Biology

More evidence on two-step cancer

It takes at least two genetic changes to make a normal cell cancerous, according to several lines of recent research. Robert A. Weinberg of the Massachusetts Institute of Technology in Cambridge recently reported at a meeting that copies of individual cancer genes will not make normal cells, taken from rat embryos, cancerous, but some pairs of these genes will transform the cells (SN: 6/18/83, p. 388). This work has now been published in the Aug. 18 NATURE, along with related work from two other groups. H. Earl Ruley from the Cold Spring Harbor (N.Y.) Laboratory reports other pairs of genes that will act in concert, but not alone, to make rat cells cancerous. And Robert F. Newbold and Robert W. Overell of the Institute of Cancer Research in Buckinghamshire, England, find that immature cells taken from the skin of newborn hamsters and treated with one of a variety of chemical carcinogens and one cancer gene become cancerous, whereas cells treated with just the carcinogen or just the gene do not.

Together these experiments indicate two separate genetic steps in the formation of cancer. One step gives cells the ability to grow indefinitely in laboratory culture, a characteristic the scientists call "immortalization." This step may be accomplished by a chemical carcinogen or one of the following cancer genes: the chicken leukemia virus gene called *myc,* the rodent cancer polyoma virus gene called large T and the human respiratory infection virus adenovirus-2 gene called *E1a.* The other step in cancer formation allows the cells to reproduce rapidly and change their surface properties to those characteristic of a malignant cell. This group of cancer genes includes the *ras* human bladder carcinoma gene, the polyoma middle T gene and the adenovirus gene called *E1b.* Others of the twenty or so cancer genes so far identified are expected to fall into these categories. But further steps, and further grouping of cancer-causing genes, may yet be identified.

Honey bee specialty job: undertaking

Visscher

Within an hour of the death of a honey bee in the hive, an undertaker arrives on the scene. This specialist bee grasps the corpse in its mandibles, flies with it from the hive and eventually drops the body as much as 400 feet away. One or two bees out of every hundred specializes in carrying from the hive corpses of its fellows, reports Kirk Visscher of Cornell University in Ithaca, N.Y. "It's remarkable that they can carry a bee that's their own body weight," Visscher says. These undertakers, who also serve as guards, probably hold the job temporarily for at least several days.

Undertaking is not just housekeeping. Although corpses in the hive may carry diseases or attract predators, most bees either ignore a dead body or poke and lick it. Visscher suspects that the undertakers act in response to a chemical emission from the corpse. In experiments, Visscher put into an active hive freshly killed bees, dead bees coated with paraffin and balsa wood models of bees. The undertakers removed the untreated corpses after as little as 3 minutes; removal of the paraffin-coated ones took three times longer. And the wood models were carried out only after more than 7 hours. Visscher says, "Dead bees elicit an especially rapid response; they are not simply treated in the same way as motionless foreign objects." And when Visscher incubated dead bees for various lengths of time before introducing them into the hive, those dead the longest were the most expeditiously removed by the undertakers.

Behavior

Extra fuel for mental retardation

The nature of the brain damage in mental retardation is unknown, but the very idea of retardation suggests less of something—less circuitry, less activity. Surprisingly, government scientists have found that mentally retarded young adults have brains that are more, not less, active than normal controls—suggesting that they are working hard (though inefficiently) at the task of thinking. "It's like they have the accelerator to the floor," one scientist says, "but they're not in gear."

Neuroscientist Neal R. Cutler and his colleagues at the National Institute on Aging in Bethesda, Md., have been using positron emission tomography (or PET) scanners to measure glucose consumption in the brains of young adults suffering from Down's syndrome, a genetic disorder and the most common form of mental retardation. The metabolism of glucose, the brain's fuel, is closely coupled with neuronal activity—both of which are significantly reduced in conditions such as Alzheimer's disease, a form of senility. Because Down's syndrome, like Alzheimer's disease, involves impaired mental ability, the scientists expected to find less fuel consumption in the retarded brains. As they report in the Aug. 19 SCIENCE, they found more—in some regions as much as 40 percent more than normal.

The researchers also studied a 51-year-old retarded man, and they found that his brain activity was not significantly different from that of normal 51-year-olds—suggesting that the excessive glucose consumption of young adulthood may decline with age. In normal, healthy people, no age-related changes in brain activity occur, so the decline seen in Down's syndrome may indicate a progession toward senility coupled with mental retardation. And in fact, Cutler notes, autopsies have shown that all middle-aged Down's syndrome victims develop the brain pathology associated with Alzheimer's disease.

Clocks for mind and body

Many people have a particular time of day at which they work most efficiently, and scientists have long suspected that this rhythm of human performance is under the control of a steadfast biological clock. Scientists have suspected furthermore that the clock controlling task performance is not the same clock dictating the sleep-wake cycle, but rather a second one controlling the rhythm of core body temperature. It may not be that simple: New research suggests that physical performance may indeed be controlled by the body temperature clock, but that thinking has a distinct rhythm that is tied to the natural cycle of sleep and waking.

Timothy H. Monk of the New York Hospital-Cornell Medical Center in White Plains, N.Y., conducted an experiment on a young male in which he intentionally desynchronized the two internal clocks. Isolated from all indicators of time, the subject was put on a rigid 25.8 hour day, one hour ahead of the natural 24.8 hour cycle of his core body temperature. Working with colleagues in New York and at Harvard University, Monk tested the man several times a day for 40 "days" for both manual dexterity and reasoning ability. As he reports in the Aug. 17 NATURE, the peaks in physical performance corresponded with peaks in temperature; complex reasoning ability, in contrast, seemed to be under the control of both internal clocks and peaked fairly soon after waking. It may be, Monk speculates, that manual dexterity is controlled by some vigilance-motivation mechanism connected to the temperature cycle, but that thinking requires, in addition, information-processing mechanisms that must be reset during sleep. This finding, Monk notes, has practical implications for those designing industrial work schedules: Because the temperature clock is much more resistant to change, physical performance is most likely to be hurt by shift rotation; and jobs requiring dexterity would seem to be inappropriate for such shifts.