irradiated cells recovered very little in the first two weeks, but then "caught up" to X-irradiated cells. Shielding half of a lens from 1000 rads of X-rays slightly decreased the immediate effects on irradiated cells and enabled the cells to recover faster.

Summary of Recent Project Activities

We presented a paper at the 23rd Annual Meeting of the Radiation Research Society, 11-15 May 1975, in Miami Beach, Florida. Copies of this paper, "Some Effects of Single or Fractionated Exposures of the Mouse Lens Epithelium to Fission Neutrons" by Richard C. Miller and Edgar F. Riley, are included with this report. We presented another paper on 23 September 1975 at the 10th Paterson Symposium sponsored by the Christie Hospital and Holt Radium Institute in Manchester, England. The title of this paper was: "A Successive Pulse Model of Cell Cycle Progression in the Rat Lens Epithelium Responding to a Mitogenic Stimulus from a Puncture Wound" by E.F. Riley. We do not have a copy or a reprint of the abstract of this paper. Two papers about recovery patterns in neutron and X-irradiated rat lens epithelia and the effects of shielding half a rat lens during X-irradiation have been accepted for the 24th Annual Meeting of the Radiation Research Society in San Francisco, 28 June - 2 July 1976.

We have derived more data about effects on the mouse lens epithelium, effects that could be observed during the first 30 days after single or fractionated doses of X-rays or fast neutrons. For example, we determined the percentages of the mitotic figures that were abnormal when the epithelial cells responded to a mitogenic wound stimulus produced at different times during the first 30 days after irradiation. Some other data were presented in our last Technical Progress Report #C00-1024-54. We have discussed this data with other radiobiologists. However, we have not decided on the best way to condense the data for publication. We hope to do this in the next few months. We have had no evidence that Mr. Hite has made any progress on a parallel study of radiation effects on the mouse skin.

Most of our efforts in the last year were focused on some rat experiments. Rat eyes were given a single dose of 1000, 850, 700, or 550 rads of X-rays or 225, 200, 175, 150, or 125 rads of fission neutrons. In some cases, half of the lens was shielded when the other half was given 1000 rads of X-rays. The ability of shielded and irradiated cells to respond to a wound stimulus was assayed at various times after irradiation. In most cases, the entire lens was irradiated and tested by wounding at 3, 14, or 28 days after irradiation. Some of the sample epithelia have been evaluated, but others are in various stages of whole mount preparation, autoradiographic preparation, and cell counting. We hope to complete and summarize these experiments in the next year.

During the summer of 1975 and extending into the fall, we did some pilot experiments to see whether or not we could assay the levels of cyclic AMP and the levels of RNA synthesis at different times after wounding the rat lens epithelium. There seemed to be a relatively high level of RNA synthesis about 4 hours after wounding. This was probably related to the preparations for DNA synthesis by responding cells. The cyclic AMP level seemed to drop to very low levels just before DNA synthesis. We think it would be worthwhile to extend this pilot study to study the effects of irradiation on the RNA and cAMP economies of epithelial cells responding to a wound stimulus.

The amount of time that the Principal Investigator was able to devote to the project has varied widely during the past year. At times the percentage of effort was probably no more than 5% and much of the time was only about 20%. The decreased time available was the result of extra duties that all of our staff have had to assume for a time after two of our colleagues died

last spring (1975). The time required for the extra duties has varied considerably. As a result, the Principal Investigator has devoted nearly 70% of his time to the project for the last month and will be able to spend at least that much time for the next two months. The percentage effort should average 30 - 40% for the current contract period.

Experiments in Progress

In some experiments, half of a lens was shielded with lead during irradiation with 1000 rads of X-rays. When the lens was wounded 1 day after irradiation, the shielded cells responded more intensively than control cells did (peak of ^3H -TdR labeling = 70% instead of about 50%). The irradiated cells were better able to respond than cells in the wholly-irradiated lens were able to do (peak of cell labeling = 28% instead of 20%). By 4 days after irradiation, the wound response in both halves was greater than in unirradiated control lens epithelia. By 14 days after irradiation, the half-shielded, half-irradiated epithelia seemed to have completely recovered their ability to respond to a mitogenic wound stimulus. Observations of the response in certain epithelia showed that X-radiation did not block the production of a mitogenic stimulus by wounding, but did block (partially suppress) the ability of irradiated cells to respond. Shielding half of the cells reduced the immediate impact of irradiation a little and accelerated recovery processes.

In other experiments, rat eyes were given a single dose of 1000, 850, 700, or 550 rads of X-radiation or 225, 200, 175, 150, or 125 rads of fission neutrons. Some rats (and lenses) were saved for periodic ophthalmoscopic examinations. The lenses given 1000 rads of X-radiation had

advanced cataracts by 10 months and complete cataracts by 12 months post-irradiation. The cataracts were not as advanced at 10 months after 225 rads-n as after 1000 rad-x. This indicates that the RBE for cataract formation was about 4.

Other lenses given single doses were tested by wounding at 3, 14, or 28 days post-irradiation. Figure 1 and Figure 2 show the percentages of abnormal mitotic figures observed in epithelial cells responding to the wound stimulus at the different times after the neutron or X-ray doses. The percentage observed at 3 days after 225 rad-n coincides with the percentage observed at the same time after 1000 rad-X. This indicates an RBE of 4.4 for this criterion of effect. The percentages observed after 1000, 850, and 700 rad-X decrease from 3 to 14 days post-irradiation. In contrast, the percentages observed after 225, 200, and 175 rad-n did not decrease from 3 to 14 days post-irradiation. This would increase the relative effectiveness of the neutrons if repeated doses were given at intervals of 7 - 14 days.

Figures 3 and 4 show the "waves" of ^3H -TdR cell labeling (DNA synthesis) at 0 - 200 μ and 200 - 400 μ from a wound produced 3 days after a dose of 550 rads of X-rays. Figures 5 and 6 show that the "wave" developed with less delay and was bigger when the lens was wounded at 7 instead of 3 days post-irradiation. Both factors indicate that some recovery took place in the intermitotic cells during the time from 3 to 7 days post-irradiation. Figures 7 and 8 show that even more recovery took place by 28 days after 550 rad-X. Figures 9 through 26 show similar patterns of recovery after the other X-ray doses. The recovery patterns based on the magnitude of response (relative areas under the waves of cell labeling) are summarized in

Figure 27. Figure 28 shows dose-effect curves based on the magnitude of the response at different days after different single doses of X-radiation. Similar data about the labeling of cells after neutron irradiation are "in progress". We expect the neutron data to show a slower rate of recovery after the neutron doses.

Figure 1.

Figure 2.

Figure 3.

Figure 4.

Figure 5.

Figure 6.

Figure 7.

Figure 8.

Figure 9.

Figure 10.

Figure 11.

Figure 12.

Figure 13.

Figure 14.

Figure 15.

Figure 16.

Figure 17.

Figure 18.

Figure 19.

Figure 20.

Figure 21.

Figure 22.

Figure 23.

Figure 24.

Figure 25.

Figure 26.