Rocking around the cell division clock

If there is any characteristic peculiar to cancer cells, as opposed to normal cells, it is uncontrollable cell division. Normal cells know when to stop dividing. Cancer cells don't; their aim is takeover of the body. In other words, something of shattering importance occurs in one or more of the four phases of division in the cancer cell. The phases, if visualized on a clock, would look like this: G_1 (three o'clock phase); S (six o'clock phase, DNA synthesis); G_2 (nine o'clock phase); M (12 o'clock phase, cell division).

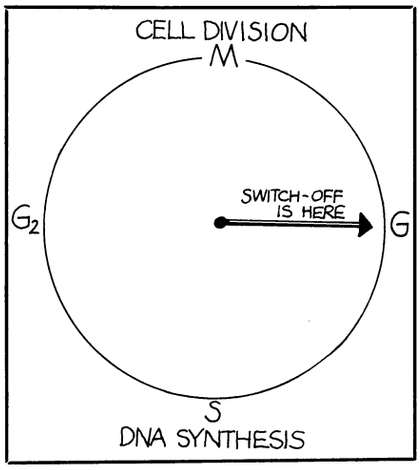
Not until the 1960's, with the development of sophisticated cell culture techniques, were cancer scientists able to study normal cell division and cancer cell division with any success. Even today, their knowledge of how normal cell division and cancer cell division differ is woefully inadequate. Still, they are making some progress toward understanding the differences, as a symposium on the control of cell division made evident last week. The symposium was part of the annual meeting of the Federation of American Societies for Experimental Biology in Atlantic City.

Howard Green of the Massachusetts Institute of Technology, for example, reported that he and his colleague, Sheldon Penman, have found that if a normal cell in the resting state is chemically stimulated to divide, the cell gears up for DNA synthesis (the first step in cell growth). And gearing up for DNA synthesis constitutes an increase in the cell's messenger RNA, transfer RNA and ribosomes. Shortly after stimulation, the amounts of tRNA and ribosomes increase, in proportional amounts. The amount of mRNA increases, more dramatically. Why might mRNA increase even more than the tRNA and ribosomes? "So that the cell can use its tRNA's and ribosomes even more efficiently than usual," Green speculates.

"It could be more efficient, or it could be for new purposes," the chairman of the symposium, A. B. Pardee of Princeton University, suggests. "The mRNA is what tells the machinery, the tRNA and ribosomes, what it is supposed to make. When you turn the machinery on, you turn it on to make different things by supplying new kinds of the mRNA."

Regardless of the reason for more mRNA, however, it appears that if there is a modest amount of mRNA in a cell, the cell is in a resting state. And if a cell contains a whopping amount of mRNA, the cell is ready to divide.

If increases in RNA or in ribosomes are disrupted, Green continues, cell division is thwarted. Thus, DNA synthesis appears to be an event necessary for normal cell division.



So, how does a cancer cell differ in division from the normal cell? Green and Pardee concur that a cancer cell gears up for division just as the normal cell does—with an increase in its equipment for DNA synthesis. And this increase in synthesis equipment probably leads, as it does in the normal cell, to DNA synthesis, then to cell division. Thus the several events that lead to cell division in the normal cell probably lead to division in the cancer cell as well. In fact, as Green and Pardee point out, a number of cancer drugs are known to combat cancer by interfering with DNA synthesis or with cell division itself.

Where the cancer cell parts company with the normal cell, then, is that once cell division gets under way, it will not turn off. The question is: What are the switches that turn on cell division in the first place? Are they the same switches that turn off cell division? Does the cancer cell have these switches or not? More than one cancer scientist would give his last grant dollar to identify the crucial switches. "They could give us the key to turning off uncontrolled cancer cell growth," Pardee says.

Although Pardee has not yet found the mythical switches, he has at least taken a firm step in that direction. He has found that the switching off of division in the normal animal cell occurs during the G_1 phase in cell division. ("G" stands for "gap." Pardee calls the "G" phases the ignorance phases.) Leland H. Hartwell of the University of Washington told the symposium that a switching off of division in the yeast cell occurs at the same phase. Thus, a crucial phase in the switching off of cell division appears to be that phase of cell division that precedes DNA synthesis, and in turn, cell division. The challenge now is to determine what the switch is, and whether it is present in cancer cells or not.

Pardee is enthusiastic about Hartwell's work, because, as he explains it, "There are enormous advantages in studying this switch in yeast cells rather than in animal cells. It is a lot simpler, and it can be handled with genetic methods too that are hard to apply to animal cells." □

Chemicals found in cities' water

The methods many American cities use to purify drinking water could add dangerous organic chemicals to the water, the Environmental Protection Agency has concluded. In a survey of 79 cities, EPA found that raw, untreated water showed no trace of the six chemicals the group sampled for in 30 cities and extremely low concentrations in the other 49 cities. Samples of treated water had, across the board, at least one of the six chemicals in it. The six chemicals chosen for the survey—two of them (chloroform and carbon tetrachloride) potentially carcinogenic—were selected because they are prevalent, easily analyzed and in some cases thought direct results of chlorine purification.

But regardless of chlorine's possible by-products, Russell Train, the agency's administrator, says chlorination remains the single most effective method of preventing serious water-borne bacterial diseases such as typhoid and cholera. "We continue to believe that the benefits of chlorine used to prevent immediate, acute biological diseases far outweigh the potential health risk from chlorine-derived organic compounds," he says.

Some scientists speculate that chlorine added to purify the water may be combining with organic substances not removed during filtration, to form the dangerous chemicals. Organic chemicals are compounds that contain carbon. They include many man-made compounds.

"People should not react with any sense of panic, but they should know there is a problem," Train told a news conference last week. Specific health problems of the pollutants, if any, are unkown but are under study. In a few cities, where more detailed studies were conducted, traces of dieldrin, a pesticide, and vinyl chloride, which has been linked to cancers in persons heavily exposed to it, were found.

The 80-city survey was triggered in part by last year's discovery that drinking water in New Orleans, originating from Mississippi water, contains traces of 66 different chemical pollutants (SN: 11/16/74, p. 311). It was with the Louisiana study that the methods for analyzing water for harmful chemicals was refined. □