The reasons why cancer develops are complex and varied. Medical scientists are beginning to unravel the molecular basis for this common disease with a view to eventually controlling it

CANCER AND ONCOGENES

Richard Vile

IMAGINE the Earth as a single "body" in which the people form the individual working parts. Each person would have a function that contributed both to the running of the constituent "organs" (the countries) and to the day-to-day operation of the body as a whole.

Such global cooperation would require intricate coordination between each and every individual. Detailed regulations would control each person's activities. Close supervision of reproduction would be necessary, to ensure that everyone would be replaced when they died, at the correct rate and in the correct proportions.

This Orwellian picture of the world may seem far-fetched, not least because of the enormously compels organisation it would require. Yet every one of the billions of cells in our bodies carries, and can read, a program of this level of complexity that tells it when and how to develop. The result is the integrated collection of cells that cooperate to form a human body.

It is when the reading of the program breaks down that we see disease. By studying he breakdowns, scientists are beginning to understand the molecular events that give rise to many genetic diseases. Cancer is one of the main diseases that result when the population controls in the program fail. Leading to uncontrolled proliferation of cells.

The information for this highly complicated program is contained, in code form, in the large molecule known as deoxyribonucleic acid. The molecule, DNA for short, is found in the nuclei of cells. The DNA consists of a linear sequence of four smaller component molecules, called bases.

The order of the bases, called A. T. C and G, forms a code which the cell copies into a messenger molecule called ribonucleic acid, or RNA. this molecule, which also consists of a sequence of bases, carries the information out of the nucleus and into the cytoplasm, where proteins are made.

Proteins form the major components of each cell. Proteins can form part of the structure of the cell; among their other functions, they can also serve as "signalling molecules" within the cell or between cells.

The code contained in the RNA determines the sequence of the building blocks, called amino acids, that make a protein.

The information needed to make proteins is carried in our genes. Broadly speaking, a gene is a sequence of bases in the DNA that specifies the structure of a protein. When a gene makes the protein that it codes for, scientists say that the gene is expressed.

Our genes are held in large assemblies, known as chromosomes, which are sometime large enough to be seen with an optical microscope. Every human cell carries, in its nucleus, 23 pairs of chromosomes (46 in all). The exceptions are sperm and egg cells (the gametes), which contain only a single copy of each chromosome.

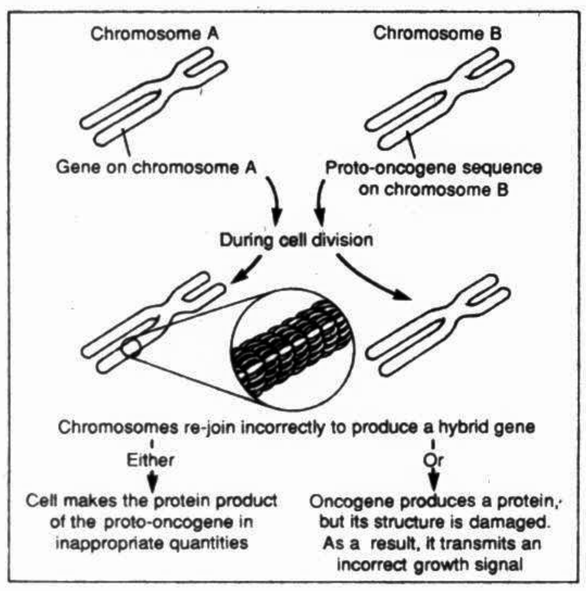
WHEN a sperm fuses with the egg, a single cell, called the zygote, results. The zygote carries the normal complement of 46 chromosomes, with two copies of each gene, one copy inherited from the egg the other from the sperm.

Every cell in an adult is derived from the zygote by a series of repeated cell divisions. As the body develops, the dividing cells become specialised, by differentiating into a variety of cell types, such as muscle, fiver or brain cells. Once a cell has reached a certain stage in the process of differentiation, known as commitment, it can no longer revert to any of the other cell types in the body.

When a cell becomes committed to a certain pathway of differentiation, one of the many specific genetic programs within its DNA becomes activated. This activation occurs in response to a wide variety of signals from the cell's environment, which are partly determined by the age and position of the cell in the developing body. The singnals may be in the form of proteins sent by the cell's near or far neighbuors. (These proteins are termed growth factors and hormones, respectively.)

All the cells of one specific type (those of the blood, for example) are described as belonging to the same differentiation compartment. Within a compartment, there are a variety of cell lineages, specialised cells with different functions.

All cells of the compartment will share the same genetic program of differentiation that has been "switched on" in the stem cells (making all the cells into blood cells, for example). The mature cells of that compartment will elaborate on the basic program to produce the specialised cells of the separate lineages. The stem cells not only express the genes required to determine the functions of the daughter cells. They also have to divide rapidly and plentifull, to ensure that each compartment has enough cells (usually many millions of cells in each lineage) to carry out its functions in the body.



So the stem cells have to express genes whose protein products drive cells through repeated divisions. These are the genes of cellular proliferation. In this way, the single cell of the zygote is eventually converted into billions of cells of varying specialisations. In the progression from stem cells to mature, differentiated cell types, the genes of cellular proliferation generally become less active. Simultaneously, the activity of those genes concerned with differentiation increases.

One way of defining a cancer is as a population of cells that has gone a certain distance along its pathway towards maturation, but in which the processes of proliferation and differentiation have become uncoupled. The result is that cancer cells divide rapidly and are no longer able to complete their program of differentiation. Cells with these qualities are said to be transformed.

A population of transformed cells usually derives from the divisions of a single cells that has accumulated damaging changes in its genes. A group of similar cells (termed "clones") derived in this way from a single parental cell in known as s clonal population.

We do not know how often potentially cancerous cells arise in the body, or exactly what the role of the immune system is in dealing with those rogue cells. But we do know that these changes can happen to most cells, diverting them from their normal program of differentiation, within most of the compartments of the body, and at many different stages between stem cell and the fully differentiated state.

Cancer eventually kills through the damage caused by the expanding number of cancer cells. The wrong types of cells progressively occupy vital room in the body : their presence hinders normal cellular activity.

Many cancer cells also eventually become able to spread form the site of origin to distant regions of the body. This process, which is called metastasis, is life-threatening as it increases the ability of the rapidly growing population of cells to damage the body.

Scientists name the study of cancer "oncology". They have known for many years that damage to a cell's DNA, known as mutation, is associated with the changes that lead to cancer, a process called carcinogenesis or oncogenesis. But current ideas on how genes change in cancer began to take shape only when researchers discovered small viruses called researchers.

By arrangement with New Scientist.

Chinese herbal medicines are not very well-known outside China and South-East Asia, but the Chinese swear by them for certain ailments, and they are becoming more and more well-known in other parts of the world.

Ginseng, Herbs, Mushroorns and Lizards

Eating Them Can Help You

Nasreen Sobhan

There are few things nastier than a bad cold. Sore throat, heavy head, blocked or running nose, and on top of everything else sometimes you lose your voice. When that happens to me, I take Chinese herbal medicines. A couple of doses of Chinese cold tablets and I am well on the way to a cleared head, and after one dose of Balangan I can talk again. Miraculous? I don't know, but it works.

Chinese herbal medicines are not very well-known outside China and South East Asia, but the Chinese swear by them for certain ailments, and they are becoming more and more well-known in other parts of the world. There are remedies for everything from age spots to insomnia to kidney stones.

Take, for example the Musk plasters. They smell quite strong, but are very effective in the relief of muscular aches and pains of all kinds. If you want something extra, use White Flower Oil, a famous Chinese liniment which is said to cure all pains starting from headaches to rheumatism. The manufacturers say that you can apply it to the affected parts, or swallow it if you so prefer. In fact they say some foreigners enjoy White Flower Oil mixed and eaten with rice !

For those who are concerned not so much with aches and pains as with more intimate problems, a cure is available for them in the form of snore drops. A couple of Datong snore drops in each nostril at bedtime are guaranteed to stop you snoring and allow your spouse a good night's sleep. If your spouse's insomnia is not however, caused by your snoring, why not let him or her try the sleep pillow, which is stuffed with a special mixture of herbs guaranteed to induce slumber in even the worst insomniac.

Having had a good night's sleep, what could be better than to greet the morning with enough vitality and energy to carry you through a working day and still enjoy a few games of squash and perhaps a night out with friends? Ginseng tea, ginseng capsules, drops and tonics are apparently failproof. According to the results of scientific experiments, ginseng helps to retard the ageing processes of brain and body cells, assists in the absorption of protein, fat and sugar, and improves stamina of all kinds.

Recently a woman who took double doses of ginseng during her pregnancy gave birth to an exceptionally hairy child, prompting speculation in the scientific community that ginseng could assist in hair growth.

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If the taking of ginseng proves to be insufficient, perhaps supplementary doses of royal jelly can help in the search for eternal youth. The queen bee feeds on royal jelly and is larger lives longer than the average bee. It may not induce growth in human beings but it is said to combat ageing and is a great tonic. One user claimed that regular doses of royal jelly had cured her sciatica; and it definitely seems to improve skin tone.

Ginseng tea, ginseng capsules, drops and tonics are apparently failproof. It helps to retard the ageing processes of brain and body cells.

Since there is a premium these days not only on youthful looks but a slim figure, help is at hand for plump people. Slimming or anti-adiposity tea, is guaranteed to help you lose weight. A cup of slimming tea at bedtime taken regularly can help the hopeful dieter lose up to several pounds a week.

Lotion 101 is the ultimate aid to good looks, for what is the use of a youthful appearance and a slim body if one has a receding hairline or worse still, is bald? Regular applications of 101 are reputed to have cured many people of baldness. It stops hair loss, and stimulates the growth of new hair on the scalp for both men and women. Sales of 101 are especially high in Japan, but it is now being exported to many other countries.

As for those who, indifferent to the uses of ginseng and slimming tea, can think only of how to relieve the agonies of gout, there is hope for them in Chinese gout medicine, which tastes awful, but has been proved to be truly effective.

The practice of Chinese traditional medicine is an ancient science which goes back many centuries. The remedies are numerous and varied, and are made up of such ingredients as herbs, deer horn and antlers, snake venom, mushrooms and dried lizards. In most cases the medicines are prescribed in the form of pills, some quite small, and taken in doses of five or six at a time. Some pills however, are as large as ping pong balls and they have to be cut up and chewed in pieces.

Apart from these oddities of shape and size, traditional medicines have been proved to be effective. Antibiotics and other modern medicines are certainly used widely in the case of more serious illness.

Although these are no cheaper than western medicines, the herbal and natural preparations have the advantage of being both effective and without side-effects. So why not try one next time you feel poorly?

• A freelance journalist who specialises in travel and health writing, Ms. Nasreen Sobhan now lives in Beijing with her Bangladeshi diplomat husband.

AIDS Orphans on the Rise

Apart from creating a large number of orphans, AIDS now seem to pose a threat to children themselves. by Nassali Tamale

ACQUIRED Immune Deficiency Syndrome (AIDS) is no mystery to the children of Rakai district in Uganda.

It is not uncommon for young children to say, "Mummy is also going to die," upon the death of their father from the disease.

Eight years after the first case of AIDS was identified in Rakai, in many villages one now finds households run by teenage AIDS orphans. These children are often malnourished, in need of proper healthcare and lacking education.

Of Uganda's two million orphans, 1.5 million have lost parents to AIDS, according to Manuel Pinto, President of the newly-formed Uganda Community-Based Association for Child Welfare (UCBAC). In Rakai district alone there are now 50,000 orphans.

Sometimes AIDS claims both parents, but children are also frequently abandoned if one parent, often the mother, survives and decides to move to a different part of the country.

While extended family networks can absorb some of these children, the scale of the problem is so great that Ugandan society's traditional safety net can no longer cope.

Even when relatives can take charge of the orphans, they are often elderly and impoverished and cannot provide proper nutrition or care. There have even been cases for young AIDS orphans who have been forced to fend for themselves in the former home of their parents.

Orphanages do not seem to offer a solution to the problem. Pinto says that when children are taken into care, they often lose their parents' property through theft or neglect.

Land is usually the most valuable asset left to them. Once the parents die, landlords seize the opportunity to evict the children, usually on the grounds that they sold the plot of land to the parents, not the children. If the land is left idle then neighbours will encroach upon it.

Robinah Kashadha, Rakai District Administrator, says that the number of land cases in which children are threatened with eviction is increasing. In many cases, the children are so helpless that she personally handles their cases for them.

Another problem with orphanages is that children who are brought up in such institutions may become uprooted from society, according to Molly Nassuna, UCBAC representatives in Rakai.

It is usually children from poor families who end up in orphanages. Rich parents often take precautions in case they should die prematurely as the recent trend of setting up trust committees involving officials from the Roman Catholic Church shows.

With the number of orphans continuing to rise, orphanages will only be a partial solution. Asks Nassuna: "Where will the resource come from to institutionalise all of them?"

Pinto is calling for a flexible community-based approach tailored to the particular circumstances of the orphans. If old enough, the eldest child can become the head of the family and a neighbour become responsible for looking after them.

Basic provisions such as clothing and food have to be provided to the many children who are left penniless because their parents use up all their income for medical treatment

Says one woman from Lwanda in Rakai district: "All along we were led to believe that children aged between five and 15 were not at risk." But recently cases have been reported of children of six and nine years being infected. -- Depthnews Science /PANOS

A Pill Against Cancer : More than Just a Dream ?

With regard to intestinal cancer molecular biologists have found an answer to the question as to the cause of malignant tumors.

A team of scientists at the Max Planck Institute for Medical Research in Heidelberg have succeeded in deciphering parts of the degenerative process of intestinal cancer. Now their efforts are being directed at methods of intervening in this process so that it can be interrupted.

As a rule cancer is triggered when certain, normally harmless genetic factors (genes) undergo mutation as a result of external causes. Here, for example, a single element in the molecular chain of this gene, the DNA, is replaced by another element. As each gene has at least hundreds, and sometimes even hundreds of thousands of such elements,this seems to be only a slight modification. Nevertheless, under certain circumstances it can have devastating consequences. The reason for this is that the gene supplies the instructions for synthesizing protein molecules, and as a result this can bring about a defective protein.

Proteins are made up out of a good 20 different amino acids. A mutation in the gene can result in an exchange of elements occurring also in the attendant proteins; valine could be incorporated, for example, instead of glycine. But this can have definite consequences for these proteins because they all have convoluted and interwoven chains of molecular structures of an extremely complex nature; and it is the structure of the respective proteins which determines their particular behavior. This is because this structure ensures that the actual and extremely minute function complex of such chains is characteristically turned outward, thus offering access point to its reaction partner. Thus, if this spatial arrangement is altered by the exchange ofjust a single amino acid, this can have fatal consequences.

It is precisely this kind of form alteration which scientists in Heidelberg have been tracing. They were able to demonstrate this on a protein called P 21 because of its low molecular weight of 21,000 units. This protein is attributed to a genetic factor which has long been known as an oncongene : a gene whose mutation can lead to the formation of tumors. Cancer researchers have so far been able to identify about 50 of these oncongenes in human genes. In the process it has been discovered that these are very often involved in the transmission of growth signals from the call surface to the cell nucleus, and that one of them reacts with an especiall energy-rich molecule, called guanosine triphosphate, better know simply as GTP. This is P 21.

In the case of intestinal cancer it was possible to show that defective P 21 was formed in 50 percent of the cases, and in cancer of the pancreas the proportion was up to 90 percent, P 21 is part of a signal chain which transmits growth instructions into the cell's interior. The trigger is a messenger substance, which makes contact on the outer wall of the cell and attaches itself to the P 21. In this condition the protein bonds itself with the energy-rich GTP and is now in the position to connect itself with a receptor molecule in the cell's interior.

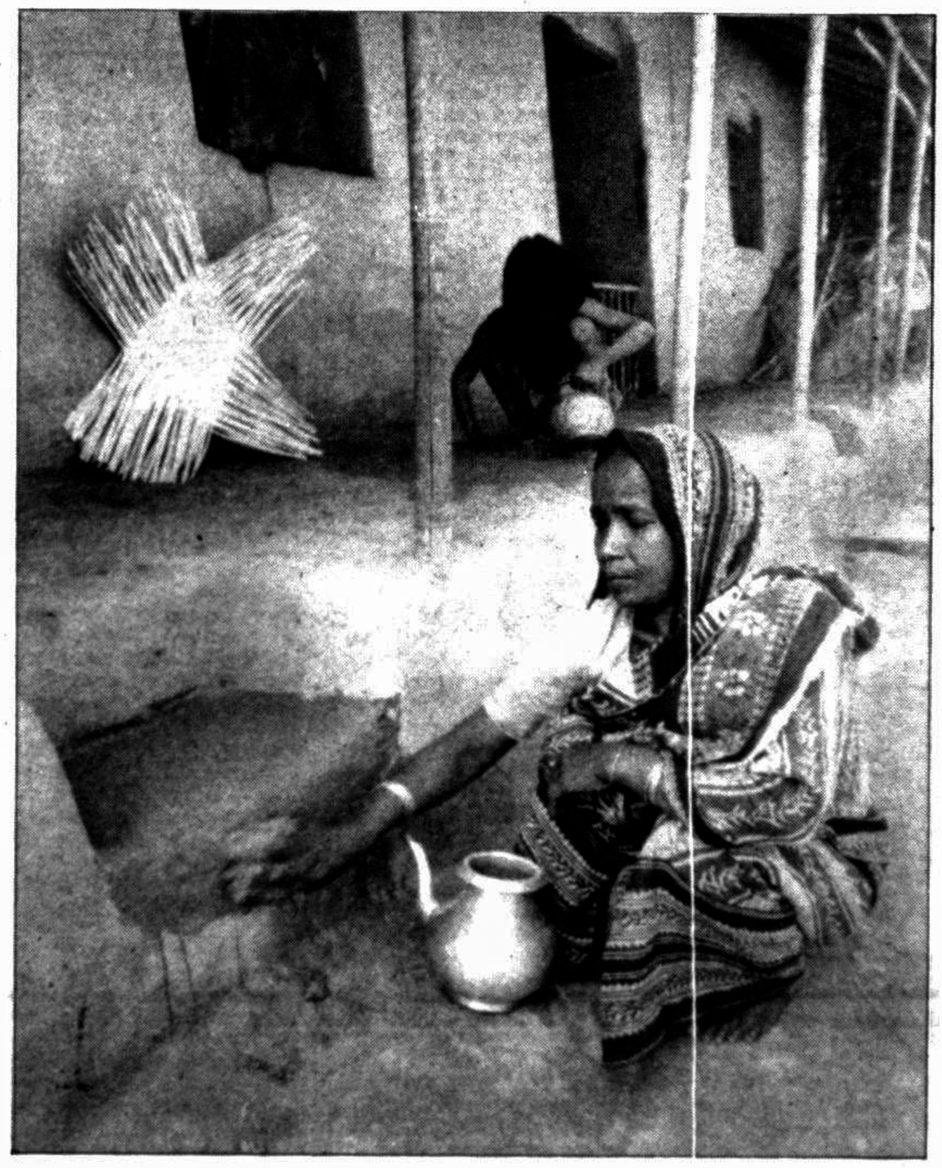
Normally this signal is immediately interrupted again due to the fact that a part of the GPT molecule is split off, which breaks the bond to the receptor molecule. However, in the case of defective P 21 the receptor molecule remains coupled and now incessantly transmits the growth and cell division instructions within the cell. Thus it is transformed into an uncontrollably multiplying cancer cell : a tumor begins to proliferate.

At the Max Planck Institute in Heidelberg, scientists succeeded in making the distinction between normal and defective P 21 literally visible. It was found that two adjacent loops protrude out of the relatively compact proteins, which have string-shaped and helical structures. One of the loops is responsible for bonding the receptor molecule, while the other is involved in the bonding of GPT. It was on the second loop where the false amino acid for defective P 21 was actually found. This tiny alteration of the characteristics of the loop prevents the splitting off and "provides the receptor molecule with a permanent parking place", as one of the scientists expressed it .

This success, which has been hailed as "pioneering", will now be pursued in two directions in Heidelberg. On the one hand, researchers are trying to discover similar disturbance mechanisms for other protein changes, which also lead to tumor developments. On the other hand, possibilities are being sought to neutralize the fatal effect of amino acid exchange.

The problem is that such an effect must be restricted to the defective proteins- normal P 21 may not be effected, so as not to interfere with the growth of healthy cells. At present, computer simulation of the molecular processes is being used to try to design suitable substances. If this is successful, it will still be many years before an appropriate medication arrives on the market.Be that as it may : "A pill against certain types of cancer is no longer pure utopia", in the opinion of Dr. Fred Wittinghofer, one of the team leaders in Heidelberg.

— GRS Feature.



'We shall not live in dilapidated houses. We shall repair our houses and work toward constructing new houses at the earliest' — is one of 16 'decisions' adopted by the Grameen Bank which offers services, among others, in health.

Cells Aid In Vitro Fertilization

Despite more than a decade of experience, the success rate of in vitro fertilization (IVF) in the United States, Britain, France, Australia and other major centres remains stubbornly low.

The initial birth in Singapore from fertilization outside the human body was in 1983, four years after the world's first IVF baby was born in Britain.

Using the standard IVF technique of mixing sperm and eggs in the laboratory before implanting the embryo in the human womb, nearly 29 per cent of the women treated by the Singapore General Hospital's centre for assisted reproduction were able to conceive and successfully carry their pregnancy to full term.

But although this was one of the highest rates of any country, it still means that an average of less than one in three of the women unable to conceive naturally can have a child with the aid of modern reproductive technology.

Research being carried out at the National University Hospital in Singapore suggests that a promising avenue for increasing the rate of test-tube fertilization, and then carrying it through the full cycle of pregnancy to healthy live birth, is to replicate a key part of the human womb in the laboratory.

In a series of experiments since 1988 that were reported in the British medicl journal Human Reproduction, a National University Hosptial research team headed by Arif Bongso, associate professor in the hospital's department of obstetrics and gynecology, has succeeded in cultivating cells of the fallopian tube and using them as a bed for producing successful IVF pregnancies.

Under natural conditions of human reproduction, eggs released by the ovaries into two fallopian tubes on either side of the uterus are fertilized by sperm deep inside the tubes.