**1959** At Columbia University, Harald Rossi introduced the concept of measuring energy deposition by ionizing radiation in small volumes, thus launching the field of microdosimetry. This concept would lead to significant advances in our understanding of the risks of exposure to low-level radiation.

**1961** In a joint effort with the NIH, a team headed by Norman Anderson developed a high-speed zonal centrifuge at Oak Ridge. By the late sixties, commercial descendants of this machine were producing highly purified vaccines for humans and animals.

**1962** Richard Setlow at Oak Ridge pinpointed the damage caused in bacteria by ultraviolet light. Two years later, he would discover the role of genetic repair mechanisms in mending such damage.

of potentially toxic agents—chemicals as well as radiation—and to reckon their effects by looking for biological change in human tissues. New cell-culture techniques and sensitive methods for assessing chromosome damage in cultured human cells led Oak Ridge researchers to the concept of biological dosimetry or *biomarkers*. In one extension of this concept, Richard Albertini at the University of Vermont quantified mutations to a specific "reporter" gene, known as HPRT, as a means for gauging human exposures to radiation and to hazardous materials. Since their introduction, biomarkers have been used successfully to estimate radiation doses to astronauts, radiotherapy patients, and radiation accident victims. They were widely used, for example, in the wake of the reactor accident at Chernobyl.

Along similar lines, engineers and physicists have directed consistent effort since the forties toward improving instrumentation for measuring radioactivity in medical, biological, and environmental samples. Early research centered around photomultiplier tubes and scintillation detectors, but a crucial breakthrough came in the sixties with the development of solid-state silicon and germanium detectors. Properly prepared, these materials produced electrical signals precisely matched to the energy of the detected x-rays—and thus pinned down the identity of the radioactive isotopes present. Now successfully commercialized by several manufacturers, many of the underlying practical discoveries arose from AEC-supported research, especially by Fred Goulding and his colleagues at Berkeley.

Then, in the seventies, with the broadening scope of ERDA, and then the DOE, concern extended to the chemical by-products of all energy production and use. Techniques have thus been developed to monitor known cancer-causing chemicals, to measure skin contamination, and to detect trace amounts of environmental contaminants. An especially notable tool is resonance ionization spectroscopy (RIS), an Oak Ridge–developed technique so sensitive that in 1977 it allowed single atoms to be detected for the first time. Spin-offs have included several RIS-based analytical techniques for studying trace materials in the environment. And in 1990, at Los Alamos, similar concepts led to another milestone, the first detection of a single molecule.

### Radiation Effects: A Closer Look

A shortcoming of epidemiological studies—and most animal studies, too, for that matter—is that they offer little insight into Why. Why does radiation cause mutations? Why are low levels of radiation often harmless? Why do the consequences of more severe exposures often appear as cancers decades later? These and similar questions fall within the province of radiation biology, which looks beyond mice and fruit flies, to uncover the underlying effects of radiation on cells and their components. One of the ground-breaking discoveries came at Oak Ridge in the early sixties, when Richard Setlow pinpointed the damage caused by ultraviolet light in the genetic material of bacterial cells, and fur-

**Damage control** In the early sixties at Oak Ridge, Richard Setlow elucidated the mechanism of DNA repair, thus opening the door to a field of inquiry that is at the center of cancer research today. Now at Brookhaven, he is shown here with fish used to study the induction of melanoma by ultraviolet light.