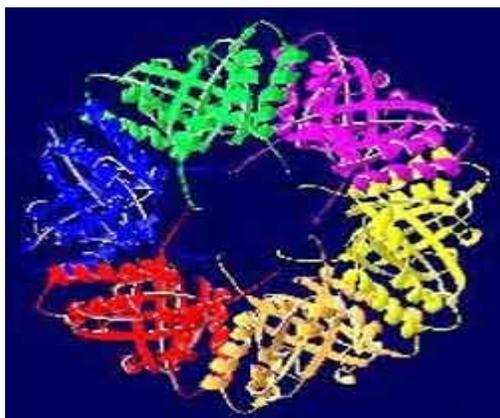




Nanotechnology Medical Applications



Breakthroughs in nanotechnology promise to revolutionize drug manufacturing, drug delivery, and medical diagnostics. By learning how substances behave differently at the individual cellular or particle level, researchers are beginning to unlock the vast medical potential of nano-scale materials. Though much of this work is still in its early stages, scientists at the University of Maryland's Nanotechnology Center are creating novel tools and developing new methods for crucial research areas of drug synthesis, drug carriers, targeting technologies, toxicity reduction, and materials optimization.

Douglas English, Philip DeShong, and Sang Bok Lee are developing stable, durable drug carriers, which can be coated with materials that enable targeting to specific cells. Their research demonstrates promising capabilities for detecting and treating diseases and tumors more efficiently and with fewer side effects.

Hamid Ghandehari uses nano-scale materials to deliver drugs directly to tumors, with minimal absorption by non-target organs. His research with polymeric biomaterials also has applications for improving cancer gene therapy and the oral administration of drugs.

Bill Bentley and his collaborators have pioneered nano-scale MEMS devices that respond to the changing biological environment. These tiny "nanofactories" can sense when and where a drug is needed and then synthesize it at the proper dosage while traveling to the delivery site.

http://www.nanocenter.umd.edu/faculty/faculty_list.php

Nanocapsules for Drug Delivery

Self-assembling nano-scale vesicles can provide the stable, long-lasting encapsulation key to targeted drug delivery. Douglas English and his team discovered that, when mixed in the right concentrations, common surfactants will spontaneously gather to form durable capsules that are highly-charged and thermodynamically stable. These capsules can attract, encapsulate, and concentrate charged organic molecules, such as pharmaceutical compounds. English's research could provide one key to ensuring that drugs are not released until they reach their intended target.

English now hopes to develop the potential of nanocapsules into detection and treatment applications for both infectious diseases and tumors. His team has already encapsulated and concentrated the anti-tumor drug doxorubicin and specifically targeted bacterial cells in vitro.

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Cell Surface Receptors Enabling Targeted Drug Delivery and Pathogen Detection

Philip DeShong has developed new pathogen-detection and drug-delivery systems by coating nanocapsules with "smart" materials that recognize targets. These smart systems promise to be much more efficient and effective than current alternatives. For example, DeShong's pathogen detection system for *Neisseria gonorrhoeae* has reduced recognition time to minutes, when current methods require days. In drug delivery, DeShong's recent data show that nanoparticles coated with specific ligands can carry anti-tumor compounds directly to the desired site with no overt signs of toxicity.

DeShong's team has already created nano-scale materials sized to prevent removal by either the kidney or liver, used surface charges to optimize biological effectiveness, and attached receptors onto optical fibers to create novel biosensors. Now the team is working to develop this research into practical applications by optimizing materials, optimizing receptor quantities, investigating new particle architectures, and determining toxicological effects.

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Nanoparticle Tubes Enabling Targeted Drug Release

Sang Bok Lee has developed nano-scale materials that overcome limitations impeding other drug targeting-and-release technologies. The hollow, tube-shaped nanostructures Lee manufactures possess the properties of ideal drug carriers: high drug presence, targets or probes, imaging capabilities, and non-toxicity. Made of magnetic materials, these structures obviate the need for bio-compatibility among components and enable the nanotubes to disperse easily in aqueous solutions. Acting like tiny capsules, the nanotubes also protect the medicine they contain from attacks such as enzymatic reactions.

Lee further discovered that adding a layer of magnetite inside the nanotube imparts magnetic properties, allowing them to be tracked with MRI systems. These properties also appear to hold the tubes at their target, providing maximum therapeutic effect.

The iron oxide Lee developed for his nanotubes is the only inorganic nano-particle approved by the FDA as an MRI enhancement contrast agent.

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Polymer "Carrier" Molecules Enabling Cancer Therapies

The University School of Pharmacy's work with protein-based polymers demonstrates dramatic potential for drug delivery and gene therapy. Recombinant DNA technology that allows manipulation of these polymers at the molecular level has revealed new possibilities for controlling drug release. Dr. Hamid Ghandehari has made HPMA copolymers that have demonstrated direct, effective delivery to Lewis Lung tumor cells in vitro and in mice. These copolymers minimize uptake by non-target organs and overcome multi-drug resistance. Polymer structures can also be correlated with gene release and transfer, for applications in cancer gene therapy. Further, Ghandehari has successfully transported PAMAM dendrimers across gastrointestinal epithelial cells with little or no toxicity, indicating that polymer-based drugs can be delivered orally as well as intravenously.

Much of the research in nanoparticle polymer-based drug delivery will now focus on the influence of architecture, charge, and drug loading, and especially on animal testing for toxicity.

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"Nanofactories" Enabling Nano-based Drug Synthesis and Delivery

Bill Bentley's team was the first to demonstrate mechanized, nano-based drug synthesis and delivery with MEMS devices. These "nanofactories" automatically collect raw materials in the local environment to synthesize drugs and deliver them to specific sites at specific times and dosages. One of Bentley's factories produces and delivers signal molecules that manipulate bacterial cells' "quorum-sensing." As the cells falsely perceive that there are sufficient numbers to become aggressive, they prematurely expose themselves to drug targeting or an immune response. Rather than transporting an antibiotic, this nanofactory targets pathogenicity, minimizing the pressure for bacteria to develop resistance.

To broaden nanofactory applications and reduce costly animal testing, Bentley experiments with "bio-fabrication," putting synthetic pathways onto nanoparticles, which then mimic the reactions of biological systems. Having manufactured fusion proteins covalently coupled and electro-deposited onto devices, Bentley's team is now determining the best applications for the process.

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