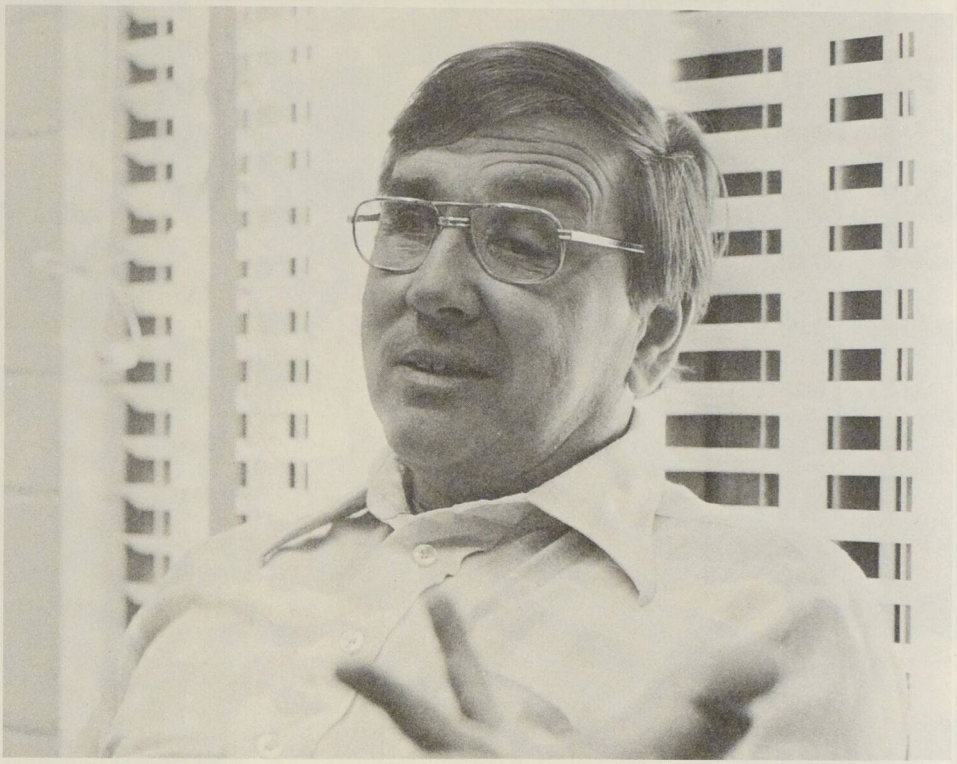
New insights into cancer
Fitting pieces into the jigsaw puzzle

Dr. James Whitfield's research on the proliferation of normal and cancerous cells has led him to believe that cancer is, by and large, not due to a mutation. Instead, it may be a disease of differentiation, the process responsible for the development of the many different types of cells or tissues that make up the adult human body. He feels that cancer may be a disruption of this orderly process.



David Gillan, NRC/CNRC

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Hundreds of thousands of people are afflicted by cancer every year, and it is estimated that by the year 2000, eight million people will die annually of the disease. Although we are now aware that certain chemicals, radiation and viruses are the most common cause, no consensus exists as to how these agents transform normal cells into cancer. Cancer essentially remains a biological mystery.

However, a few researchers are now proposing a new theory which may infuse new vigor and insights into the long struggle against this dread disease. NRC's Dr. James Whitfield explains some essential differences between the old and new theories. "The old concept of cancer insisted that it is a product of a mutation, a change in the DNA (deoxyribonucleic acid — the genetic material of living things) of one of the cells in the body. To produce a change which would be inherited from one cell generation to the next, the DNA had to be altered either by a mutation or some other physical rearrangement of its sequence. When it was discovered that cancer cells could be grown indefinitely in test tubes, and that the daughter cells were exactly like the parent cell, it was automatically assumed that, when the original cell had become cancerous, its DNA had mutated.

"But now we have some other clues which force us to reexamine this concept, partly as a result of the vast amount of research done in the fields of differentiation and cancer, and perhaps as a result of straightening our thinking. The following three facts are central in disproving the mutational theory for cancer. The cells in any given cancer in the body are not identical to one another; often, cancerous cells will produce non-proliferating differentiated cells which appear in all ways to be normal and resemble the healthy tissue. Moreover, in some cases when mouse cancer cells were injected into early mouse embryos, those cells reverted to normal mouse cells. Finally, no altered or structurally abnormal proteins have been found in any of the cancer cells that have been examined. Such facts are hardly consistent with a mutational origin." What they do suggest is that cancer is a disease of differentiation.

Differentiation occurs during early development in higher animals. Development, of course, begins when the fertilized egg cell divides and produces first, two cells, then four, and so on until there are thousands of cells in the early embryo and, ultimately, the billions that make up the adult animal. At some time during this process, the destinies of the cells in the different areas of the embryo are sealed permanently — some cells will give rise to eyes, others to skin, and still others to muscle. Yet, through each division and physical change that leads toward these different tissues, exactly the same DNA is passed on to each and every cell as was originally present in the fertilized egg cell. That is the great mystery of differentiation in molecular biology — how all the various types of cells in the body arise when they all contain the same DNA.

According to Whitfield, it is also possible for normal cells to change irreversibly into cancer cells without the DNA undergoing a change. He feels that most cancers are not due to an actual mutation in the DNA, but instead arise from a persistent or heritable change in the processes which control gene expression (and thus differentiation). In epithelial tissues or the surface cell layers of, for example, the cervix, intestine, or skin, the mutational theory for cancer would give rise to only one type of cancer cell. "In fact, what we observe is cancerous cells giving rise to other cells which differ from the original not only in appearance but also in that they do not proliferate. Since proliferating cancerous cells predominate in a cancer, the affected part of the tissue grows excessively, producing a lump or tumor."

If, in the tumor, the cancer cells stay in their "homeland", the tumor will be benign, but if they begin to emigrate and form colonies elsewhere it will be malignant. One of the factors which normally regulate tissue growth and prevents cells from colonizing is physical contact to a surface and their position relative to one another. An example of this is the control of the growth of skin tissue.