

NCI Alliance for
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in Cancer

Cancer Nanotechnology – An Opportunity for Early Diagnosis and Novel Therapy: *Developed vs Developing World Cost and Accessibility*

Piotr Grodzinski, Ph.D.
*Director, NCI Nanotechnology Alliance
National Cancer Institute*

Fight against cancer – US

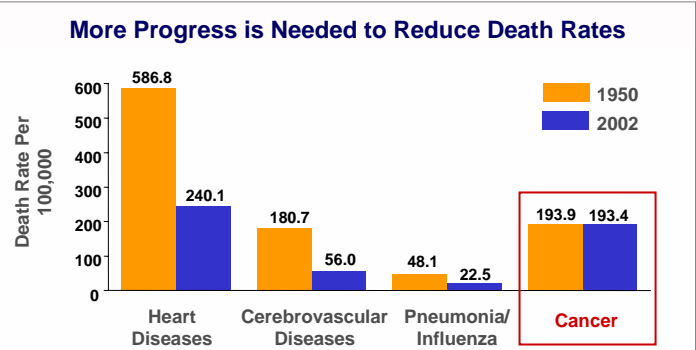
Need for New Approaches to Diagnosis and Therapy

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Cancer is now the #1 killer of Americans under 85

- 570,280 Americans will die of cancer this year
- 1,372,900 Americans this year will hear the words “you have cancer...”
- \$192 billion = Costs of cancer in 2004

More Progress is Needed to Reduce Death Rates

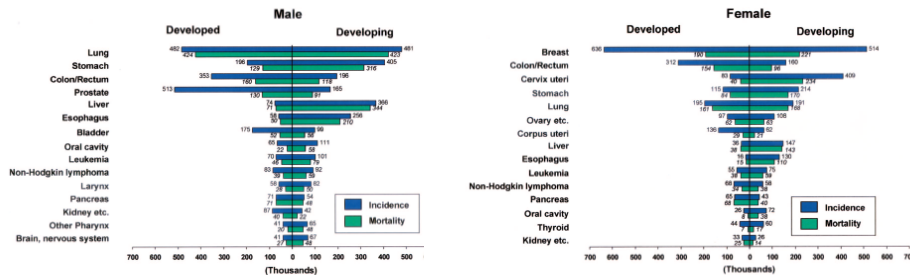


Disease	1950	2002
Heart Diseases	586.8	240.1
Cerebrovascular Diseases	180.7	56.0
Pneumonia/Influenza	48.1	22.5
Cancer	193.9	193.4

Source: American Cancer Society.

Cancer Statistics - Worldwide

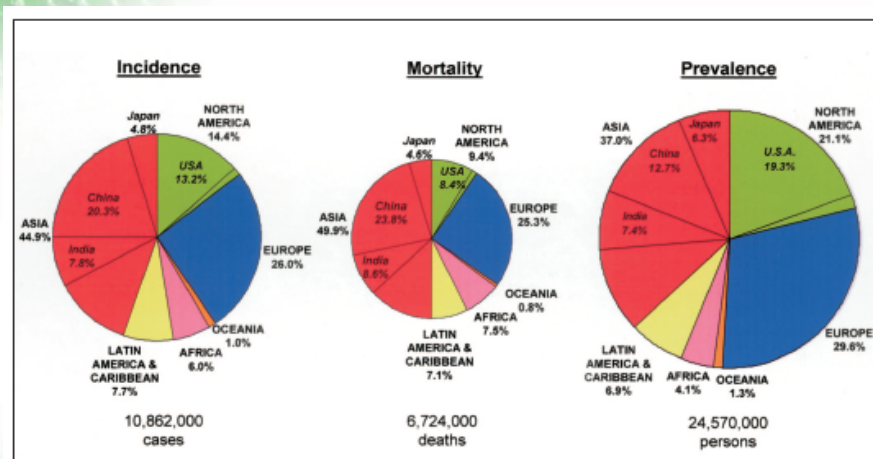
Parkin, Bray, Ferlay, Pisani, CA Cancer J Clin 55, 74–108 (2002)



- Comparable ratio of incidence/mortality (developed vs developing world) rates for cancers with poor prognosis: lung, liver
- Value of early diagnosis to reduce mortality in developed countries for cancers with better prognosis: colon-rectum, breast, leukemia, cervix)
- Variation in incidence for some cancers (prostate, liver, cervix) – impact of the environment (life style, infections)
- Vaccines for HBV (liver cancer) and HPV (cervical cancer)

Early Diagnosis and Effective Treatment – Key to Higher Survival Rates

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Parkin, Bray, Ferlay, Pisani, CA Cancer J Clin 55, 74–108 (2002)

Nanotechnology and Cancer

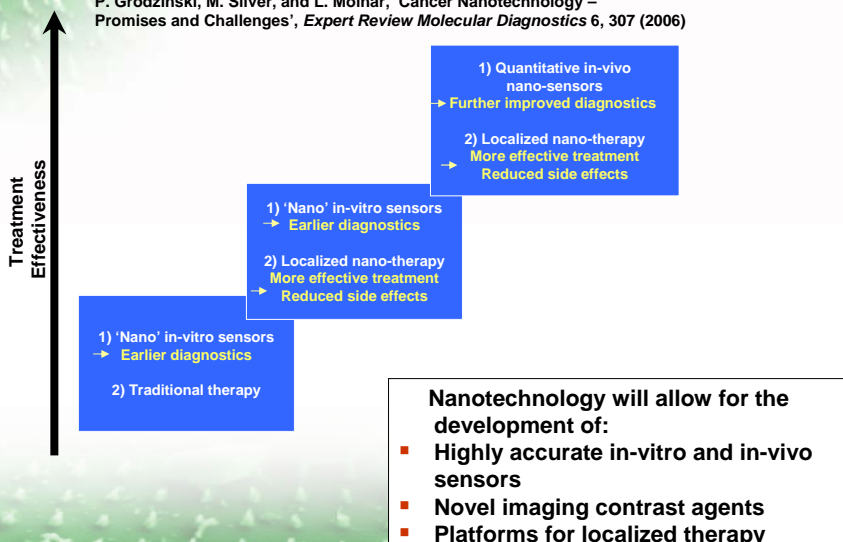
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- Prevention and Control of Cancer
 - Developing early screening methods based on in-vitro tests
 - Developing nanoscale devices that can deliver cancer prevention agents
 - Designing multicomponent anticancer vaccines using nanoscale delivery vehicles
- Imaging Diagnostics
 - Designing targeted contrast agents that improve the resolution of detection to the single cell level
- Multifunctional Therapeutics
 - Developing nanoscale devices that deliver therapy locally at lower dose and higher efficacy
 - Creating “smart” therapeutic devices that can control the spatial and temporal release of therapeutic agents while monitoring the effectiveness of these agents
- Quality of Life Enhancement in Cancer Care
 - Designing nanoscale devices that can optimally deliver medications for treating conditions that may arise over time with chronic anticancer therapy, including pain, nausea, loss of appetite, depression, and difficulty breathing

Nanotechnology for Cancer: Evolution and Progress

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P. Grodzinski, M. Silver, and L. Molnar, 'Cancer Nanotechnology – Promises and Challenges', *Expert Review Molecular Diagnostics* 6, 307 (2006)

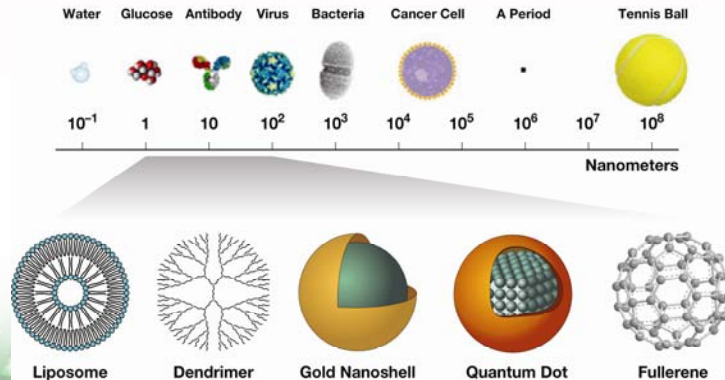


Nanoparticles in Cancer Diagnosis and Treatment

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“Research and technology development at the atomic, molecular or macromolecular scale leading to the controlled creation and use of structures, devices and systems with a length scale of approximately 1 – 100 nanometers (nm).”

(Source: National Nanotech Initiative)



Nanotechnologies for Developing World

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- **Energy storage, production and conversion** →
- **Agricultural productivity enhancement**
- **Water treatment and remediation**
- **Disease diagnosis and screening** →
- **Drug delivery systems** →
- **Food processing and storage**
- **Air pollution remediation**
- **Construction**
- **Health monitoring** →
- **Vector and pest detection and control**

Potential impact on cancer

F. Salamanca-Buentello, P.A. Singer et al., PLoS Medicine 2, e97 (2005)

Push for Nanotechnology Role in Developing World

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Comprehensive initiative on healthcare?

- Inexpensive diagnostic tests
- New vaccines
- Novel methods of drug delivery

Multiplexed Diagnostic Assays

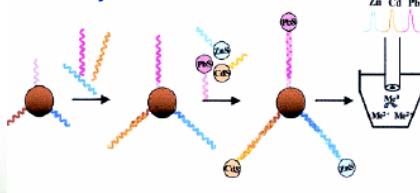
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Q-dots

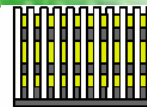


Alivisatos et al.

Nanocrystals for E-chem det.



J. Wang, *Analytica Chimica Acta* 500 (2003) 247

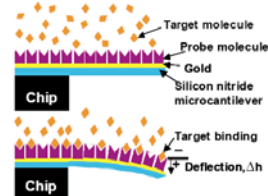


Nanorods



Nicewarner-Pena et al.,
Science 294, 137 (2001)

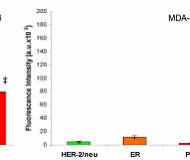
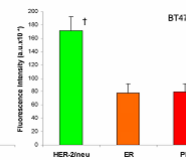
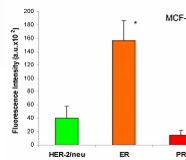
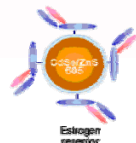
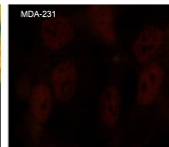
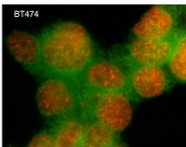
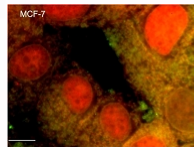
Cantilevers



G. Wu and A. Majumdar,
Nature Biotech 19, 856 (2001)

Monitoring of Breast Cancer Biomarkers Using Quantum Dots

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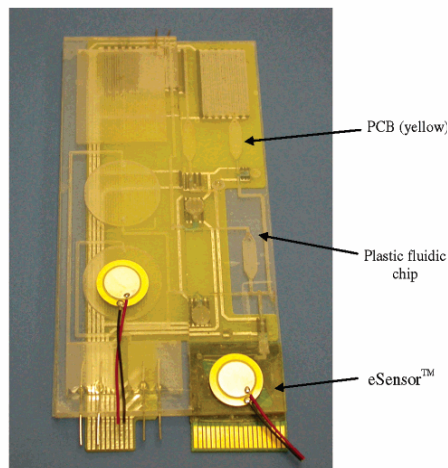
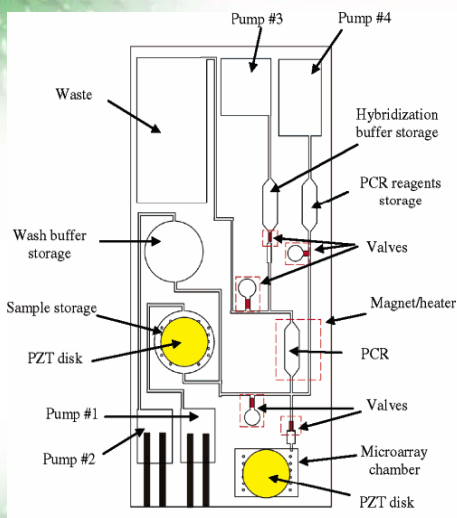


- ER, PR, and HER2 can be detected using multiplex QDs simultaneously on specimens of breast cancer cell lines
- ER, PR and HER2 detected using QD-Abs can be quantified using spectrometry
- Detection/quantification of ER, PR and HER2 using QD-Abs correlated well with standard methods (IHC and Western Blotting)

O'Regan et al., submitted to *PNAS*

Microfluidics for Diagnostics

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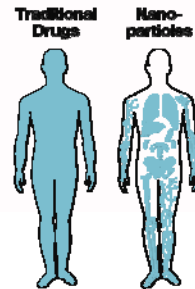
R.Liu, P. Grodzinski, *Anal Chem* 76, 1824 (2004)

Drug Delivery

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Problem:

- Non-specific
- Cannot reach tumor
- Insoluble
- Systemic chemotherapy is often toxic



Solution:

- Payload: large quantities of multiple drugs delivered directly to tumor sites
- Delivery device minimizes alterations needed to drug
- Therapeutic index shifts
- Enables nucleic acid delivery

Multi-Functional Nanoparticle-based Therapies

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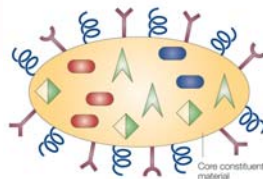
■ Multi-functional platforms:

- Targeting
- Delivery
- Reporting, biosensing



→ In one package

Free drug formulations do not possess multi-functional characteristics



Therapeutic or imaging payload	Biological surface modifier
Drug A	PEG
Drug B	Targeting moieties
Contrast enhancer	
Permeation enhancer	

First generation of nano-delivered drugs (no targeting) approved by FDA – Abraxane®

M. Ferrari, Nature Reviews 5, 161 (2005)

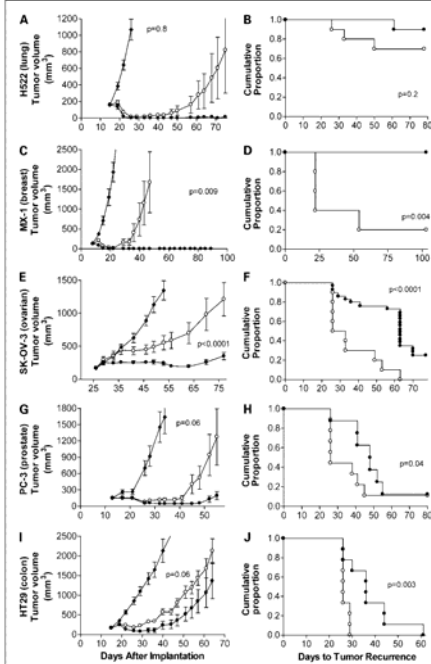
Abraxane

First generation of nano-delivered drugs approved by FDA – Abraxane®

Abraxane is albumin-bound, 130-nm particle form of paclitaxel. It was developed to avoid solvent-related toxicities in free paclitaxel and to exploit albumin receptor-mediated endothelial transport.

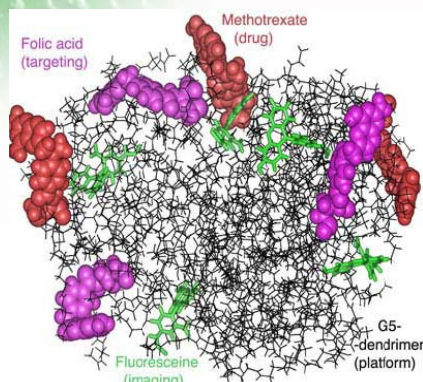
Antitumor activity and mortality were assessed in nude mice bearing human tumor xenografts in lung (H522), breast (MX-1), ovarian (SK-OV-3), prostate (PC-3), and colon (HT29)]

N. Desai, P. Soon-Shiong,
Clin Cancer Res 12, 1317 (2006)



New Experiments Multifunctional Nano-platforms: Find-Detect-Treat

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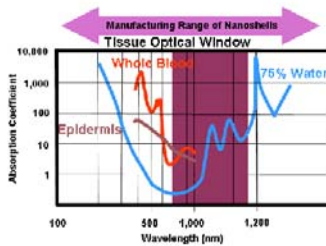
KB human tumor grown in mice



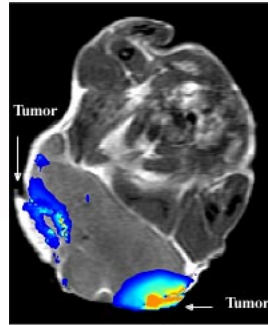
Kukowska-Latallo, Baker et al., *Cancer Research*, 65, 5317 (2005)

New Experiments Multifunctional Nano-platforms: Find-Detect-Treat

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Naomi Halas and Jennifer West,
Rice University and Nanoshells, Inc.

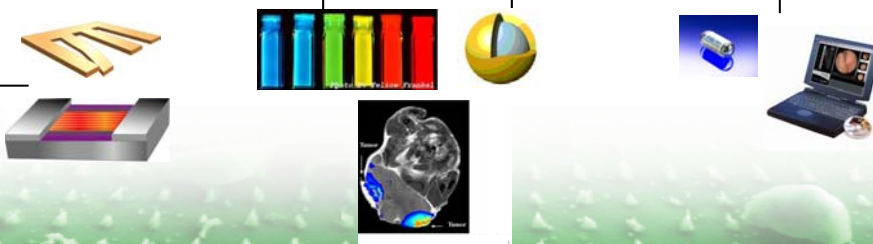


Two tumors in a mouse are simultaneously ablated. The colored areas (blue and yellow) represent temperature levels conducive to ablation. The nanoshells injected into the tumor in the upper left are being irradiated from the laser on the other flank of the mouse.

Nanotechnology – Cancer Prevention

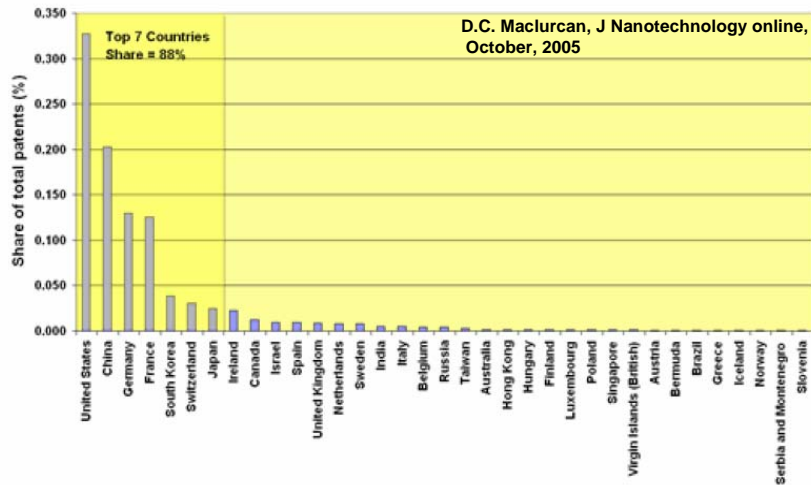
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- Genetic profiling using highly multiplex in-vitro platforms
- Early imaging enabled through the use of 'smart' nanoparticles
- Development of in-vivo sensing techniques which will detect (and possibly kill tumor cells) at very early stage
- Reduced discomfort of routine exams – for example endoscopy using in-vivo integrated sensor/imaging/data transfer devices



Nanotechnology – Innovation Worldwide

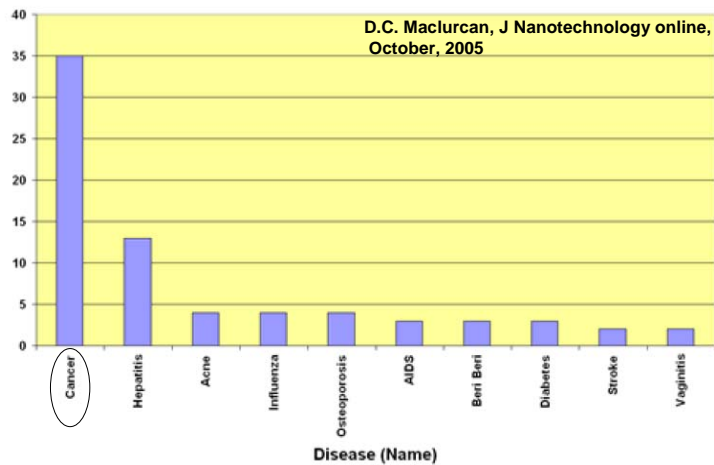
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Patent activity (1975 – 2004) in nanotechnology for biomedical applications

Nanotechnology – Innovation Worldwide

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Patent activity by disease

Nanotechnology Development: Path Forward Challenge: Integration of Disciplines

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- Silos of activity among private and public domains
- Disciplines are not used to working with each other
 - No common language
 - No common scientific literature
 - No common funding mechanisms
 - Few integrated training programs

Engineering

Materials Science

Physics

Information Technology

Math

Medicinal Chemistry

Biology

NCI's Commitment to Cancer Nanotechnology

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- \$144.3M initiative
- Designed to "ignite" nano-product development and commercialization
- Encompasses public and private sectors
- Launched September 2004

- Centers of Cancer Nanotechnology Excellence
- Multidisciplinary Research Teams
- Nanotechnology Platforms for Cancer Research
- Nanotechnology Characterization Laboratory



Nanotechnology – Environmental and Safety Concerns

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- **Hazard identification**
 - In vitro toxicity
 - Acute in vivo toxicity
 - Subchronic/chronic toxicity
 - Route of exposure
- **Dose response**
 - External dose
 - Internal dose
 - Biologically effective dose
- **Exposure assessment**
 - Human exposure

Nanomaterials production

Chronic exposure of the worker

Nanomaterials use for biomedical applications

Dose and patient response



Summary

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- **Nanotechnology clearly provides unique solutions to problems which can not be addressed otherwise**
- **New approaches to diagnosis:**
 - In vitro diagnostic assays
 - New imaging contrast agents
- **New approaches to therapy:**
 - Local drug delivery
 - Lower side effects
- **Nanotechnology and prevention**

Developing world:

- Inventor or importer?
- Cost?
- How soon?