

NEWS ITEM

IISc researchers dispatched directly proteins into cells, first of its kind

In a breakthrough that might have huge medical implications, researchers at Bengaluru's Indian Institute of Science (IISc) have used a novel strategy to directly deliver proteins into mammalian cells. Proteins are big molecules and so cannot enter the cells on their own. So a team led by Govindasamy Mugesh from the institute's Department of Inorganic and Physical Chemistry substituted a hydrogen atom of the protein with an iodine atom to achieve a nearly sixfold increase in protein uptake by cells. The increased protein uptake was seen even when the molecular weight of the protein was 28,000 dalton, meaning the protein was much bigger in size than most of the therapeutic small molecules. The researchers also tried replacing a hydrogen atom with an atom of bromine and chlorine but the uptake was way lower than when iodine was used. In the case of bromine, the uptake of proteins increased by only about two times, while the uptake increased only marginally when chlorine was used. The results were published in the journal *Angewandte Chemie*. Other researchers have tried tagging the protein with cell-penetrating peptides, supercharged proteins and even used virus-like particles to ferry the proteins into cells. But these approaches have severe limitations including altering the protein function inside the cell. For this reason, most of the applications involving proteins are directed to extracellular targets. Proteins inside the cells get impaired during diseased conditions such as neurodegenerative and cardiovascular disease. Supplementing the cellular protein in such cases becomes important and this is where the method used by the IISc team will come in handy. The team had to first synthesise a green fluorescent protein with one hydrogen atom being replaced with an iodine atom. Iodine forms a halogen bond with a specific receptor (caveolin) that transports the protein from the cell membrane surface to inside the cells. To be functionally useful, the proteins must enter the cytoplasm of the cell. However, the moment proteins are ferried into the cell by the receptor they are trapped inside the endosomes and transported to lysosomes, where the proteins are degraded. Significant decrease in protein concentration as measured by the fluorescence intensity was seen by the researchers after 24 hours. To overcome the problem of protein degradation, the team treated the cells with a peptide (ppTG21).

Detection of oral cancer is possible through lymph node biomarkers

By looking out for five biomarkers, it is now possible to tell in advance if a person with oral cancer of the gum and cheek has lymph node metastasis even before surgery is undertaken, a study has found. The ability to correctly predict absence/presence of lymph node metastasis in oral cancer patients is 80-90% based on the five biomarkers, a team led by Partha Majumder from the National Institute of Biomedical Genomics, Kalyani, West Bengal, has found. As a result, an oral cancer patient can be spared of a neck dissection to investigate if the cancer has spread to the lymph nodes in case the five biomarkers are absent. Lymph node dissection increases morbidity. However, if the patient tests positive for even one biomarker then an aggressive treatment would be required. An oral cancer patient with cancer spread to the lymph node has a 50% lower chance of survival for five years or more compared with patients in whom it has not spread to the lymph node.

In oral cancer patients, the cancer cells tend to commonly spread to the lymph node in the neck. But not all oral cancer patients have the tendency for the cancer to spread to other organs (metastasis). So in some patients, the cancer would have spread to the lymph node even at an early stage of oral cancer, while in some patients with advanced (T4 stage) oral cancer, the cancer would not have spread. To find out what determines lymph node metastasis in oral cancer patients, the team studied two groups of patients — those with lymph node metastasis and those with advanced oral cancer but without lymph node metastasis. Totally, 72 patients belonging to these two groups were studied by a team led by Dr. Rajiv Sarin, Director of Advanced Centre for Treatment, Research and Education in Cancer (ACTREC), Tata Memorial Centre, Mumbai and co-author of the paper. The team found that lymph node metastasis was associated with five genomic biomarkers. The results were published in *International Journal of Cancer*. There are five genomic features or biomarkers of lymph node metastasis in oral cancer patients. Two of these are rare, heritable DNA changes in BRCA2 and FAT1 genes. The remaining three are non-heritable (somatic) DNA alterations. The somatic DNA alterations can occur in genes belonging to three different pathways — mitotic G2/M cell-cycle pathway, homologous recombination (HR) and non-homologous end joining (NHEJ) DNA-repair pathways. The protein product of FAT1 gene functions as an adhesion molecule that keeps the

cells together. In the case of cancer, cellular adhesion property is sometimes lost and the cells tend to spread. A cell duplicates to produce two daughter cells. Many genes are involved in this cell-cycle pathway, called mitotic G2/M pathway. If DNA of one or more genes of this pathway is altered, then many adverse cellular events take place. Most importantly, chromosomes become unstable and abnormal chromosomal changes occur, eventually leading to metastasis.

Researchers from JNCASR synthesised novel molecule for spinal cord injury

Spinal cord injury can now be repaired using a small molecule (TTK21) synthesised by a team led by Tapas Kumar Kundu from the Molecular Biology and Genetics Unit at Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), Bengaluru, a study has found. The small molecule tested both on mice and rat models promoted regeneration and growth of new sensory and motor axons leading to recovery of sensory and motor functions in the animals with spinal cord injury. Since the small molecule cannot cross the blood-brain barrier and enter the brain, the researchers used 400 nanometre-size carbon nanospheres made using glucose, which is self-fluorescent, and attached the molecule to its surface. The non-toxic nature of the small molecule has already been demonstrated in animals. The JNCASR researchers in collaboration with a French team had in October 2018 used the same molecule to recover long-term memory in mice with Alzheimer's disease. When the spinal cord is injured, the tails (axons) of nerve cells that stretch up and down the spine are either damaged or even completely cut.

For the first time Black hole image was unearthed:

This image released on April 10, 2019 by Event Horizon Telescope shows a black hole. Scientists revealed the first image ever made of a black hole after assembling data gathered by a network of radio telescopes around the world. Photo: Event Horizon Telescope Collaboration/Maunakea Observatories. This image released on April 10, 2019 by Event Horizon Telescope shows a black hole. Scientists revealed the first image ever made of a black hole after assembling data gathered by a network of radio telescopes around the world. Scientists have been

puzzling over invisible "dark stars" since the 18th century, but never has one been spied by a telescope, much less photographed. Astronomers on April 10 unveiled the first photo of a black hole, one of the star-devouring monsters scattered throughout the Universe and obscured by impenetrable shields of gravity. The image of a dark core encircled by a flame-orange halo of white-hot gas and plasma looks like any number of artists' renderings over the last 30 years. Scientists have been puzzling over invisible "dark stars" since the 18th century, but never has one been spied by a telescope, much less photographed. The supermassive black hole now immortalised by a far-flung network of radio telescopes is 50 million lightyears away in a galaxy known as M87. The unprecedented image — so often imagined in science and science fiction — has been analysed in six studies co-authored by 200 experts from 60-odd institutions and published on April 10 in *Astrophysical Journal Letters*. The Universe is filled with electromagnetic "noise", and there was no guarantee M87's faint signals could be extracted from a mountain of data so voluminous it could not be delivered via the Internet.

Post doc opportunities:

1. Tata Institute for Genetics and Society- Bengaluru, Karnataka: Post-doctoral Fellow with the Tata Institute of Genetics and Society, inStem, Bangalore, Karnataka. To be part of a team of scientists working on gene editing in mammalian stem cells. Refer concerned website.

2. Institute for Stem Cell Biology and Regenerative Medicine- Bengaluru, Karnataka: A post-doctoral fellow position is available for a candidate with cell and molecular biology expertise. The position is to work on the molecular mechanisms of Alzheimer's disease reporting to Prof. Mahendra Rao at inStem, Bengaluru. Refer website instem.res.in

3. Indian Institute of Technology Hyderabad - Hyderabad, Telangana: Postdoctoral Position on Stem Cell Engineering and Regenerative Medicine at eNARM Lab, Department of Biomedical Engineering, IIT Hyderabad. Refer iith.ac.in.