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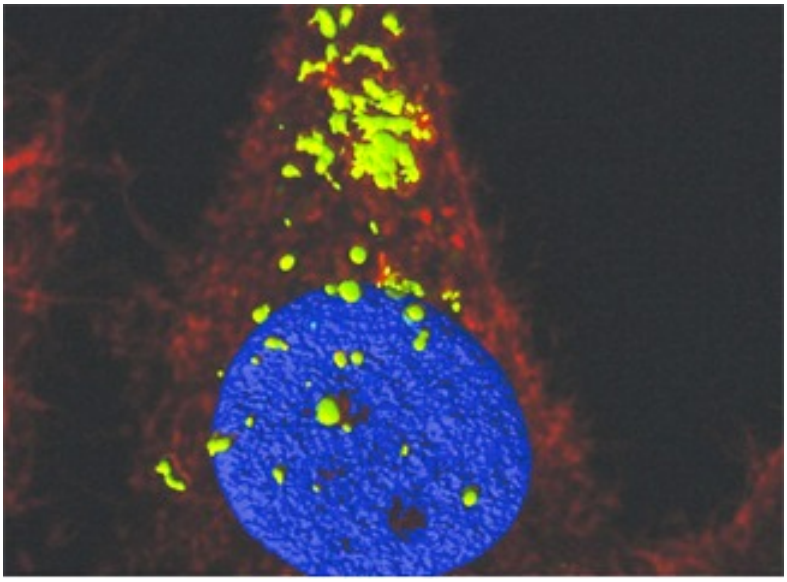
Genetic material inserted in cell nucleus using nanodisks



Researchers at UAB have discovered a novel gene therapy method using particles measuring only a few nanometres which encapsulate genetic material and introduce themselves directly into the cell nucleus. The nanodisks, as researchers have named the particles, travel rapidly to the interior of the cell until reaching the nucleus, thus increasing the efficiency of the gene transfer process.

One of the challenges of gene therapy -a set of methodologies aimed at treating several nucleic acid diseases (DNA or RNA)- is to assure that this material arrives directly to the nucleus of the cell without losing a substantial amount along the way and without producing any undesired side effects. With this aim, scientists experiment with the use of different types of vectors, molecules capable of transporting genetic material to the correct place. Presently, natural "deactivated" viruses are the most commonly used vectors in clinical trials, their side effects however often limit therapeutic application.

One of the most promising alternatives in this field is the use of artificial viruses. These viruses can be constructed through genetic engineering by assembling minute protein structures made

up of peptides, the building blocks of proteins.

The team of scientists, led by Antonio Villaverde, lecturer of the Department of Genetics and Microbiology, researcher at the UAB Institute of Biotechnology and Biomedicine and of the Biomedical Research Networking Center in Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), demonstrated that the peptide R9, formed by a specific type of amino-acid (arginine), can encapsulate genetic material, assemble itself with other identical molecules to form nanoparticles and enter directly into the cell nucleus to release the material it contains. The nanoparticles have the shape of a disk, with a diameter measuring 20 nanometres and a height of 3 nm.

The study was published recently in the journals *Biomaterials* and *Nanomedicine* and describes how scientists studied the performance of R9 nanodisks in the interior of the cells using confocal microscopy techniques provided by the UAB Microscopy Service and applied by Dr Mònica Roldán. The images show that once the cell membrane is passed, particles travel directly to the nucleus at a rate of 0.0044 micrometres per second, ten times faster than if they dispersed passively in the interior. Nanoparticles accumulate in the interior of the nucleus and not in the cytoplasm -the thick liquid between the cell membrane and nucleus- and therefore increase their level of effectiveness.

Participating in this discovery were researchers from the Institute of Material Science of Barcelona (ICMAB-CSIC), the Catalan Institute for Research and Advanced Studies (ICREA), and the Technical University of Catalonia. The discovery represents a new category of nanoparticles offering therapeutic benefits. According to Dr Esther Vázquez, director of the project, "nanodisks assemble automatically, move rapidly, remain stable and travel to the interior of the nucleus. This makes them a promising tool as a prototype for the safe administration of nucleic acids and functional proteins".

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References

"Protein nanodisk assembling and intracellular trafficking powered by an arginine-rich (R9) peptide". Esther Vazquez, Mónica Roldán, César Diez-Gil, Ugutz Unzueta, Joan Domingo-Espín, Juan Cedano, Óscar Conchillo, Imma Ratera, Jaume Veciana, Xavier Daura, Neus Ferrer-Miralles, Antonio Villaverde. Nanomedicine February 2010, Vol. 5, No. 2, Pages 259-268.

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