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Peeping into the living cell

Another step has been taken to understand goings-on within living cells, says S.Ananthanarayanan.

The last two centuries have seen great strides in understanding the process of life. It was nearly 200 years after the first glimpse of cells through the microscope, in 1665, that living things were seen to be made up of cells, within which the vital functions of life take place and which arise as copies of other cells. With advances in technology, in molecular biology and genetics, many of the components of cells and their interactions are now largely known. But there is a long way to go, as the work of a team at the ***Max Planck Institute for Biology of Ageing***, Cologne, with associates from Italy, Sweden, the UK and Korea have found. In their paper just published in the journal, ***Cell Biology***, Mugen Terzioglu, Benedetta Ruzzenente, Julia Harmel, Arnaud Mourier, Elisabeth Jemt, Marcela Davila Lopez, Christian Kukat, James B. Stewart, Rolf Wibom, Caroline Meharg, Bianca Habermann, Maria Falkenberg, Claes M. Gustafsson, Chan Bae Park, and Nils-Goran Larsson, have shown by a real life trial that a firm conclusion reached after laboratory tests is not true.

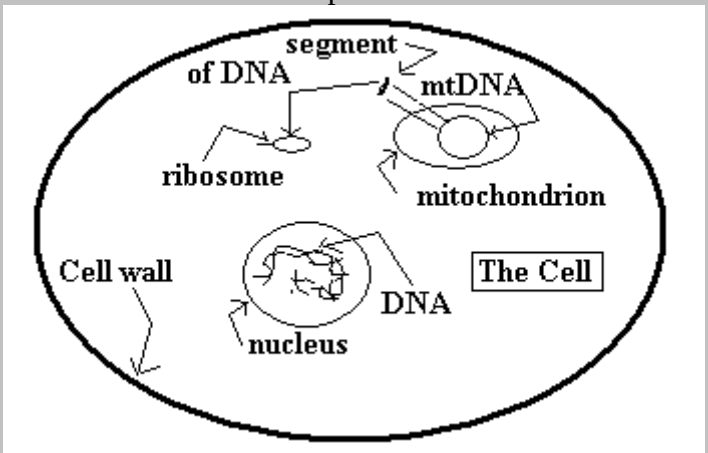
Cell structure

Animal and plant cells consist of a membrane envelope that contains compartments which have different functions. The most important is the ***nucleus***, which contains the ***DNA***, which is the code molecule which spells out the action and functions of the cell. The actions of the cell are actuated by different proteins, each of which brings about a specific action because of its special chemical profile or shape. And it is the DNA which tells the cell what proteins to make and hence, what actions to carry out.

The DNA molecule is sequence of groups of three chemical units. There are only 4 of these units and so there can be 4x4x4=64 different groups of three. But many groups are treated as stand-byes or start and end markers and finally, the sequence, which can be millions of units long, consists of choices from only 20 different groups. Each group helps synthesise a chemical unit called an ***amino acid*** and each segment of the DNA chain, then, specifies a sequence of amino acids, which makes up the protein. And then,

there is the process by which the cell picks up the information from the DNA and transfers it to cell components that join amino acids and assemble proteins.

The segments of DNA that specify proteins are first copied on to messenger units called ***mRNA***, which resemble the bit of DNA that they represent. mRNA carry the information to the next important component of the cell, the ***ribosomes***, where proteins are assembled. This assembly uses other DNA-like units called transfer or ***tRNA*** and ribosomal or ***rRNA*** to collect and link amino acids to form the protein.



The other important component of the animal cell is the ***mitochondrion.*** Mitochondria are bodies within the cell, which, among other functions, generate the chemical units used for transfer of energy within the cell. For this role, they are called the '***powerhouse of the cell'***. Cells need huge energy, the pancreas cell to create insulin, or the brain cell to fire an electrical signal to start and action, or a thought, and so on. This energy is made available by he mitochondria and some cells have thousands of these 'energy converters'. But mitochondria have other important functions too, like creating the proteins that help the cell convey and receive signals, to develop the cell as a particular kind of cell, regulating the cell's growth and also its death and hence the ageing process. They are also involved in the production of substances like cholesterol and components of haemoglobin, in the blood. The sperm cell, which only needs to move, has only one mitochondion, while the ovum, which has to grow into the embryo, has thousands. The result, incidentally, is that at fertilization, the single mitochondrion of the sperm cell is lost and when the fertilized egg multiplies, the mitochondria are all from the mother. Mitochondria also have their own nucleus and DNA, called mtDNA, which is in addition to the DNA within the nucleus of the cell.

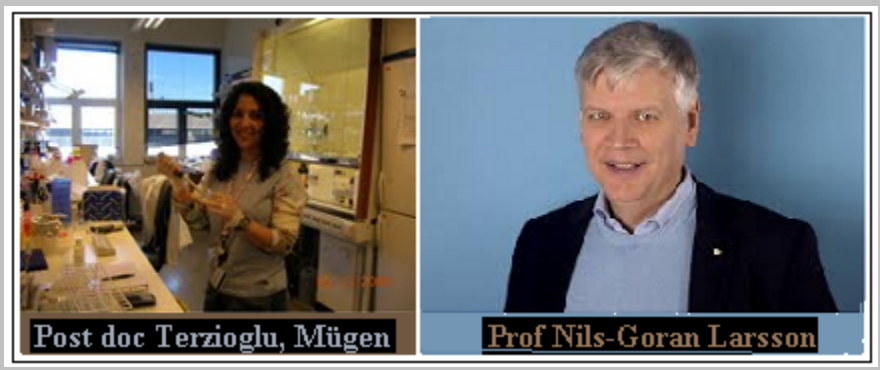
The Mitochondrion DNA is similar in many ways to the DNA of bacteria and it is thought that Mitochondria may have arisen through a capture of a bacterium by the cell, sometime in the course of its evolution. The mtDNA is contained in several copies, in the form of a circle, as found in bacteria. The proteins that arise from the code in the mtDNA are for the action of using oxygen and glucose for generating energy transfer units, and also to create some of the RNA of ribosomes, including the 22 tRNA that are required for converting the information from mRNA into protein. How the mtDNA function or any defects in the function, which are associated with a number of diseases and ageing, are thus areas of great interest. One gene in the DNA, and the associated protein,

Mitochondrial transcription termination factor 1, MTERF1, has been identified as an important agent in the process of decoding DNA information mRNA and the generation of proteins in ribosomes. *"MTERF1 has been reported to couple rRNA gene transcription initiation with termination and is therefore thought to be a key regulator of mammalian mitochondrial ribosome biogenesis,."* say the authors in the abstract of their paper in ***Cell Biology***.

Details of the action of MTERF1 have been worked out through tests conducted on cell cultures and the role of MTERF1 has been considered as known and understood for 20 years. But the team at the Max Planck Institute made an assay of the role of the protein in a living model, and arrived at surprising results.

In vivo trial

The mitochondrial DNA is known to have two strands, the heavy (H) and the light (L) strands. The copying of the sequence of the strands has been proposed to be regulated by the MTERF1 protein, strongly promoting correct copy of segments of the H strand. But studies ***in vitro***, or using cell cultures in the lab, have yielded different results and have not answered many questions, perhaps because all real conditions cannot be created outside a living organism. –Post-doc researcher, ***Mugen Terzioglu*** and colleagues used genetic engineering methods to modify mtDNA in living mice so that the MTERF1 gene was not expressed. '***Knocking out'*** the gene and hence the protein should have blocked the strong effect that was attributed to the protein and resulted in mice with several deficiencies. Surprisingly, all functions of the gene-depleted mitochondria were intact and the gene-depleted mice were thriving. Analysis of different organs and cell components of the 'knock-out' mice resulted in all parameters, particularly of generation of energy transfer units, being found unaffected. –Studies of the action at the places in the mtDNA sequence, where MTERF1 was known to bind, again showed no changes despite there being no MTERF1 proteins. It appears the protein has no effect on the H strand of the DNA, but serves, instead, to block the L strand, which became active in 'knock out' mice.



The finding will change the way scientists have looked at proteins and their role within cells. In particular, they open a new perspective into the mechanism of translation of DNA information. "The findings also illustrate the fact that ***in vitro*** systems like cell culture can only to a certain extent represent a natural physiological condition. Consequently, the insights gained in vitro must always be verified in vivo," says Mügen Terzioglu, the lead author of the paper.