

# Cancer Detection using Nanoparticles

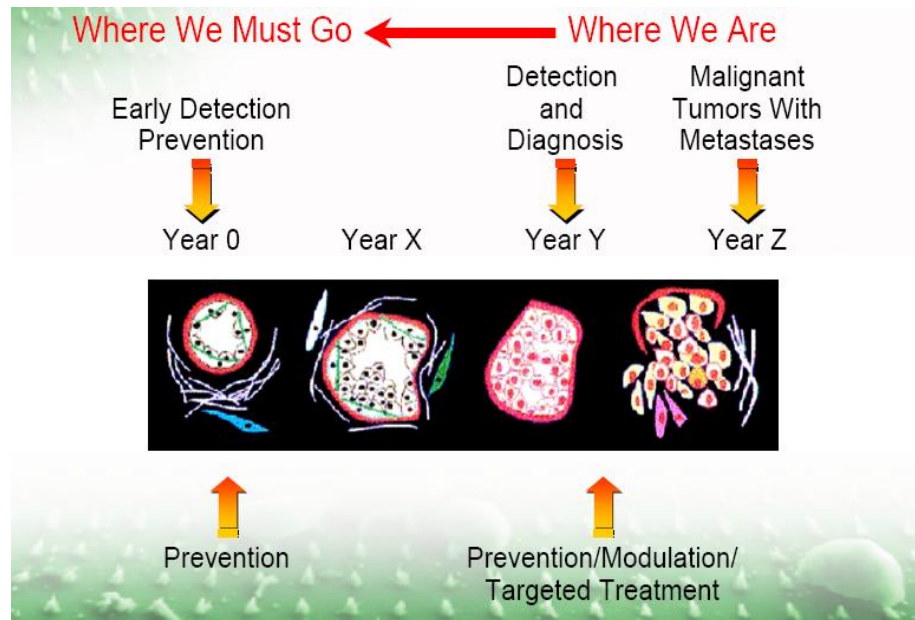
ECG653 Project Report submitted by  
Kranthi Kumar Potteti, Fall 2008  
pottetik@unlv.nevada.edu

## Introduction:

Cancer is a difficult disease to treat, contain, and identify. There are many different ways for treating cancer such as surgery, chemotherapy, radiation and many others. These methods are effective if the cancer tumor is caught soon enough. However, these treatments are not effective enough because they do not only target the affected cells, they also affect healthy cells. There is new technology that is showing promise in detecting cancer cells along with destroying cancer cells using chemicals found in nature and man-made chemicals. This new technology, which is a subcategory of nanotechnology, is less painful and targets the infected cells. Today nanoparticles are being studied and used for detecting and destroying cancer cells in mice. In this report we are going to look at the different ways for detecting cancer by using nanoparticles.

## Project Description:

One of the key problems in the treatment of cancer is the early detection of the disease. Methods for the early detection of cancer are of utmost importance and are an active area of current research. Blood tests are a common and straightforward means of screening people for cancer in its early stages. If a chemical in the blood that signals the presence of even a small tumor can be detected, the cancer could be treated sooner and would be more likely to be cured. Often cancer is detected in its later stages, when it has comprised the function of one or more vital organ systems and is wide spread throughout the body.



**Fig 1 Emerging Possibility to Define the Natural History of Cancer –Move to Prevention vs. Current Paradigm**

In figure 1 we can see the different stages of cancer cells, where the prevention is possible when it is detected in its early stage. Using the present techniques we are able to detect and diagnose the cancer when the cancer cells grow to a physically detectable size.

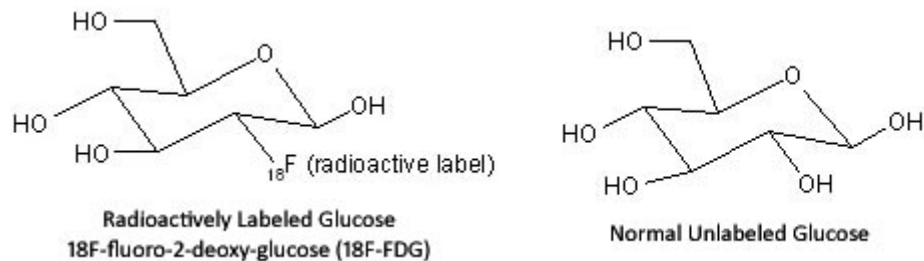
### General Detection and Diagnostic Techniques:

In general the detection and diagnostic techniques used for cancer are classified into 3 categories

1. Non-invasive techniques
2. Invasive techniques
3. Analysis of Biopsy

In Non-invasive technique the most commonly used methods are

- i. Ultrasound scanning also known as a sonography, is an imaging technique used to detect many different kinds of cancers. It uses sound waves and their echoes to image the body's internal structures.
- ii. MRI, or magnetic resonance imaging, is a non-invasive way to look at organs, tissues, bones, and other structures inside the body. It uses large magnetic fields and radio waves to produce images of the body.
- iii. A Positron Emission Tomography (PET) scan is an imaging technique that uses radioactive molecules to create a dynamic image of internal tissues and organs. PET scans produce images that reveal the activity of living tissues. This is in contrast to techniques that reveal structure but not activity.



**Fig 2 Difference in unlabeled and radioactively labeled Glucose**

- iv. A Computed Tomography (CT) scanner uses x-rays in the same way as a conventional x-ray but instead of taking one image a CT scanner takes multiple images, or slices. A computer gathers all the images and compiles them to create a 3 dimensional image of the internal structures being examined.

There are two Invasive techniques

- i. Fine Needle Aspiration (FNA) is done with a small, 20-27 gauge, needle (same size or smaller than most needles used in ordinary blood test, a larger gauge corresponds to a smaller needle). The area is sterilized with alcohol to prevent infection. The needle is then inserted and aimed at the center of the lesion. When the needle reaches the lesion a very small piece is removed by suction. This is repeated to ensure that a proper amount of usable sample is obtained.

- ii. Core needle biopsy is similar to a fine needle aspiration (FNA), except that a larger (11-18 gauge) needle is used and the pathology report is different. Because the needle is larger than in a FNA, local anesthesia is used to numb the area before insertion.

Techniques used in analysis of biopsy are

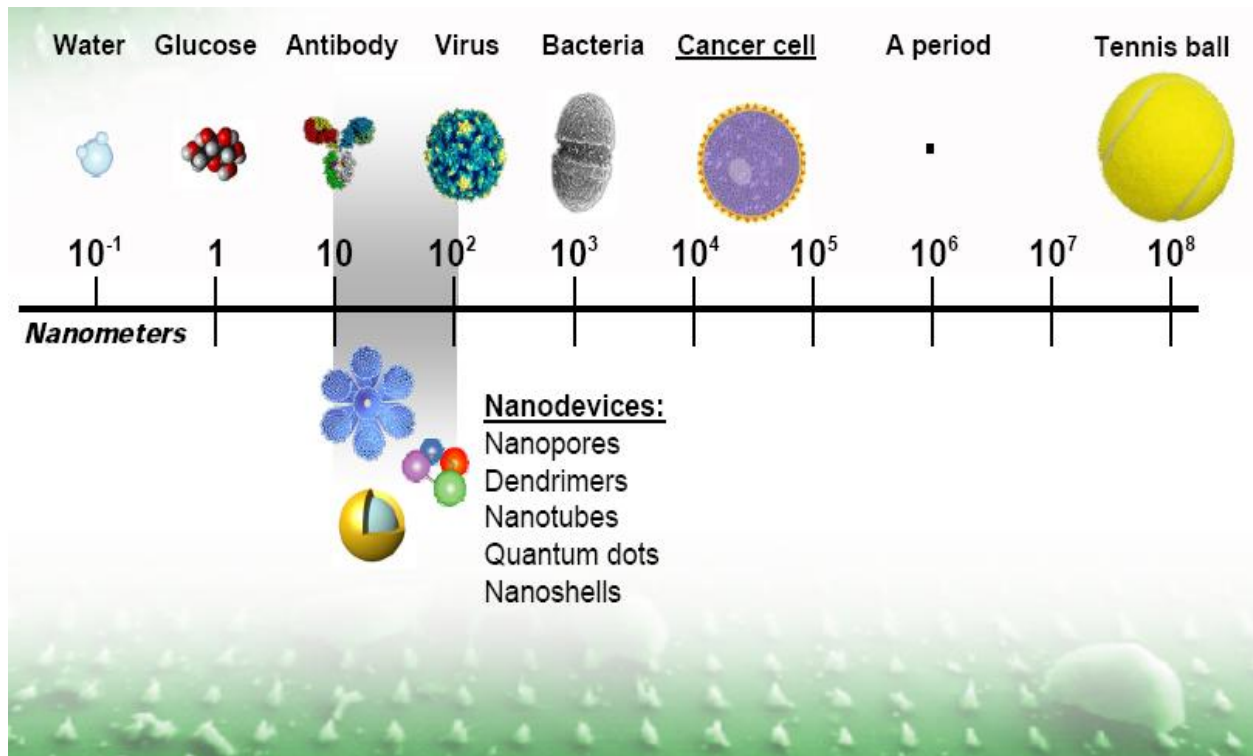
- i. Immunohistochemistry (IHC) is a technique used to determine the presence and level of specific cellular proteins. IHC measures protein expression using specially labeled antibodies that can bind to the proteins of interest.
- ii. Fluorescence in Situ Hybridization (FISH) is a technique that measures gene amplification using fluorescently labeled DNA (probe).

All these techniques are useful in cancer detection but has some limitations in terms of

- Accuracy
- Can't detect all cancers
- Requires more number of infected cells to identify the tumor
- Only effective in detecting tumors that are close to the skin surface
- May identify a potential area of concern that is not malignant (high false results)
- Inherent technical limitations

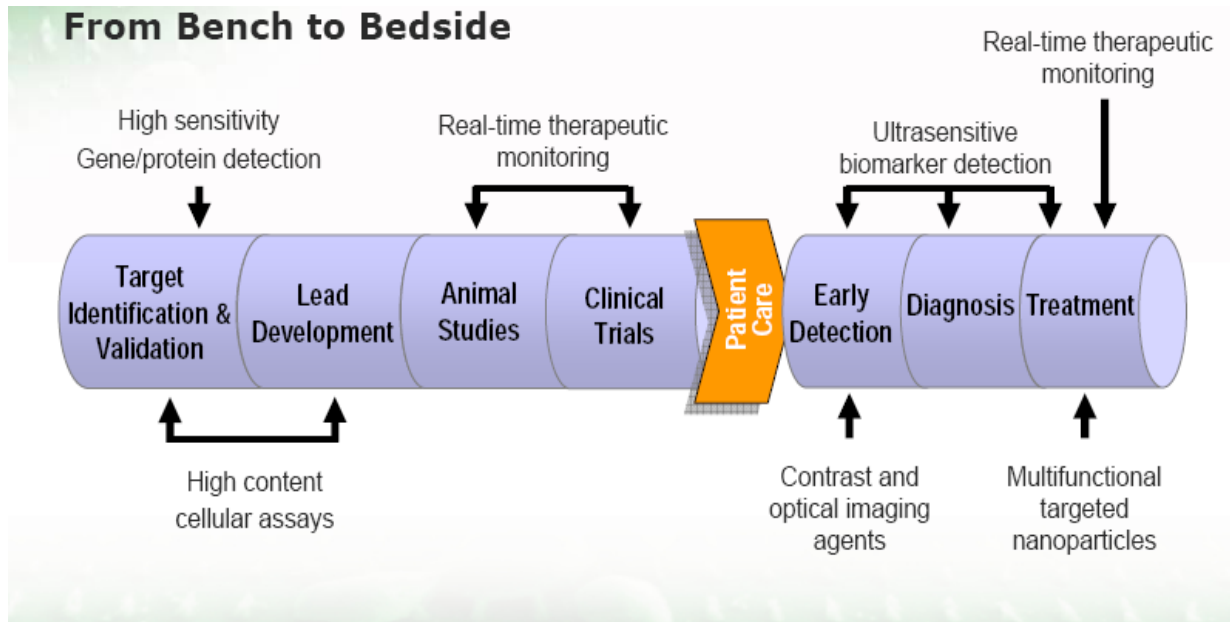
**Nanotechnology in Perspective:**

Nanotechnology has found many new ways in detecting cancer cells and how far the disease has spread throughout the body.



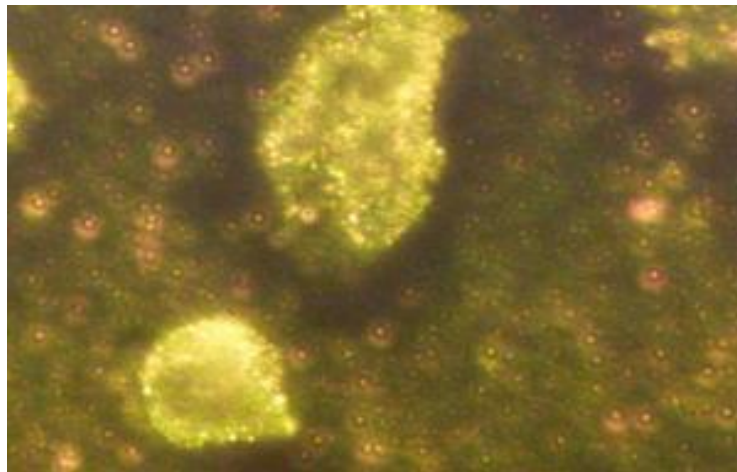
**Fig 3 Nanodevices having feature size less than a cancer cell**

Nanotechnology has multiple applications; it can be used for detection, treatment and prevention



**Fig 4 Applications of Nanotechnology at different stages of cancer detection and diagnosis**

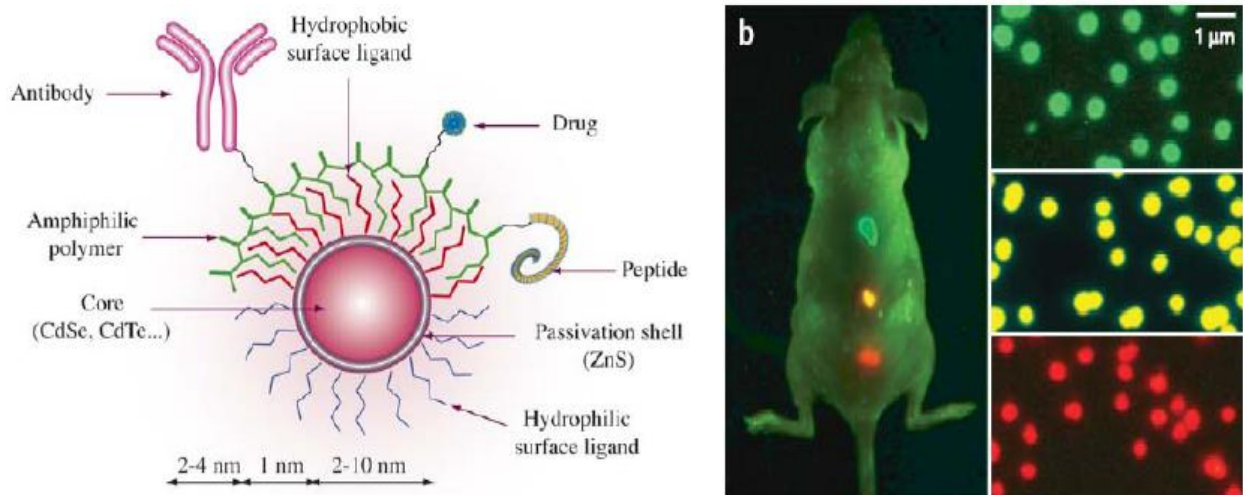
A couple of new cancer detecting nanoparticles are gold nanoparticles and magnetic iron oxide nanoparticles encased in a biocompatible material. Gold nanoparticles can be used as both detecting and destroying cancer cells. Gold nanoparticles are very good at scattering and absorbing light. Cancer cells have a protein called Epidermal Growth Factor Receptor (EGFR) which the gold nanoparticles attach themselves to. If we add this conjugated nanoparticle solution to healthy cells and cancerous cells and we look at the image, we can tell with a simple microscope that the whole cancer cell is shining. The healthy cell doesn't bind to the nanoparticles specifically, so we don't see where the cells are. With this technique, if we see a well defined cell glowing, that's cancer.



**Fig 5 Gold nanoparticles stick to cancer cells and make them shine**

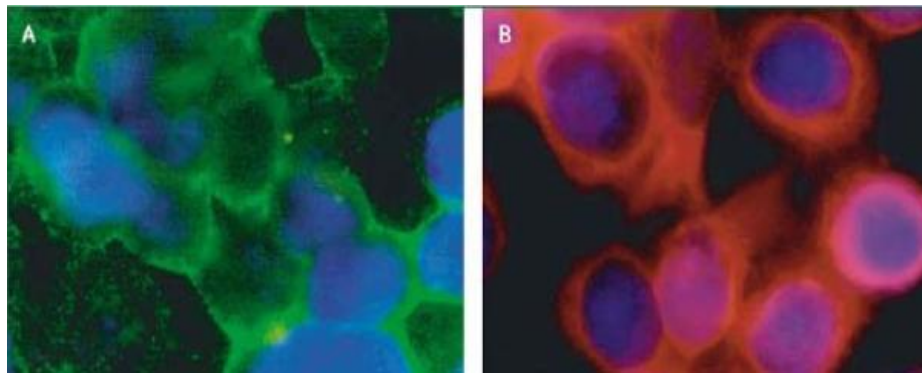
There are various benefits to using gold nanoparticles such as being less expensive since all we need is a microscope and white light. Also the results are immediately found; there is no wait period to find out if a person has cancer. This means that treatment can start immediately which could save lives. This process also is not toxic to healthy human cells.

Similar to gold nanoparticles is quantum dots. These use cadmium selenide nanoparticles which glow when under ultraviolet light which makes it easier to extract the tumor.



**Fig 6 Structural diagram of quantum dot and different quantum dots used to detect tumors**

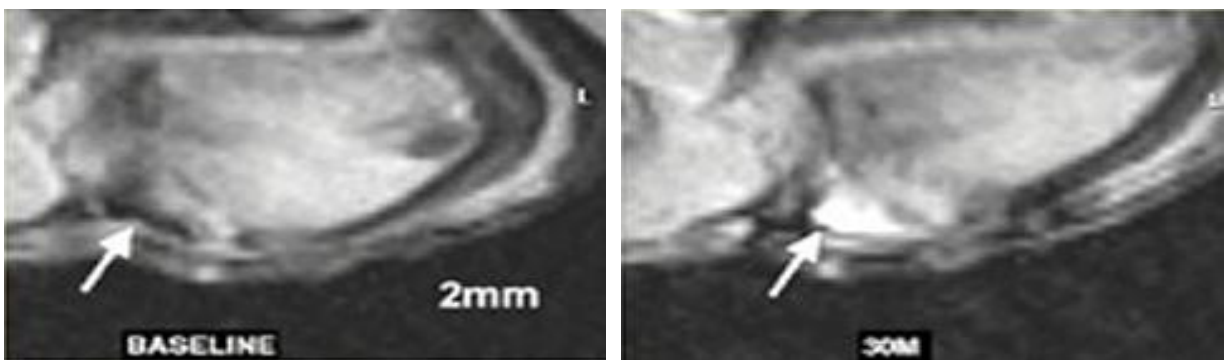
Quantum Dot contains a central core and a protective organic coating shell. Quantum dots can emit powerful fluorescence between 450 nm and 850 nm. In breast cancer, 3 crucial biomarkers can be detected and accurately quantified by use of quantum dots they are; Estrogen Receptor (ER), Progesterone Receptor (PR) and ERBB2 protein. These biomarkers are currently detected using Immunohistochemistry (IHC) and Fluorescence in Situ Hybridization (FISH) techniques. But the use of fluorescence has its limitations in terms of Photo bleaching and an Autofluorescence. Quantum dots are used to replace fluorophore.



**Fig 7 (A) FISH of E-cadherin mRNA and (B) Protein with quantum dots in androgen-repressed prostate cancer cells**



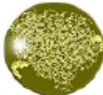
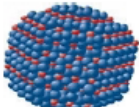


Magnetic iron oxide nanoparticles encased in a biocompatible material can make detecting cancer cells easier, even if the cancer cells are small and clearer so there is less mistakes in the detecting process. These particles stick to the tumor cells turning them into little magnets which are then attracted to the tip of a biopsy needle. It might also be possible to detect cells from breast, prostate, and ovarian cancers that have spread to other parts of the body in amounts too tiny to sample with an ordinary needle. Instead of using biopsies, MRI's can be used to distinguish malignant lymph nodes which can help in telling how far prostate cancer has spread. "Researchers in the Netherlands and Boston, Massachusetts, recently reported in the New England Journal of Medicine that an MRI contrast agent consisting of highly lymphotropic iron oxide nanoparticles enabled clinicians to detect small nodal metastases that otherwise would have gone undetected in 33 of the 80 patients with prostate cancer."

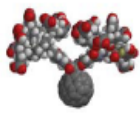


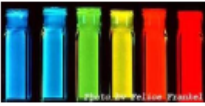


**Fig 8 The right image shows an MRI of a melanoma tumor without nanoparticles. The left one shows the same tumor lightened up by nanoparticles**

Nano-based devices and drugs for cancer and all diseases are increasing. There is around 68% increase in the clinical pipeline from 2005, 130 nanotech-based drugs and delivery systems and 125 devices or diagnostic tests.

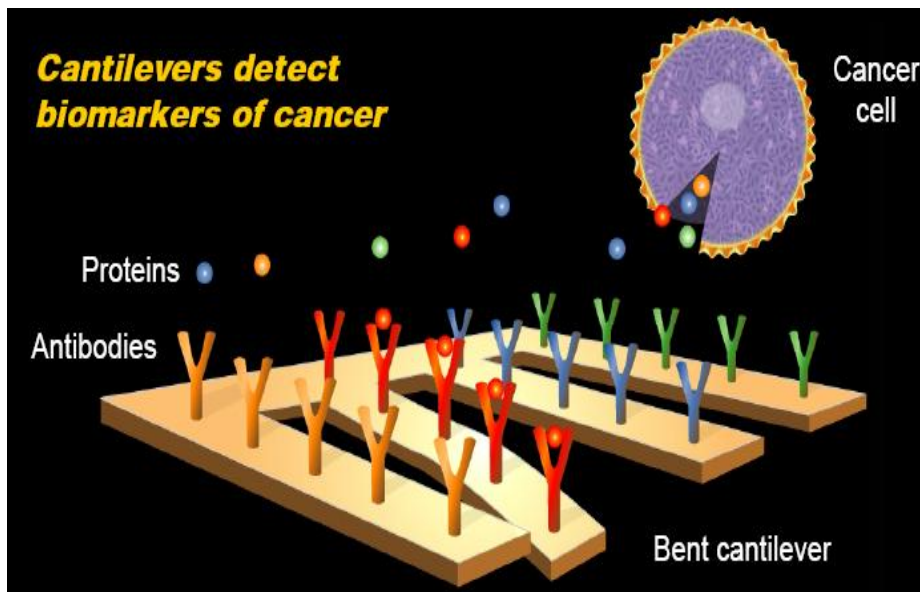
<i>Modality</i>		<i>Potential Applications</i>
<b>Cantilevers</b>		<ul style="list-style-type: none"> <li>• High-throughput screening</li> <li>• Disease protein biomarker detection</li> <li>• DNA mutation detection (SNPs)</li> <li>• Gene expression detection</li> </ul>
<b>Carbon Nanotubes</b>		<ul style="list-style-type: none"> <li>• DNA mutation detection</li> <li>• Disease protein biomarker detection</li> </ul>
<b>Dendrimers</b>		<ul style="list-style-type: none"> <li>• Target sequestration</li> <li>• Controlled release drug delivery</li> <li>• Image contrast agents</li> </ul>
<b>Nanocrystals</b>		<ul style="list-style-type: none"> <li>• Improved formulation for poorly soluble drugs</li> </ul>

**Fig 9 Different Nanodevices with different applications**

<b>Modality</b>	<b>Potential Applications</b>
<b>Nanoparticles</b> 	<ul style="list-style-type: none"> <li>• Multifunctional therapeutics</li> <li>• Targeted drug delivery, permeation enhancers</li> <li>• MRI and ultrasound image contrast agents</li> <li>• Reporters of apoptosis, angiogenesis, etc.</li> </ul>
<b>Nanoshells</b> 	<ul style="list-style-type: none"> <li>• Deep tissue tumor cell thermal ablation</li> <li>• Tumor-specific imaging</li> </ul>
<b>Nanowires</b> 	<ul style="list-style-type: none"> <li>• High-throughput screening</li> <li>• Disease protein biomarker detection</li> <li>• DNA mutation detection (SNPs)</li> <li>• Gene expression detection</li> </ul>
<b>Quantum Dots</b> 	<ul style="list-style-type: none"> <li>• Optical detection of genes and proteins in animal models and cell assays</li> <li>• Tumor and lymph node visualization</li> </ul>

**Fig 10 Different Nanodevices with different applications**

These Nanodevices offer potential cancer prevention applications. Early detection is possible by the use of highly multiplex in-vitro platforms in the form of new biomarker libraries like cantilevers. Early imaging enabled through the use of ‘smart’ nanoparticles which are used as novel contrast agents for improved resolution in imaging.



**Fig 11 Nanoscale Cantilevers**

The biomarker proteins are affinity-bound to the cantilevers and cause them to deflect. The deflections can be directly observed with lasers.

Here are some of the current alliance projects with cancer prevention applications

- Novel semiconducting nanocrystals for cancer detection (MIT-Harvard CCNE)
- Ultrasensitive chemical probing at the single molecule level using surface enhanced Raman scattering in local optical fields of gold nanoparticles (MIT-Harvard CCNE)
- Molecular beacons and activatable probes for cancer detection and analysis (Emory-GT CCNE)
- Multiplexed Raman nanotags for cancer molecular profiling (Emory-GT CCNE)
- Ex vivo sensors and “phenotypers” for cancer cells (UCSD CCNE)
- Nanofluidics devices for rapid single cell analysis (UNC CCNE)
- Development of bio-barcode assays for early cancer detection (Northwestern CCNE)

References:

*Technical Papers:*

- “Nanotechnology and Cancer Prevention” by Anna D. Barker, Ph.D.
- “Nano-Oncology Phototherapy” by Zagreb

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