Nano Sponges for Drug Delivery and Medicinal Applications

These non-toxic nano sponges are a means to deliver a drug or payload to cells in an extended-release fashion.

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This invention is a means of delivering a drug, or payload, to cells using non-covalent associations of the payload with nano-engineered scaffolds; specifically, functionalized single-walled carbon nanotubes (SWNTs) and their derivatives where the payload is effectively sequestered by the nanotube's addends and then delivered to the site (often interior of a cell) of interest.

Polyethylene glycol (PEG) and other water-soluble organic molecules have been shown to greatly enhance the solubility of SWNTs in water. PEG groups and other water-solubilizing addends can act to sequester ("sponge") molecules and deliver them into cells. Using PEG that, when attached to the SWNTs, the SWNT/PEG matrix will enter cells has been demonstrated. This was visualized by the addition of fluorescein isothiocyanate (FITC) to the SWNT/PEG matrix. Control studies showed that both FITC alone and FITC/PEG did not enter the cells. These observations suggest that the FITC is highly associated with the SWNT/PEG matrix that brings the FITC into the cells, allowing visualization of SWNTs in cells.

The FITC is not covalently attached, because extended dialysis in hot DMF will remove all fluorescence quickly (one week). However, prolonged dialysis in water (1–2 months) will only slowly diminish the fluorescence. This demonstrates that the SWNT/PEG matrix solubilizes the FITC by sequestering it from the surrounding water and into the more solubilizing organic environment of the SWNT/PEG matrix of this type. This can be extended for the sequestering of other molecules such as drugs with PEG and other surfactants.

For example, it was shown that the water-insoluble anti-cancer drug paclitaxel (Taxol) could be effectively dissolved in water via the sponging action of the SWNT/PEG matrix in solution. When one milligram of paclitaxel dissolved in 70 µL of ethanol is added into 1 mL of water, the drug will immediately precipitate out of solution once in contact with the water. However, when the same amount of dissolved paclitaxel is added into 1 mL of the SWNT/PEG matrix solution in water, no paclitaxel precipitates out of solution. This is attributed to the paclitaxel being sequestered from the water and into the more favorable SWNT/PEG matrix. In this way, water-soluble solutions of paclitaxel were made.

In preliminary studies, using the well established MIT assay, the "sponged" paclitaxel was shown to have comparable cell-killing ability as the cremophor-stabilized Taxol used in current clinical cancer treatment. The SWNT/PEG matrix, which was shown to be non-toxic to cells, could be an effective alternative for the drug delivery vehicle cremophor, which is known to cause debilitating side effects in some cancer patients. The nano sponge should behave similarly in the solubilization of other molecules with limited or no water solubility. In addition, the material also serves as a protective barrier, sheltering the drug or payload from premature destruction within the body before it reaches the final destination of the cell. Moreover, one could simply add the functionalized SWNTs into a solution of the drug or fluorescent tag of choice, incubate in order to have the SWNT/PEG matrix sequester the drug or tag, and then administer the entire solution for delivery.

This work was done by James M. Tour, Rebecca Lucente-Schultz, Ashley Leonard, Dimitry V. Kosynkin, Brandi Katherine Price, and Jared L. Hudson of Rice University; and Jodie L. Conyers Jr., Valerie C. Moore, S. Ward Casscells, Jeffrey N. Myers, Zvonimir L. Milas, Luka Milas, and Kathy A. Mason of the University of Texas for Johnson Space Center. For further information, contact the JSC Innovation Partnerships Office at (281) 483-3809.

In accordance with Public Law 96-517, the contractor has elected to retain title to this invention. Inquiries concerning rights for its commercial use should be addressed to:

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Refer to MSC-24504-1, volume and number of this NASA Tech Briefs *issue, and the page number.*

Molecular Technique to Understand Deep Microbial Diversity

NASA's Jet Propulsion Laboratory, Pasadena, California

Current sequencing-based and DNA microarray techniques to study microbial diversity are based on an initial PCR (polymerase chain reaction) amplification step. However, a number of factors are known to bias PCR amplification and jeopardize the true representation of bacterial diversity. PCR amplification of the minor template appears to be suppressed by the exponential amplification of the more abundant template. It is widely acknowledged among environmental molecular microbiologists that genetic biosignatures identified from an environment only represent the most dominant populations. The technological bottleneck has overlooked the presence of the less abundant "minority population," and underestimated their role in the ecosystem maintenance.

To generate PCR amplicons for subsequent diversity analysis, bacterial l6S rRNA genes are amplified by PCR using universal primers. Two distinct PCR regimes are employed in parallel: one using normal and the other using biotin-labeled universal primers. PCR products obtained with biotin-labeled primers are mixed with streptavidin-labeled magnetic beads and selectively captured in the presence of a magnetic field. Less-abundant DNA templates that fail to amplify in this first round of PCR amplification are subjected to a second round of PCR using normal universal primers. These PCR products are then subjected to downstream diversity analyses such as conventional cloning and sequencing. A second round of PCR amplified the minority population and completed the deep diversity picture of the environmental sample.

This work was done by Parag A. Vaishampayan and Kasthuri J. Venkateswaran of Caltech for NASA's Jet Propulsion Laboratory. For more information, contact iaoffice@jpl.nasa.gov. NPO-47993

Methods and Compositions Based on Culturing Microorganisms in Low Sedimental Fluid Shear Conditions

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The benefits of applying a low sedimental fluid shear environment to manipulate microorganisms were examined. Microorganisms obtained from a low sedimental fluid shear culture, which exhibit modified phenotypic and molecular genetic characteristics, are useful for the development of novel and improved diagnostics, therapeutics, vaccines, and bio-industrial products. Furthermore, application of low sedimental fluid conditions to microorganisms permits identification of molecules uniquely expressed under these conditions, providing a basis for the design of new therapeutic targets.

This work was done by C. Mark Ott of Johnson Space Center; Cheryl A. Nickerson, James W. Wilson, and Shameema Sarker of Arizona State University; Eric A. Nauman of Purdue University; Michael J. Schurr of the University of Colorado Health Science Center; and Mayra A. Nelman-Gonzalez of Wyle Laboratories. For further information, see http://www.wipo.int/pctdb/en/wo.jsp?WO=2009036036

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Refer to MSC-24584-1, volume and number of this NASA Tech Briefs *issue, and the page number.*