NANOTECHNOLOGY IN CANCER: TOOLS TO RELIEVE HUMAN SUFFERING

For several years, the National Cancer Institute (NCI) has supported exploratory work integrating nanotechnology into cancer research. The NCI is moving the science of nanotechnology into the clinic to change the way we diagnose, treat and prevent cancer.

Today, nanodevices are used in detecting cancer at its earliest stages, pinpointing its location within the body, delivering anticancer drugs specifically to malignant cells, and determining if these drugs are killing malignant cells. As research continues and nanodevices are evaluated for safety and efficacy, nanotechnology will result in significant advances in early detection, molecular imaging, assessment and therapeutic efficacy, targeted and multifunctional therapeutics, and the prevention and control of cancer.

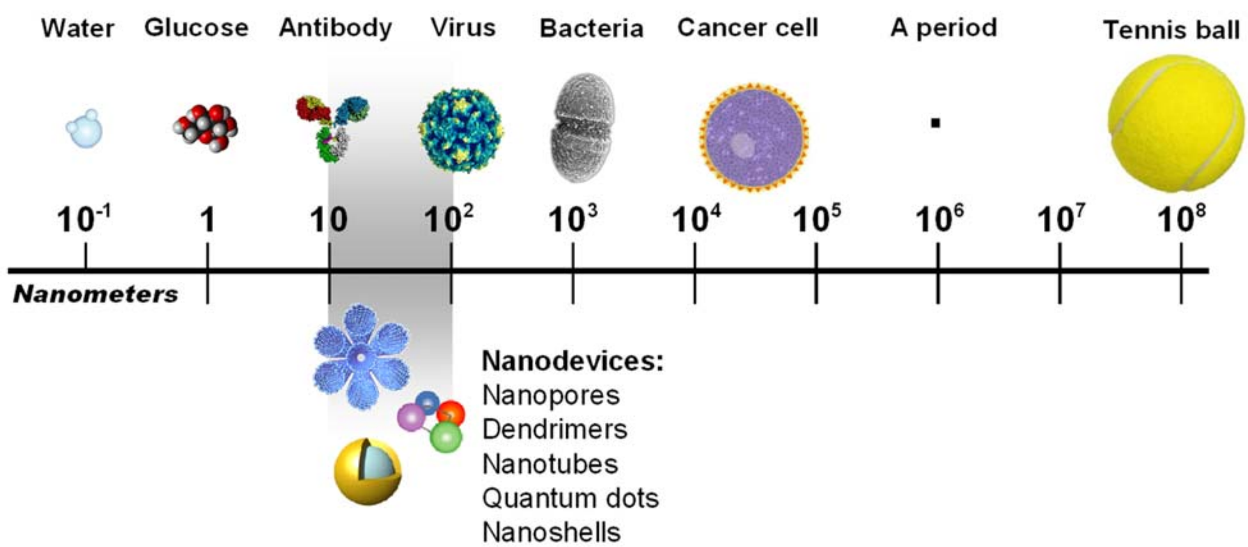
Over the next five years, the NCI will fund $144.3 million in research and development through the NCI Alliance for Nanotechnology in Cancer. This Alliance will direct research efforts and facilitate partnerships across the scientific and research communities and the public and private sectors. These efforts capitalize on the multidisciplinary nature of nanotechnology development and will hasten its application to the elimination of suffering and death due to cancer.

What is Nanotechnology?

Nanotechnology is the development and engineering of devices so small that they are measured on a molecular scale. This emerging field involves scientists from many different disciplines, including physicists, chemists, engineers, information technologists, and material scientists, as well as biologists. Nanotechnology is being applied to almost every field imaginable, including electronics, magnetics, optics, information technology, materials development, and biomedicine.

The Size of Things

Nanoscale devices are one hundred to ten thousand times smaller than human cells. They are similar in size to large biological molecules ("biomolecules") such as enzymes and receptors. As an example, hemoglobin, the molecule that carries oxygen in red blood cells, is approximately 5 nanometers in diameter. Nanoscale devices smaller than 50 nanometers can easily enter most cells, while those smaller than 20 nanometers can move out of blood vessels as they circulate through the body.



Because of their small size, nanoscale devices can readily interact with biomolecules on both the surface and inside cells. By gaining access to so many areas of the body, they have the potential to detect disease and deliver treatment in ways unimagined before now.

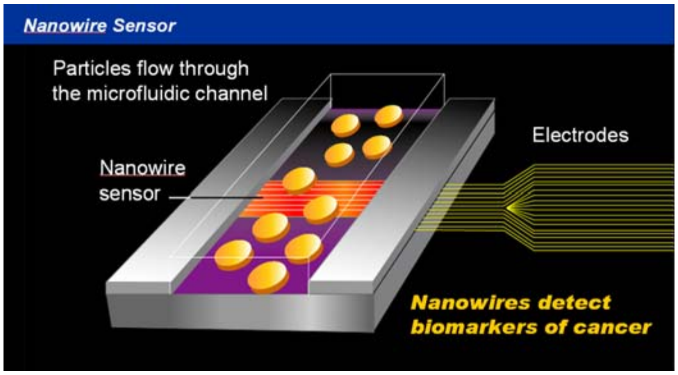
Nanotechnology in Cancer Diagnosis and Therapy

Biological processes, including events that lead to cancer, occur at the nanoscale. Nanotechnology offers unprecedented access to the interior of living cells, and therefore provides researchers with the opportunity to study and interact with normal and cancer cells in real time, at the molecular and cellular scales, and during the earliest stages of the cancer process.

Nanodevices can provide rapid and sensitive detection of cancer-related molecules by enabling scientists to detect molecular changes even when they occur only in a small percentage of cells. They also have the potential to radically change cancer therapy for the better and to dramatically increase the number of highly effective therapeutic agents. Nanoscale constructs can serve as customizable, targeted drug delivery vehicles capable of ferrying large doses of chemotherapeutic agents or therapeutic genes into malignant cells while sparing healthy cells, greatly reducing or eliminating the side effects that accompany many current cancer therapies.

Examples of Nanotechnologies

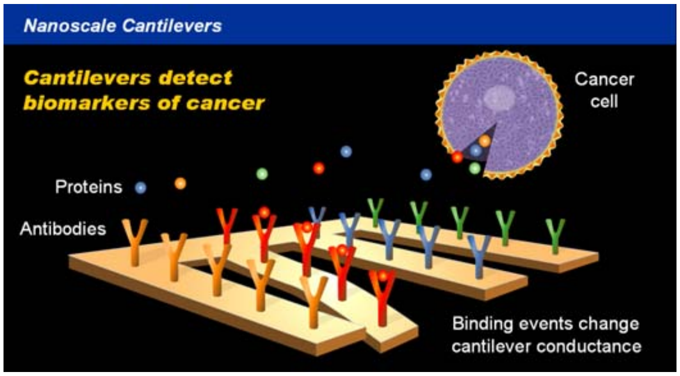
- **Nanowires**



Nano sized sensing wires lay across a microfluidic channel. These nanowires by nature have incredible properties of selectivity and specificity. As particles flow through the microfluidic channel, the nanowire sensors pick up the molecular signatures of these particles and can immediately relay this information through a connection of electrodes to the outside world.

These nanodevices are man-made constructs made with carbon, silicon and other materials that have the capability to monitor the complexity of biological phenomenon and relay the information, as it is monitored, to the medical care provider. They can detect the presence of altered genes associated with cancer and may help researchers pinpoint the exact location of those changes.

- **Cantilevers**

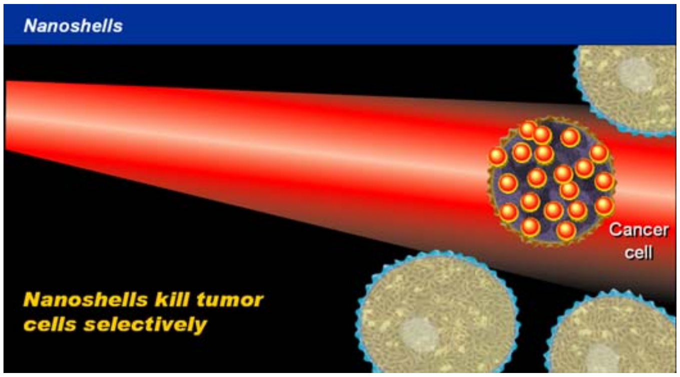


Nanoscale cantilevers – microscopic, flexible beams resembling a row of diving boards – are built using semiconductor lithographic techniques and coated with molecules capable of binding to the biomarkers of cancer.

As a cancer cell secretes its molecular products, the antibodies coated on the cantilever fingers selectively bind to these secreted proteins, changing the physical properties of the cantilever and signaling the presence of cancer. Researchers can read this change in real time and provide not only information about the presence and the absence but also the concentration of different molecular expressions.

Nanoscale cantilevers, constructed as part of a larger diagnostic device, can provide rapid and sensitive detection of cancer-related molecules.

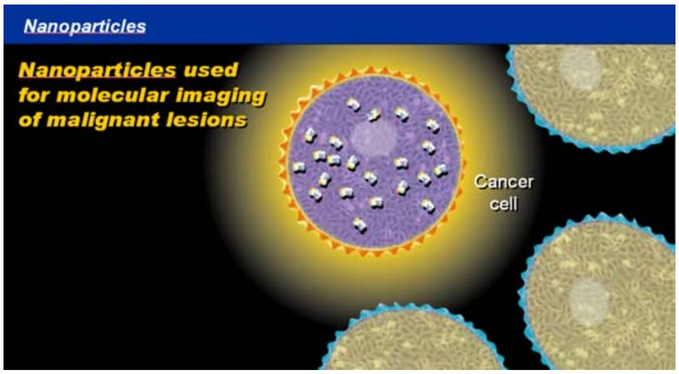
- **Nanoshells**



Nanoshells have a core of silica and a metallic outer layer. Scientists can link the nanoshells to antibodies that recognize tumor cells. Once the cancer cells take them up, scientists apply near-infrared light that is absorbed by the nanoshells, creating an intense heat that selectively kills the tumor cells and not neighboring healthy cells.

The result is greater efficacy of the therapeutic treatment and a significantly reduced set of side effects.

- **Nanoparticles**



Nanoparticles can be engineered to target cancer cells for use in the molecular imaging of a malignant lesion. Large numbers of nanoparticles are safely injected into the body and preferentially bind to the cancer cell, defining the anatomical contour of the lesion and making it visible.

These nanoparticles give us the ability to see cells and molecules that we otherwise cannot detect through conventional imaging. The ability to pick up what happens in the cell — to monitor therapeutic intervention and to see when a cancer cell is mortally wounded or is actually activated — is critical to the successful diagnosis and treatment of the disease.

Nanoparticulate technology can prove to be very useful in cancer therapy allowing for effective and targeted drug delivery by overcoming the many biological, biophysical and biomedical barriers that the body stages against a standard intervention such as the administration of drugs or contrast agents.

Strategic Implementation: The Cancer Nanotechnology Plan

The Cancer Nanotechnology Plan (CNPlan) is a focused strategy to capitalize on past NCI investments in nanotechnology and direct those and new efforts on the immediate mission of the NCI. The plan carries an aggressive timeline and specific milestones to achieve the NCI goals. The projects initiated under the CNPlan will be integrated, milestone driven, and product oriented. The efforts will include targeted objectives and goals, and will use a project-management approach to help capitalize on today's opportunities to create the tools that both cancer researchers and clinicians need.

Based on the input NCI solicited from researchers and clinicians, the cancer community will be extremely involved in the implementation of the plan. NCI will continue to utilize traditional funding mechanisms to further promising research, and will supplement these efforts with a targeted approach that stresses interdisciplinary team efforts involving partners from across the cancer research and nanotechnology development communities.

The NCI Alliance for Nanotechnology in Cancer is a comprehensive, systematized initiative encompassing the public and private sectors, designed to accelerate the application of the best capabilities of nanotechnology to cancer. The Alliance is one of the first steps in implementing the CNPlan and focuses on applying research and translating it into clinical products in six key programmatic areas:

- Molecular imaging and early detection – diagnostics to detect cancer in the earliest, most easily treatable, pre-symptomatic stage;
- In vivo imaging – targeted contrast agents that improve the resolution of cancer and address the diversity of tumors at the single cell level;
- Reporters of efficacy – systems to provide real-time assessments of therapeutic and surgical efficacy;
- Multifunctional therapeutics – multifunctional targeted devices to deliver multiple therapeutic agents directly to cancer cells;
- Prevention and control – agents to monitor predictive molecular changes and prevent precancerous cells from becoming malignant; and
- Research enablers – research tools to identify new biological targets, opening new pathways for research.

For additional information about the NCI Alliance for Nanotechnology in Cancer, please visit: http://nano.cancer.gov.