Using enemy resources

THE ENERGY SOURCE OF CANCER CELLS MAY BECOME THEIR UNDOING, SAYS **S ANANTHANARAYANAN**

Except that they have started multiplying rapidly, cancer cells are really the body's very own. Methods to destroy cancer cells thus attack healthy cells as well, and this is the great challenge in therapy. Different ways have, hence, been devised for getting drugs only to the cancer cells and leaving the healthy ones alone. A leading strategy involves putting the drug into a container that is opened only when needed. Other methods are to control the size of particles to make them more likely to enter and stay within the tumours, or even methods of guiding containers by magnetic effects or opening them with sound signals.

Ran Mo, Tianyue Jiang, Rocco DiSanto, Wanyi Tai and Zhen Gu of the University of North Carolina and at Nanjing, China, report in *Nature Communications* a method of encapsulating the drug in a container that needs energy to be opened. As cancer cells are rich in energy sources, this feature helps both in delivery of the drug as well as selecting the cancer cells. The method developed proves a principle that could dramatically improve the effectiveness of current cancer therapy.

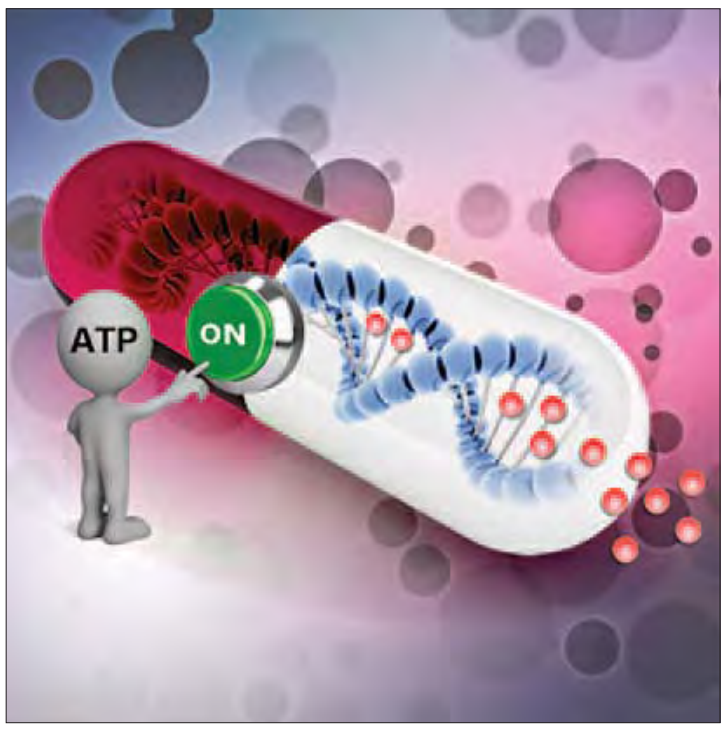
Drug delivery systems now use nanocarriers of drugs, with methods to improve targeting, so that drugs accumulate where the tumours are found and then their release within the tumour cells, triggered by different stimuli. The carriers could be *liposomes*, which are tiny spherical containers with a thin, fatty surface or hollow particles made of polymers or inorganic substance. And the triggering stimuli could be external, like temperature, light, magnetic fields or sound, or physiological, like how acid the environment has become, chemical activity, the presence of catalysts, like enzymes, or the level of glucose.

For example, a particle that becomes engulfed by a cell would release its contents if it had an acid sensitive surface to react with the interior of the cell. Variations of an abundance of agents that affect polymer covers of particles allow the release of drugs within cells where the concentration is right. Specific enzymes that are produced inside specific tumours can also be the agents to release drugs encapsulated in the relevant outer cover.

The North Carolina and Nanjing group took a different route and looked at the level of available energy sources within cells to trigger the release of drugs contained in biomolecular packaging. While the transfer of energy is mechanical in normal circumstances, like when a reaction is brought about by heat, the activity within cells is powered by energy released by reversible chemical changes. Energy from photosynthesis, for instance, is not transferred directly to generate hydrocarbons but is first stored as the energy of conversion of a specific molecule, called Adesnosine Triphosphate (ATP), which changes form from its precursor, Adenosine Diphosphate (ADP). This molecule then stores a unit of energy that it can give up and activate another chemical or electric change to enable metabolic action of the cell by switching back to ADP.

ATP can come about by different processes and is then used by enzymes and some proteins to bring about different cellular processes. ATP gets generated usually by the conversion of glucose into carbon dioxide, a process called *cellular respiration*, or by the conversion of glucose into other forms within cells, a process called. *Glycolysis*, or by processes that involve by-products of a breakdown of carbohydrates and fats.

ATP keeps getting converted back to ADP and again to ATP and is recycled many times. The human body, for instance, contains only 250 grams of ATP and this intermediates all processes of the body, which turns ATP over to the equivalent of the body weight itself within a day.



ATP and drug release

To use ATP as the trigger for drug release, the researchers created drug carriers in the form of a nanogel that consisted of DNA, protein and sugar. The DNA strand was tuned to detect ATP and also to hold the drug *Doxorubicin* within its structure. DOX is a model anti-cancer drug, used against many types of the disease, including cancer of the breast and ovaries and acute leukaemia. When the carrier attaches to ATP, this causes a change in its structure, which releases the drug. The other components of the carrier helped compress the carrier structure and to dock with portions that are found on cancer cells.

Trials, which were done with live mice that had been induced to grow cancerous, and also human breast cancer cells, showed a positive, clearly ATP-level dependant release of the drug in the fluid found within the cell. The medium around the cell contains little ATP, while the interior of the cell has ATP to enable metabolism. In the case of cancer cells, there is enhanced metabolism and many cancer cells contain enhanced levels of ATP. Control tests, with ATP analogues or a non-ATP responsive carrier, were negative, which validates the positive results.

The method was, thus, an ATP-triggered drug release system that offers new avenues for exploration of more sophisticated drug delivery, which joins hands with the processes that go on within cancerous cells and makes use of the cell resources to select the cells and deliver the drugs once inside the cells.

THE WRITER CAN BE CONTACTED AT simplescience@gmail.com

Reduction in tumour size at Day 14 under different forms of treatment.

ORGANISATION OF DNA

GENOME SIZE IS LESS IMPORTANT THAN THE NUMBER AND IDENTITY OF FUNCTIONAL GENES AND THE SEQUENCES THAT CONTROL THEIR EXPRESSIONS, WRITES **TAPAN KUMAR MAITRA**

The genome of an organism or virus consists of DNA (or for some viruses, RNA) that contains one complete copy of all the genetic information of that organism or virus. For many viruses and prokaryotes, the genome resides in a single linear or circular DNA molecule, or a small number of them.

Eukaryotic cells have a nuclear genome, a mitochondrial genome, and, in the case of plants and algae, a chloroplast genome as well. Mitochondrial and chloroplast genomes are single, usually circular DNA molecules, resembling those of bacteria. The nuclear genome generally consists of multiple DNA molecules dispersed among a haploid set of chromosomes. A haploid set of chromosomes consists of one representative of each type of chromosome, whereas a diploid set consists of two copies of each type of chromosome, one copy from the mother and one from the father. Sperm and egg cells each have a haploid set of chromosomes, whereas most other types of eukaryotic cells are diploid.

Genome size is usually expressed as the total number of base-paired nucleotides, or base pairs (bp). For example, the circular DNA molecule that constitutes the genome of an E. coli cell has 4,639,221 bp. Since such numbers tend to be rather large, the abbreviations Kb (kilobases), Mb (megabases) and Gb (gigabases) are used to refer to a thousand, a million or a billion base pairs, respectively. Thus, the size of the E. coli genome can be expressed simply as 4.6 Mb.

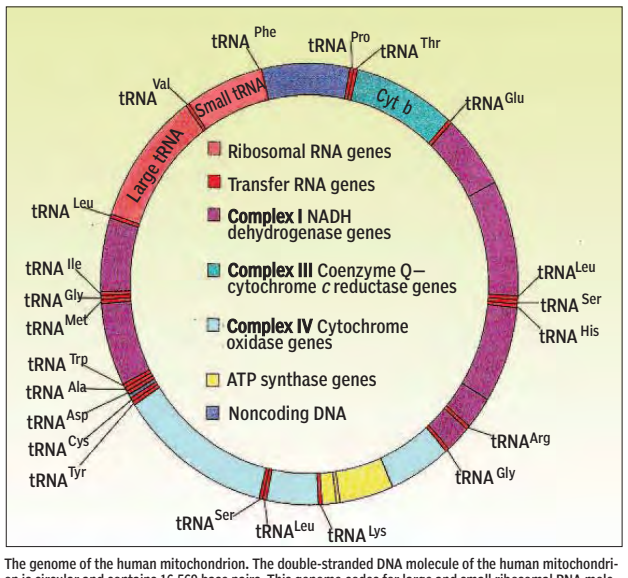
The range of genome sizes observed for various groups of organisms reveals a spread of almost eight orders of magnitude, from a few thousand base pairs for the simplest viruses to more than 100 billion base pairs for certain plants and amphibians. In terms of the total length of DNA, this corresponds to a range of less than 2 μm of DNA for a small virus, such as SV40, to roughly 34 metres of DNA (more than 100 feet!) for certain plants, such as the wildflower Trillium.

Broadly speaking, genome size increases with the complexity of the organism. Viruses contain enough nucleic acid to code for only a few or a few dozen proteins, bacteria can specify a few thousand proteins and eukaryotic cells have enough DNA (at least in theory) to encode for hundreds of thousands of proteins. But a closer examination of such data reveals some puzzling features. Most notably, the genome sizes of eukaryotes exhibit great variations that do not clearly correlate with any known differences in organismal complexity. Some amphibians and plants, for example, have gigantic genomes that are tens or even hundreds of times larger than those of other amphibians or plants, or of mammalian species.

Trillium, for example, is a member of the lily family that has no obvious need for exceptional amounts of genetic information. Yet its genome size is more than 20 times that of pea plants and 30 times that of humans. Moreover, a single-celled amoeba has a genome that is 200 times the size of the human genome. We have no idea why lily plants and amoebae possess so much DNA. Its presence highlights the fact that most eukaryotic genomes carry large amounts of DNA of no known function, a phenomenon we will discuss shortly.

In the final analysis, genome size is less important than the number and identity of functional genes and the DNA sequences that control their expression.

THE WRITER IS ASSOCIATE PROFESSOR, HEAD, DEPARTMENT OF BOTANY, ANANDA MOHAN COLLEGE, KOLKATA, AND ALSO FELLOW, BOTANICAL SOCIETY OF BENGAL, AND CAN BE CONTACTED AT tapanmaitra59@yahoo.co.in



The genome of the human mitochondrion. The double-stranded DNA molecule of the human mitochondrion is circular and contains 16,569 base pairs. This genome codes for large and small ribosomal RNA molecules, transfer RNA (tRNA) molecules (each identified by a superscript with the three-letter abbreviation for the amino acid it carries), and sub-units of a number of the proteins that make up the mitochondrial electron transport system complexes. The tRNA genes are very short because the RNA molecules they encode each contain only about 75 nucleotides.

Scientists said gamma rays coming from the centre of the galaxy could not be explained by any known phenomenon — except dark matter itself.

'We may be seeing dark matter for the first time'

ADAM WITHNALL REPORTS ON AN IMAGE OF MYSTERIOUS GAMMA RAYS FROM THE CENTRE OF THE MILKY WAY

Scientists in Boston have released an image of what they say could be the first time dark matter has ever been captured on a National Aeronautics and Space Administration telescope. The new study of gamma rays captured by the US space agency's Fermi apparatus picked up a signal that "cannot be explained by other alternatives" — meaning that by the process of elimination, what we are seeing has a high chance of being the elusive substance.

Dark matter makes up most of the material universe and yet we know very little about what it consists of or how it interacts with everything else. But by analysing an image of gamma rays coming from the Milky Way, a joint team from Harvard, the University of Chicago and the Massachusetts Institute of technology in Boston has been able to pick out a bright core at the centre of our galaxy that is only currently explained by models of dark matter itself.

Experts have speculated for some time that dark matter is most likely to be observed at the centre of the galaxy — large quantities of dark matter attract normal matter, forming a foundation upon which visible structures, such as galaxies, are built.

"This is the most compelling signal we've had for dark matter particles — ever," said Dan Hooper, speaking to *New Scientist* from the Fermi National Laboratory in Batavia, Illinois. "At this point, there are no known or proposed astrophysical mechanisms or sources that can account for this emission," he said. "That doesn't rule out things that no one's thought of yet, but we've tried pretty hard to think of something without success."

The team took publicly available images of gamma ray light shot out from the Milky Way and, piece by piece, removed every pixel that could be explained by a known phenomenon like a supernova or particles colliding with interstellar gas.

"Our case is very much a process-of-elimination argument. We made a list, scratched off things that didn't work, and ended up with dark matter," said co-author Douglas Finkbeiner, a professor of astronomy and physics at Harvard.

"Our case is very much a process-of-elimination argument. We made a list, scratched off things that didn't work, and ended up with dark matter," said co-author Douglas Finkbeiner.

One possible theory suggests that dark matter is made up of brilliantly named Weakly Interacting Massive Particles — or Wimps — which would collide to produce gamma rays at the energies detected by the Fermi telescope.

Tracy Slatyer, a theoretical physicist at MIT, said, "This is a very exciting signal, and while the case is not yet closed, in the future we might well look back and say this was where we saw dark matter annihilation for the first time."

THE INDEPENDENT

PLUS POINTS

The amount of anigorufone, a natural compound lethal for nematodes, found in the Ykm5 variety is twice that in the more popular GN variety.

Inbuilt resistance

Banana yield the world over is severely hampered by a burrowing nematode pathogen, *Radopholus similis*, which penetrates the root and topples the plant. One of the major banana cultivars, Grade Naine (GN), is highly susceptible to nematode infection but the Yangambi km5 (Ykm5) variety is resistant. A study published in *Proceedings of the National Academy of Sciences* on 7 January indicates which phytoalexins are behind Ykm5's resistance to nematodes.

Phytoalexins are phenolic compounds responsible for resistance of banana to nematodes. Researchers extracted nine phytoalexins from both GN and Ykm5 and found that phytoalexins (2S,3R)-2,3-Dihydro-2,3- dihydroxy-9 phenylphenalen-1-one, isoanigorufone, and anigorootin present exclusively in Ykm5. Methylirenolone was found only in GN. Compared to GN, twice as much anigorufone was found in Ykm5.
Using modern imaging techniques, spectroscopic analysis and bioassays, the researchers also found that plants accumulated phenylphenalenones (a kind of phytoalexins) specifically in the infected root tissues of both resistant and susceptible varieties. "Pathogen resistance is not due to lone production of phenolic compound, rather it is because of its variant concentrations in specific root regions that are highly susceptible to nematode attack," said Dirk Holscher, lead author of the study.

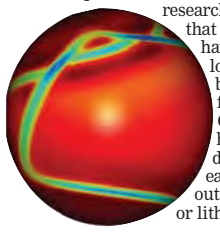
The preliminary findings indicate that of all the compounds screened, lipid soluble anigorufone is the one that is highly toxic to the pest. Inside the infected root tissues, anigorufone accumulates as lipid droplets and causes a metabolic dysfunction in the nematode. "This is the first study wherein researchers were able to dissect a part of the resistance mechanism in Ykm5 variety," says Dirk De Waele from the department of biosystems, University of Leuven, Belgium.

"We believe that such studies will provide substantial evidence for the development of recombinant banana varieties which are nematode resistant. It would also help reduce the pesticide load in banana plantations that poses serious threat to both humans and the environment,"? says? Rony? Swennen, professor at the University of Leuven, Belgium, who led the research team.

SMRITI SHARMA/CSE-DOWN TO EARTH FEATURE SERVICE

Tectonic plates

In what could be a probable answer to an enduring puzzle about how earth's tectonic plates were created, thrilling research indicates that these may have taken as long as one billion years to form. Geophysicists have discovered that earth's outermost layer, or lithosphere, was weakened by movement in viscous layers below it — a process when one plate dives below another.



Simulation shows how plate-tectonic boundaries emerged because of inherited damage following a shift in plate-tectonic driving forces.

Starting roughly four billion years ago, cooler parts of earth's crust were pulled downwards into the warmer upper mantle, damaging and weakening the surrounding crust. The process happened again and again until the weak areas formed plate boundaries.

"Over a much longer period, the same process could have created many tectonic plates. We have got a physical mechanism to explain how it could have happened," study author David Bercovici from Yale University explained. The process began about four billion years ago and caused complete fractures some three billion years ago. To investigate how the plates formed, Bercovici and Yanick Ricard of the University of Lyon in France developed a computer model of earth's crust as it may have existed billions of years ago. It included a low-pressure zone at the base of the crust that caused a piece of the crust to sink into the upper mantle — mimicking conditions thought to have occurred early in the earth's history. As the process repeated over time, it created a large tectonic plate with an active subduction zone.

According to Robert Stern, a geologist at the University of Texas in Dallas, there is no firm evidence of plate tectonics earlier than one billion years ago, but the new mechanism behind plate formation is "the first interesting example of how it might have occurred".

INDIA ABROAD NEWS SERVICE