Radiation's Own Version of Chemotherapy

Scientists have identified a previously unrecognized mechanism by which radiation indirectly kills certain tumor cells. "This is the first time you can explain radiation's mechanism of action by some means other than its direct effect on [a cell's] DNA," says Ralph R. Weichselbaum, the radiation oncologist who led the University of Chicago study. While noting that the findings are very preliminary, the researchers say they believe the toxic chemical they've isolated from irradiated human cancer cells may ultimately hold promise as a drug to boost radiotherapy's effectiveness.

Weichselbaum says his team happened onto the finding while conducting experiments on radiation survival of tumor cells. They found entire populations of cells dying from what should have been sublethal radiation exposures. After ignoring the problem for about six months – initially suspecting it resulted from technician errors – "I finally got the bright idea of decanting the [culture] medium" in which the cells grew, Weichselbaum says. When he added the cell-free fluid to new cultures of healthy cancer cells and observed that it immediately began killing these nonirradiated cells, he realized that the cells irradiated in the first tests must have manufactured some lethal poison.

In the December PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES (Vol.86, No.24), Weichselbaum and his co-workers describe their experiments and identify the toxic substance as tumor necrosis factor (TNF) – an immune system protein normally made by the body to aid in healing or to fight infections and tumor growth. Other researchers are testing TNF as an anticancer therapy in humans, but to date it has shown little promise.

The Chicago team found that in some cell lines, adding TNF – either before or up to four hours after irradiation – to cells that hadn't initially produced it could increase the number of cells that ultimately succumbed.

The gene that triggers enhanced production of TNF "is the only mammalian gene found to have increased expression after exposure to ionizing radiation," the researchers assert. Weichselbaum told SCIENCE NEWS he hopes to determine exactly how irradiation activates this gene and several other candidate genes his group is investigating.

Some researchers, among them cancer biologist Keith Laderoute at SRI International in Menlo Park, Calif., argue that even before this study, scientists had identified at least one other mammalian gene – coding for DNA repair – as being activated by damage to DNA. However, he adds, the "intriguing" new report "does appear to show real, new effects – that some tumors may be sensitized to radiation by TNF."

"This is certainly an interesting paper," comments radiobiologist Eric J. Hall at Columbia University in New York City, "though my reaction is guarded until the experiments are repeated in other systems" – other cell types or animals. For example, though the Chicago team claims evidence of a potential synergy between radiation and TNF, Hall notes that the data presented in the research report suggest their effects may be merely additive, with the TNF killing off particularly radiation-resistant cells. "That isn't to say that the two together are not useful," he adds.

TNF is a cytokine, one of a group of powerful cell-secreted chemicals that include growth factors and interferon. But it is not the only cytokine shown to modify cancer cells' response to radiation, notes Robert M. Sutherland, a cancer biologist at SRI International. In the July 5, 1989 JOURNAL OF THE NATIONAL CANCER INSTITUTE, he and Tim Tak Kwok reported that the presence of epidermal growth factor – a normally nonlethal cytokine – enhanced the radiation sensitivity of human squamous carcinoma cells. Sutherland says the SRI and Chicago findings, taken together, appear to "open up an interesting new area worthy of more investigation" – the role of natural cell-derived chemicals in modulating radiation sensitivity. *– J. Raloff*

Sun-like stars may offer clues to climate

Satellite measurements show that the sun's brightness has varied by about 0.1 percent during the current 11-year solar cycle, but astronomers lack precise records of earlier cycles. Two researchers now propose a way to extend the record back for centuries by comparing solar activity with observations of other stars. Their approach may yield clues not only to past trends in solar activity but also to future climate trends on Earth.

The key, says Sallie Baliunas of the Harvard-Smithsonian Center for Astrophysics in Cambridge, Mass., lies in comparing changes in the sun's surface activity with those of other stars of similar age and mass. Some of these solar-type stars show variations as great as 0.4 percent, up to four times those observed for the sun. These changes presumably reflect the coming and going of "starspots," say Baliunas and Robert Jastrow of Dartmouth College in Hanover, N.H. They described their work this week at a meeting of the American Astronomical Society in Arlington, Va.

Though representing only the current solar cycle, data from the Earth-orbiting Solar Maximum Mission and Nimbus 7 satellites suggest the sun's activity rises and falls with changes in its magnetic field, Baliunas reports. Solar magnetic variations leave a long-term record in the form of carbon-14 in tree rings, she notes, because when the magnetism is stronger, less carbon-14 is produced in Earth's upper atmosphere and less finds its way into the tree rings. "The amount of carbon-14 in trees over time maps the history of solar magnetism," she says, and "the tree rings thus provide a timeline of the magnetic history of the sun." One well-known period of low solar magnetism identified from tree-ring studies is the Maunder minimum, which lasted from about A.D. 1640 to 1710. Researchers have remained uncertain, however, whether solar magnetism correlates with brightness from solar surface events.

For the last 23 years, scientists working at Mt. Wilson Observatory near Los Angeles have tracked the magnetic activity of 13 solar-type stars by measuring the intensity of their calcium emissions. Baliunas, who is involved in the effort and who now draws upon its data, says variations in these emissions show that nine of the stars go through activity cycles ranging from about eight to 13 years. Activity levels of the remaining four have remained almost flat, as though they are in the process of undergoing Maunder minima of their own.

"Our sun has spent about a third of its time over the last millennium in this relatively inactive state," Baliunas says, calling the Mt. Wilson project "a portrait of what the sun would do over time, if we waited long enough."

If the Maunder minimum on Earth indeed reflects a lower solar brightness during that 70-year period – a possibility the Mt. Wilson observations support – the correlation "has implications for the explanation of climate changes over time scales of decades to centuries," Baliunas and Jastrow say. Climate forecasters and others have long espoused the notion of a "solar constant," in which the long-term brightness remains unchanged despite short-term cyclic fluctuations. However, the researchers say, "confirmation of these tentative results would call into question the assumption of a constant sun in current [long-range] climate forecasts." *– J. Eberhart*