Nanomaterials for Cancer Diagnosis and Therapy

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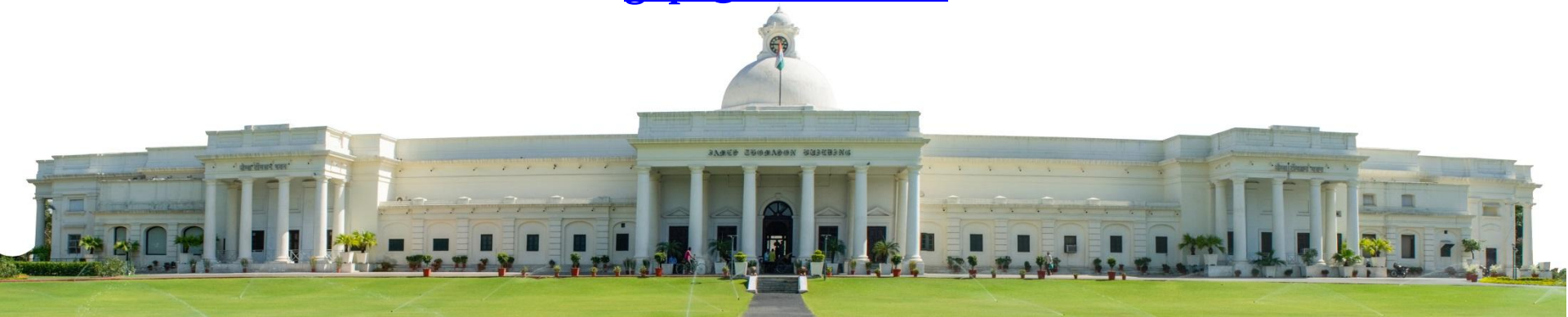


What is a nanoparticle?

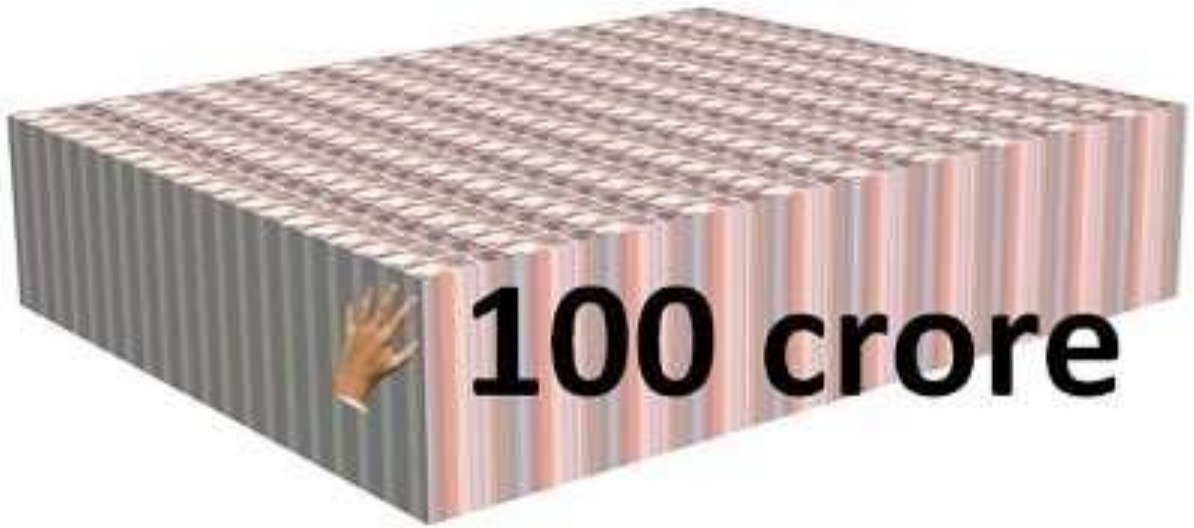
- Nanoparticle is any material having atleast one of its dimensions in the range of 1-100 nm.
- "Nano" – derived from a Greek word "Nanos" meaning DWARF or small.
- 'Norio Taniguchi, 1974' -- coined the term nanotechnology
- A nanometer is ***one billionth of a meter*** (10^{-9} m).

Nano- Simple example

- The population of India is one billion or 100 crores. Each Indian – you or me is nano in comparison with the total population of India.

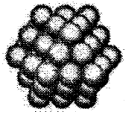
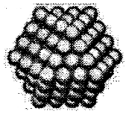
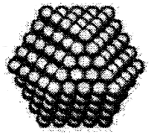
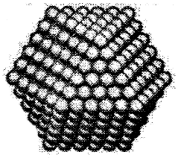
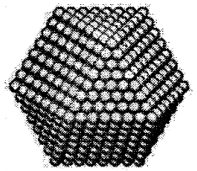
Nano- Simple example

One rupee



- One rupee in 100 crore rupees

Why small is Good?

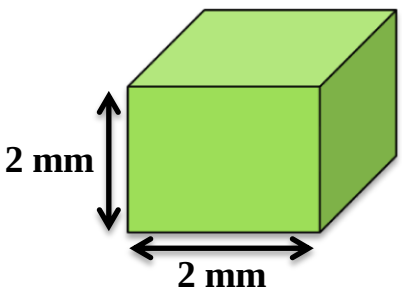
Full-shell Clusters		Total Number of Atoms	Surface Atoms (%)
1 Shell		13	92
2 Shells		55	76
3 Shells		147	63
4 Shells		309	52
5 Shells		561	45
7 Shells		1415	35

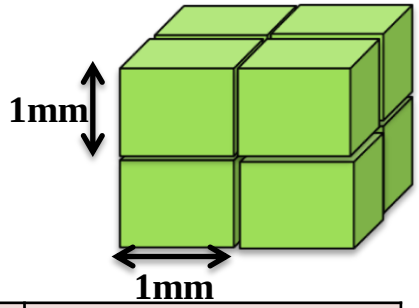
Surface area increases as size decreases

Nano-objects are:

- **Faster**
- **Lighter**
- **Can get into small spaces**
- **Cheaper**
- **More energy efficient**
- **Different properties at very small scale**

Surface area-to-volume ratio

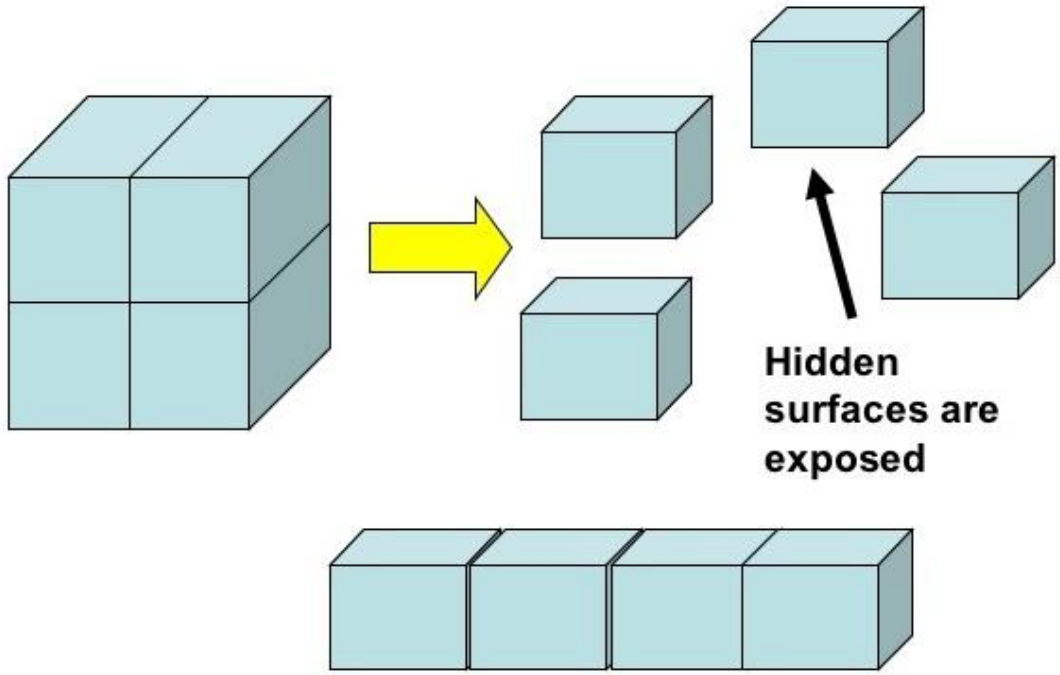




Surface Area (mm)	Surface area= Height x Width x No. of sides x No. of cubes	24 (2x2x6x1)	48 (1x1x6x8)
Volume (mm)	Volume=Height x Width x Length x No. of cubes	8 (2x2x2x1)	8 (1x1x1x8)
Surface Area/Volume ratio	Surface area/Volume	3 (24:8)	6 (48:8)

Surface area-to-volume ratio

- As surface to volume ratio increases
- A greater amount of a substance comes in contact with surrounding material
- This results in better catalysts, since a greater proportion of the material is exposed for potential reaction



Nanotechnology is not new!

window glass
(Medieval times)

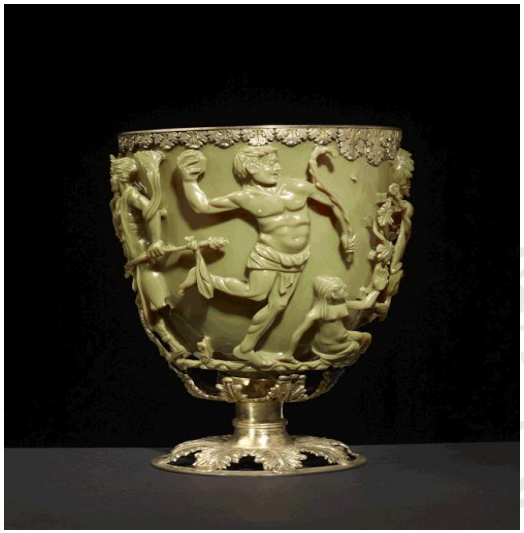
Transmitted light

Reflected light

- Thousand years ago, Chinese used gold nanoparticles as an inorganic dye to introduce red color into ceramic porcelains.

In 1857, Faraday prepared gold colloids that was stable for almost a century before being destroyed during World War II.

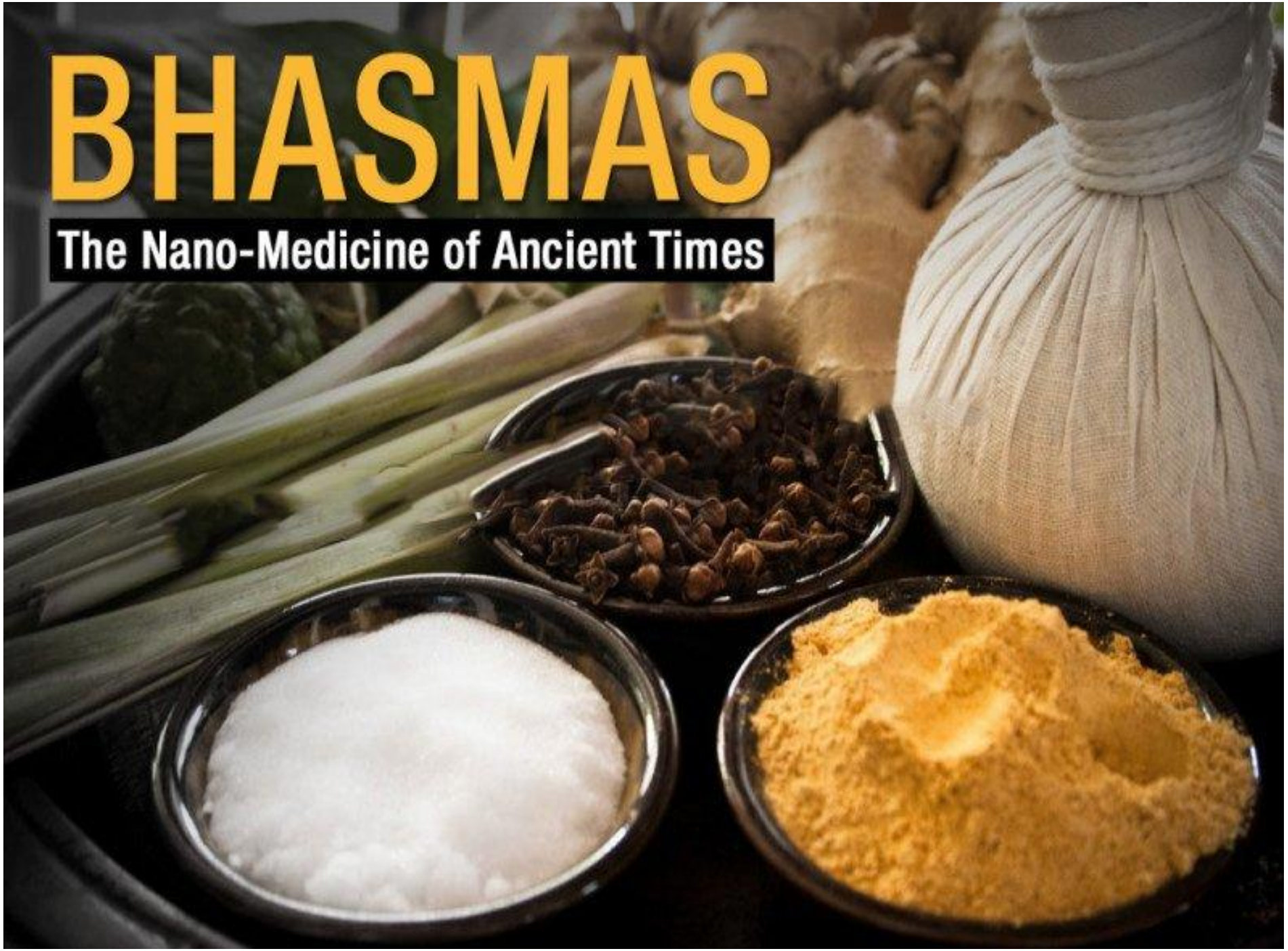
The Lycurgus cup



The Lycurgus Cup is a 4th-century Roman glass cage cup made of a dichroic glass.

Red when light from behind and green when light from in front. (**red** in transmitted light and **green** in scattered light)

The dichroic effect is achieved by making the glass with tiny proportions of nanoparticles of gold and silver "dispersed“ in colloidal form throughout the glass material.


BHASMAS
The Nano-Medicine of Ancient Times

How to make Nanostructures?

Top-down Approach

Building something by starting with a larger component and carving away material (like a sculpture)

In nanotechnology: patterning (using photolithography) and etching away material, as in building integrated circuits

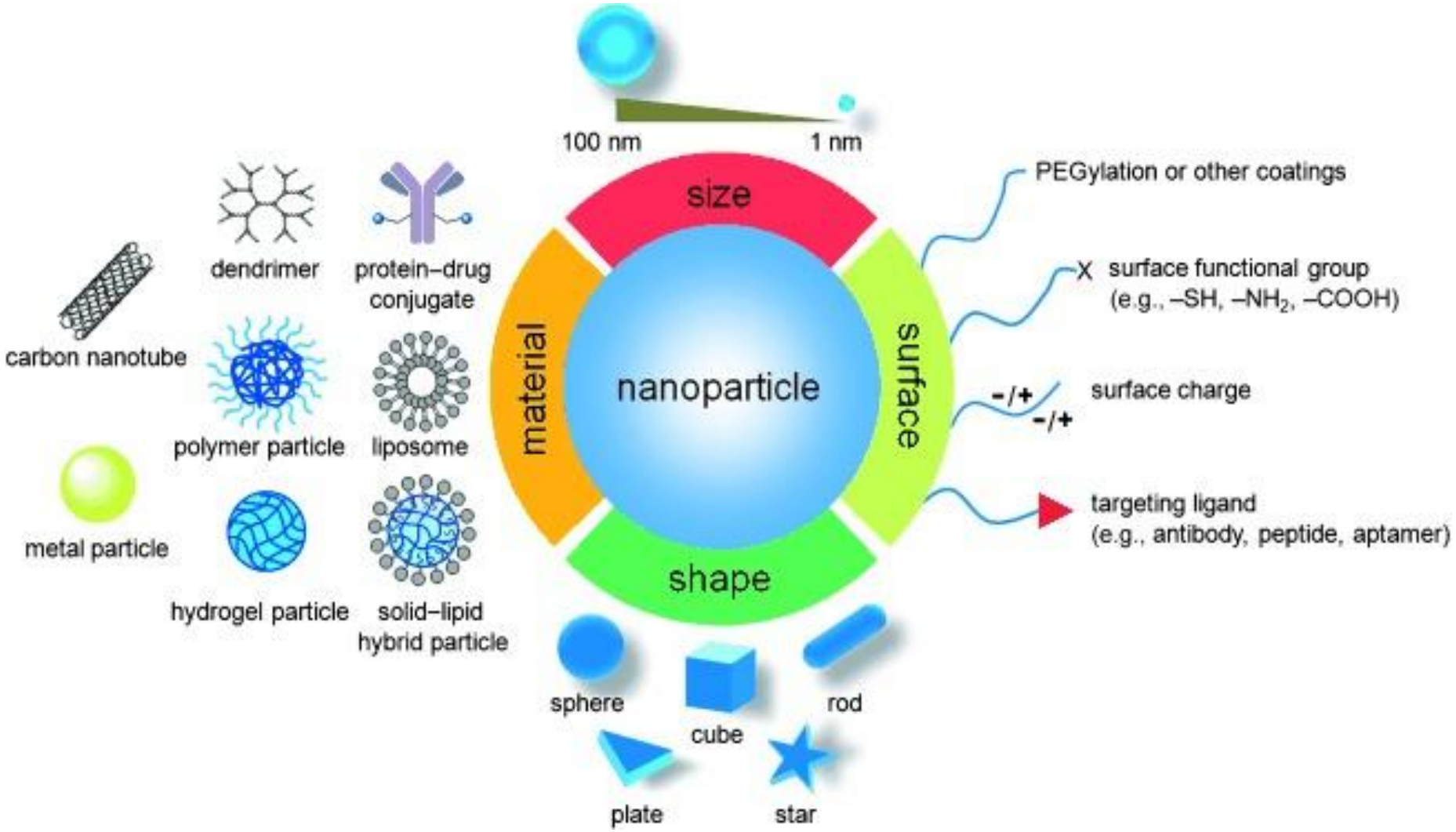
Rock **Statue**

How to make Nanostructures?

Bottom-up

Building something by assembling smaller components (like building a car engine), atom by atom assembly.

In nanotechnology: self-assembly of atoms and molecules, as in chemical and biological systems



Source: Angew. Chem. Int. Ed. 2014, 53, 12320 – 12364

Nanoscience & Nanotechnology

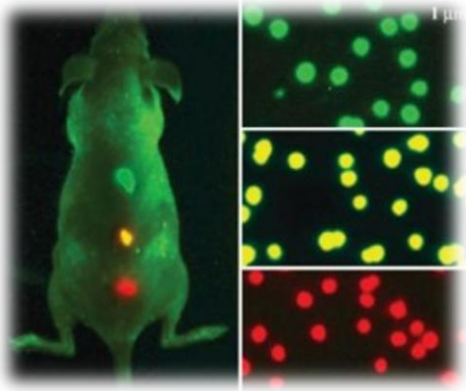
Nanoscience – is the study of nano-materials, their properties and related phenomena.

Nanotechnology – is the application of nanoscience to produce devices and products.

http://www.androidauthority.com/quantum-dot-vs-oled-explained-659321/

Nanobiotechnology & Bionanotechnology

- Nanobiotechnology / Nanobiology: Nanomaterials/tools for biological applications



Bio imaging

- Bionanotechnology: Understanding biological nanostructures and its potential applications

DNA Nanotechnology

Cancer Nanotechnology

Cancer &Tumor

Cells that continue to replicate, and become immortal.

1. **Malignant**: A tumor that grows indefinitely and spreads (metastasis)--also called cancer: kills host
2. **Benign**: A tumor that is not capable of metastasis: does not kill host

Types of Cancer

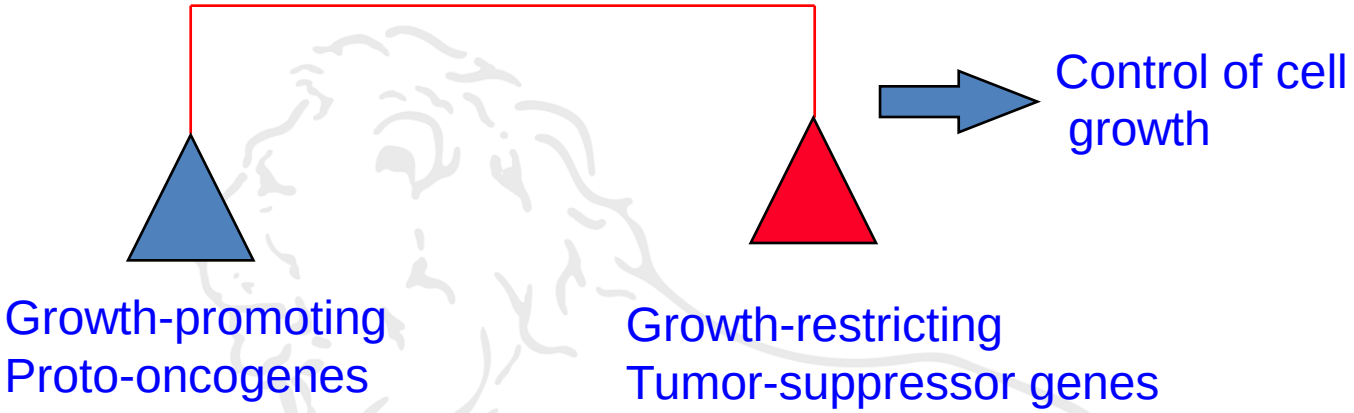
1. **Carcinoma:** arising from epithelial tissue, such as glands, breast, skin, and linings of the urogenital, digestive, and respiratory systems (89.3% of all cancers)
2. **Sarcoma:** solid tumors of muscles, bone, and cartilage that arise from the embryological mesoderm (1.9% of all cancers)
3. **Leukemia:** disease of bone marrow causing excessive production of leukocytes (3.4% of all cancers)
4. **Lymphoma, Myeloma:** diseases of the lymph nodes and spleen that cause excessive production of lymphocytes (5.4% of cancers)

Etiology of Cancer

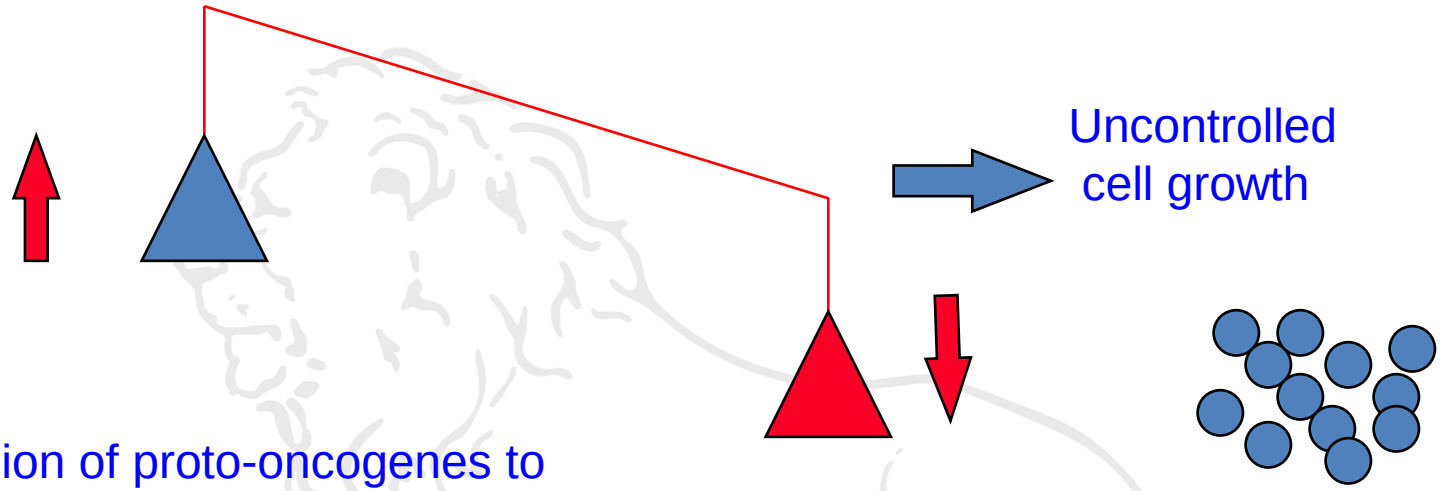
1. **Genetic factors:** mutations, translocation, amplifications
2. **Environmental factors:** UV, chemicals, viral infections

- Conversion of proto-oncogenes (potential for cell transformation) to oncogenes (cell transformation)
- Alteration in tumor suppressor genes

Cell Growth


Control of cell growth
Growth-promoting
Proto-oncogenes
Growth-restricting
Tumor-suppressor genes

Molecular Basis of Cancer



Did you know?

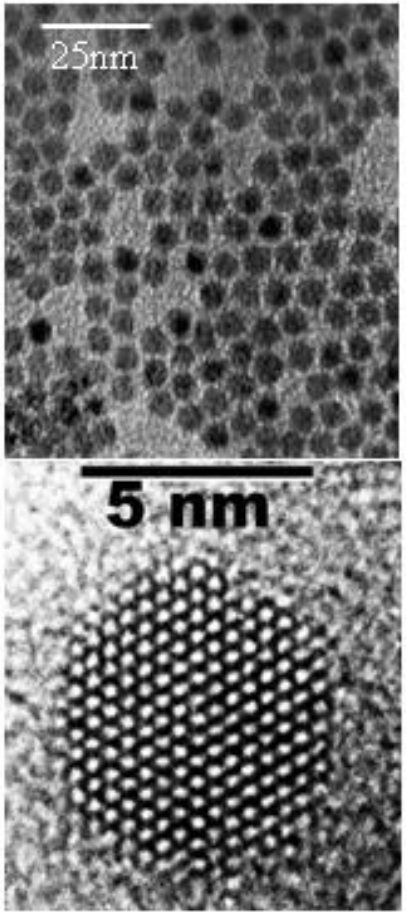
THE HUMAN TOUCH OF CHEMISTRY

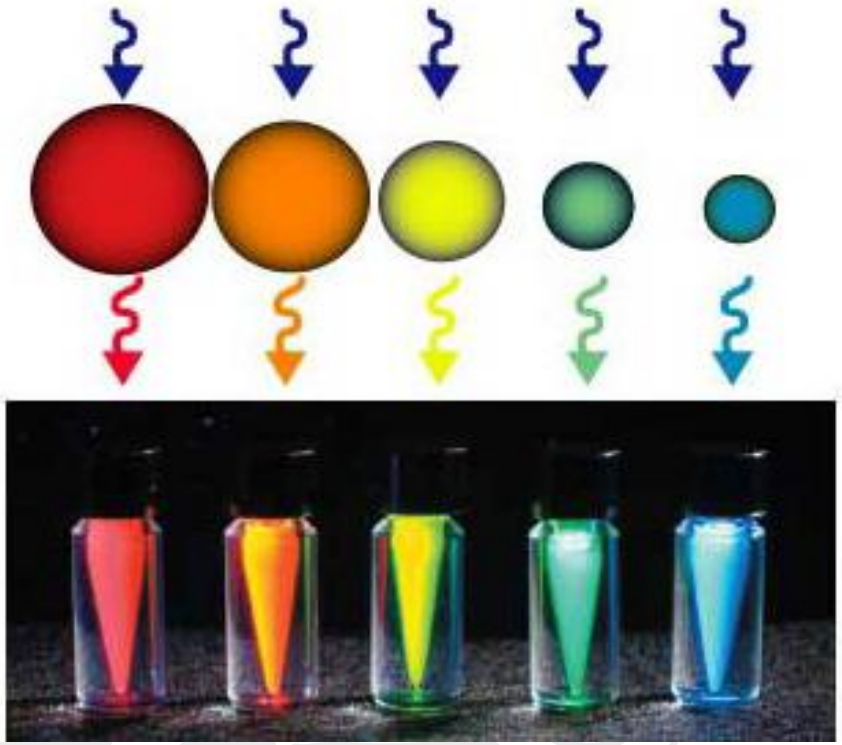
At least once a day your immune system destroys a cell that would become cancer if it lived.

T -cells Vs Cancer cells

What are Quantum Dots (QDot)?

Highly fluorescent, nanometer-size, single crystals of semiconductor materials





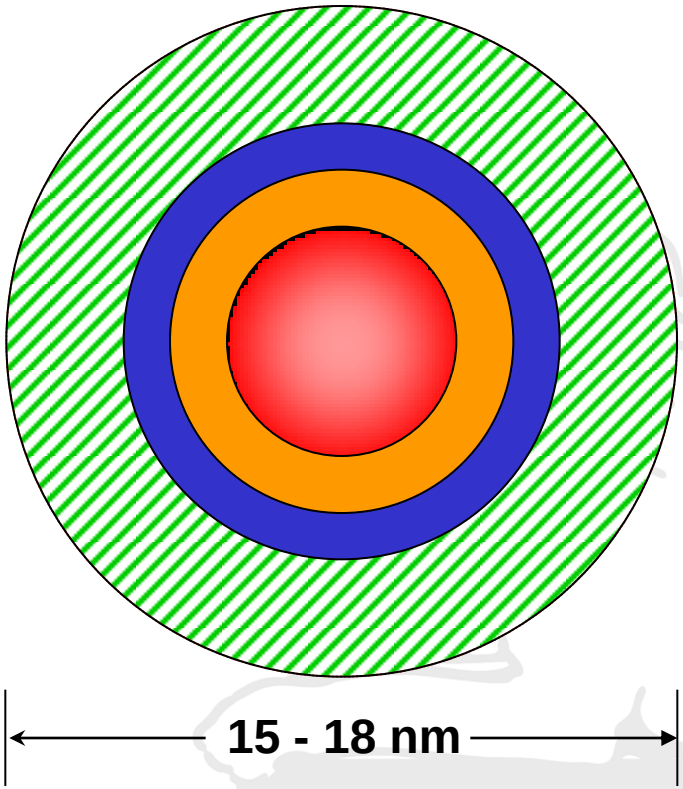
655 605 585 565 525 nm

Size of the nanocrystal determines the color

Size is tunable from ~5-15 nm (±3%)

Size distribution determines the spectral width

Qdot Conjugates are Engineered



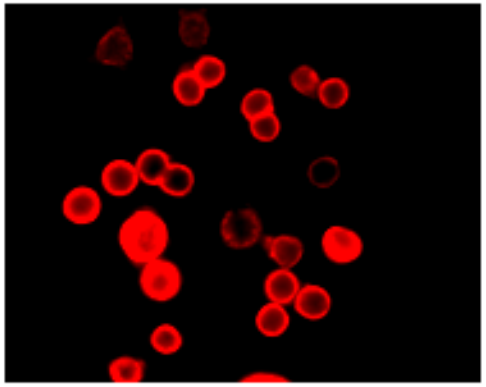
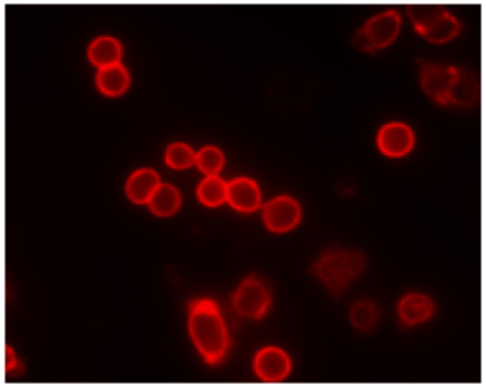
Core Nanocrystal (CdSe)
- Determines color

Inorganic Shell (ZnS)
– Improves brightness and stability

Organic Coating
- Provides water solubility and functional groups for conjugation.

Biomolecules
-Covalently attached to polymer shell
- Immuoglobulins (Abs)
- Streptavidin, Protein A
- Receptor ligands
- Oligonucleotides

Excellent Brightness and Photo-stability

Quantum dot	Organic dye
	
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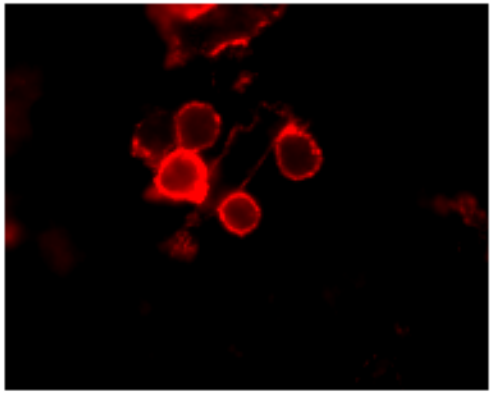
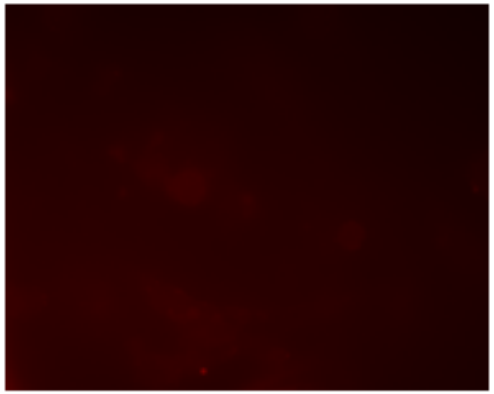
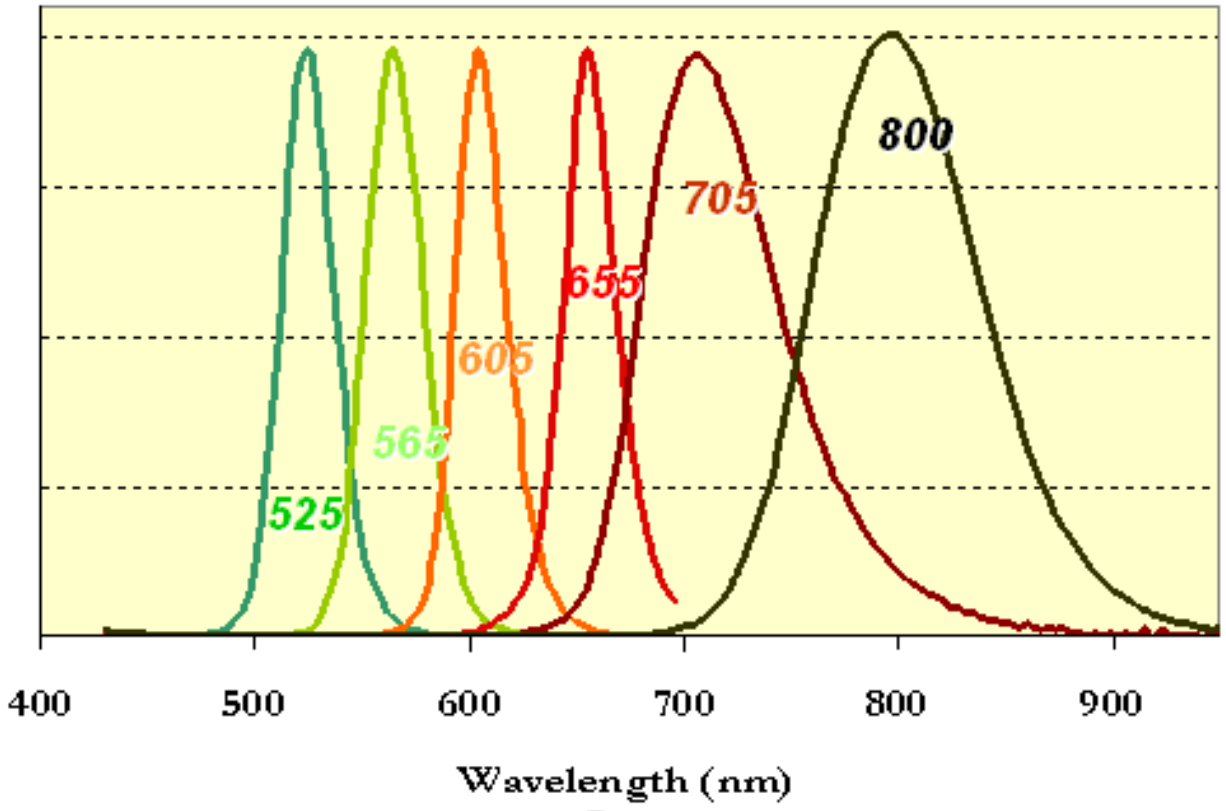
	
Exp. Time: 0.44 seconds	8.12 seconds

- High level Her 2/neu expression in SK-BR-3 cells
- Quantum dots is up to 50x brighter.

- Low level of Her 2/neu expression in MDA-MB-231 cells
- Organic dye is undetectable.

Sharp and distinguishable peaks enable multi-color detection

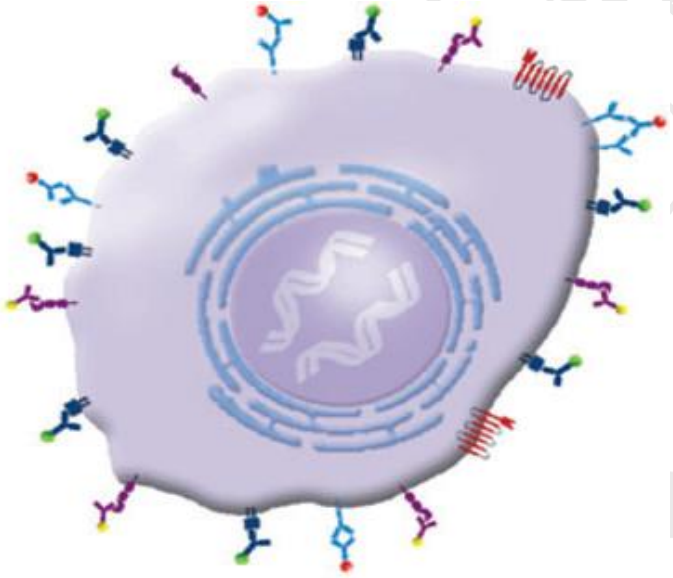


Minimal (<5%) cross-talk using 20nm bandpass filters

Diagnosis

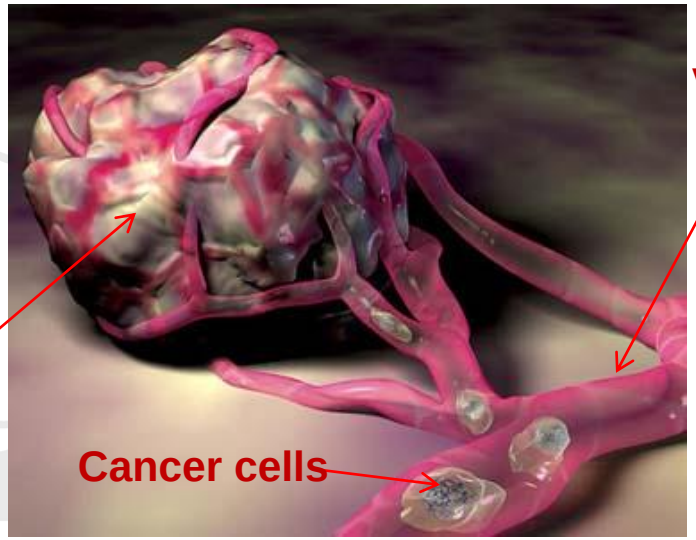
A. It must be multiplexed, i.e. multiple biomarkers must be detected simultaneously

B. A specific phenotype of cancer cells has a particular combination of biomarkers on its membrane



C. Different phenotypes show different aggressiveness on their metastatic behavior

D.



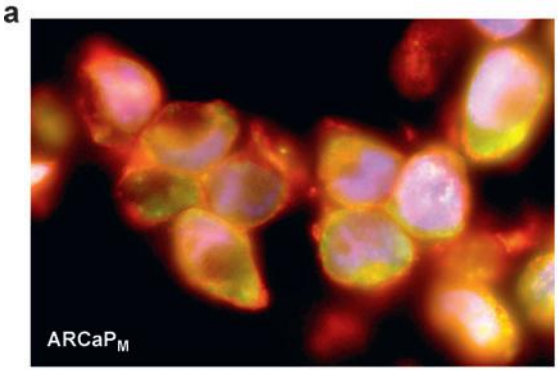
metastasis

Source: www.cancernews.com

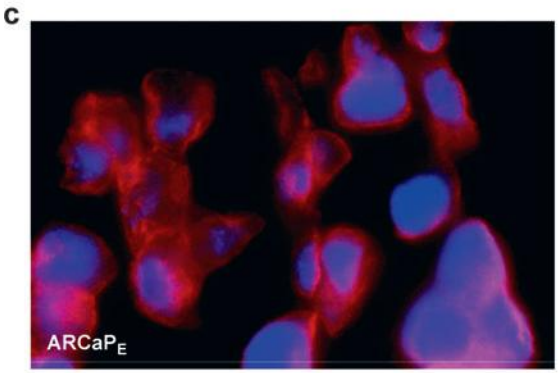
Multiplex Diagnosis

A. Four quantum dots of different diameter (i.e. different color) are respectively functionalized with four different antigens. Allowing for the distinction of two distinct phenotypes

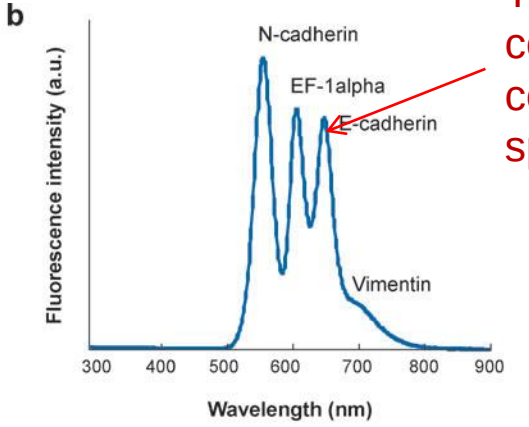
As a result cancer cells of different phenotype are colored differently



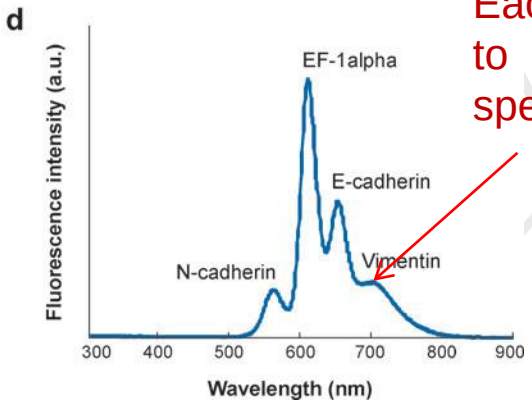
Aggressive cancer cells



Mild cancer cells

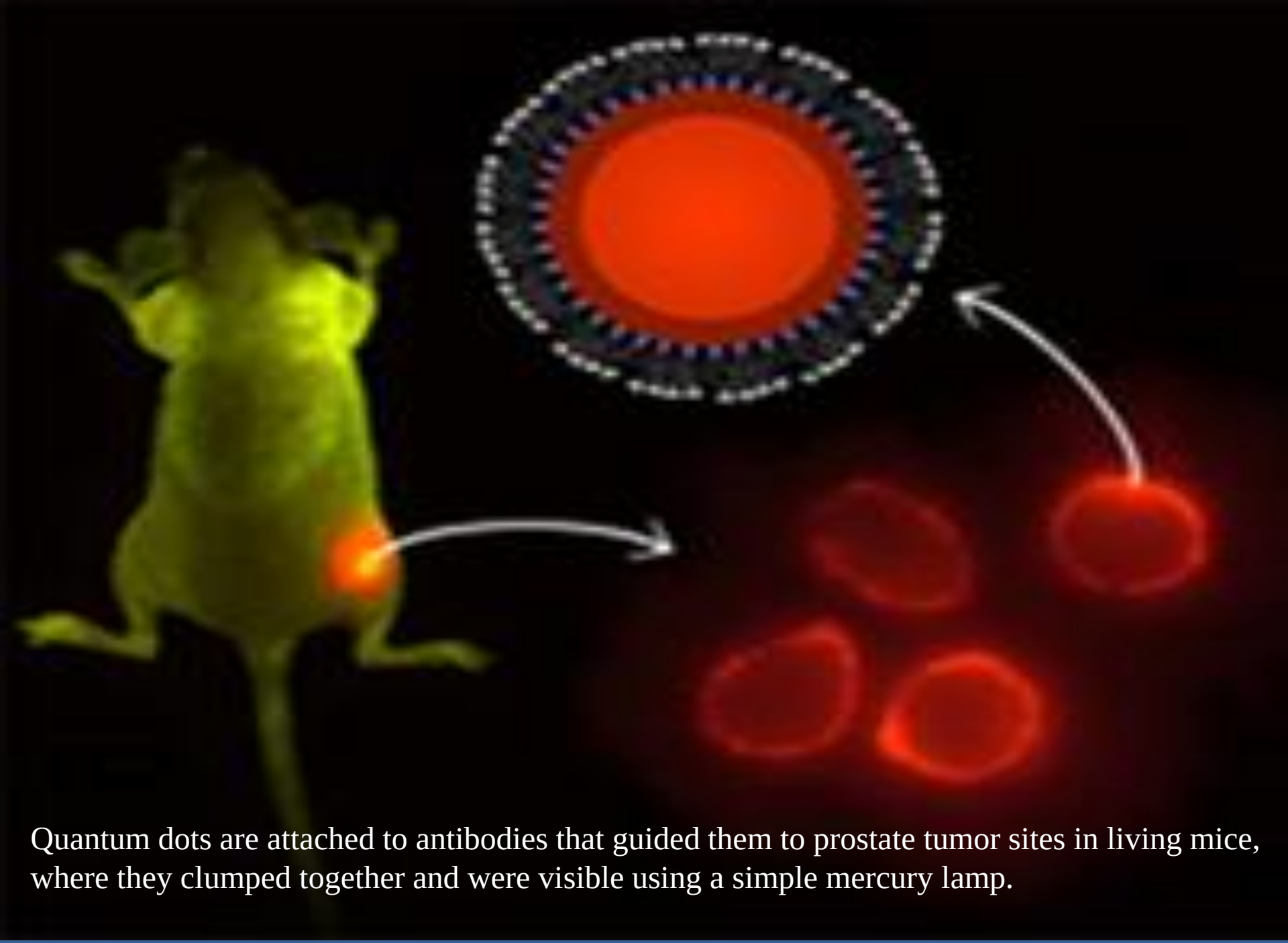


The peak intensity correlates to the concentration of a specific QD



Each peak correspond to the emission of a specific QD/antigen

Nature Protocols 2007. Vol. 2, pp. 1-15



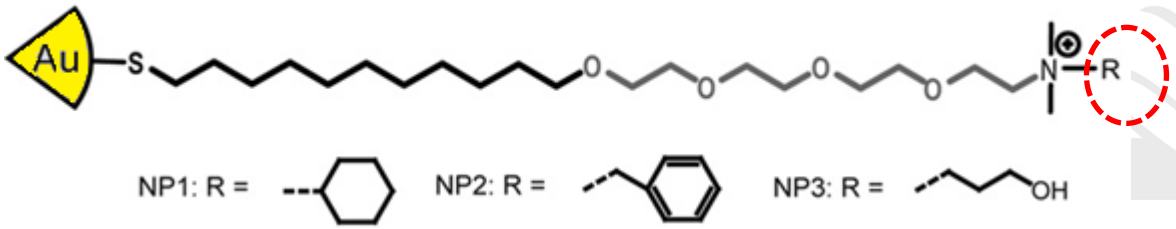
Quantum dots are attached to antibodies that guided them to prostate tumor sites in living mice, where they clumped together and were visible using a simple mercury lamp.

A Chemical Nose (Multiplex Detection)

A. Determining if a an apple is rotten or not, doing a thorough chemical analysis can be a very frustrating job. Due to the complex chemistry of the membrane, so can it be determining if a cell is sick or healthy.

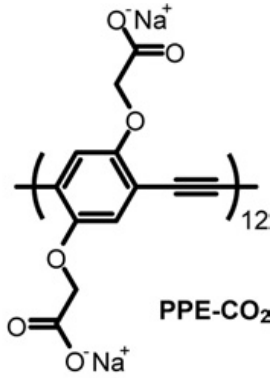
B. As well as our noses response to the overall chemistry of the apple, we can device an experiment that responses to the overall chemistry of the cell using the elements below

C.



Three sets (NP1,NP2,NP3) of functionalized gold nanoparticles

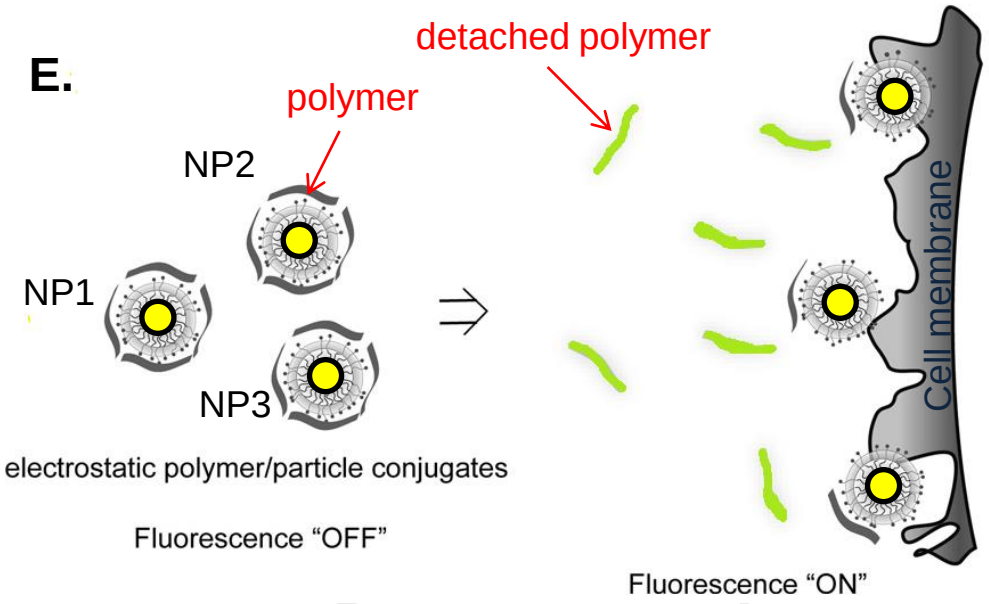
D.



A fluorescence reporter polymer

PNAS 2009, Vol. 106, pp.10912-10916

A Chemical Nose (Multiplex Detection)



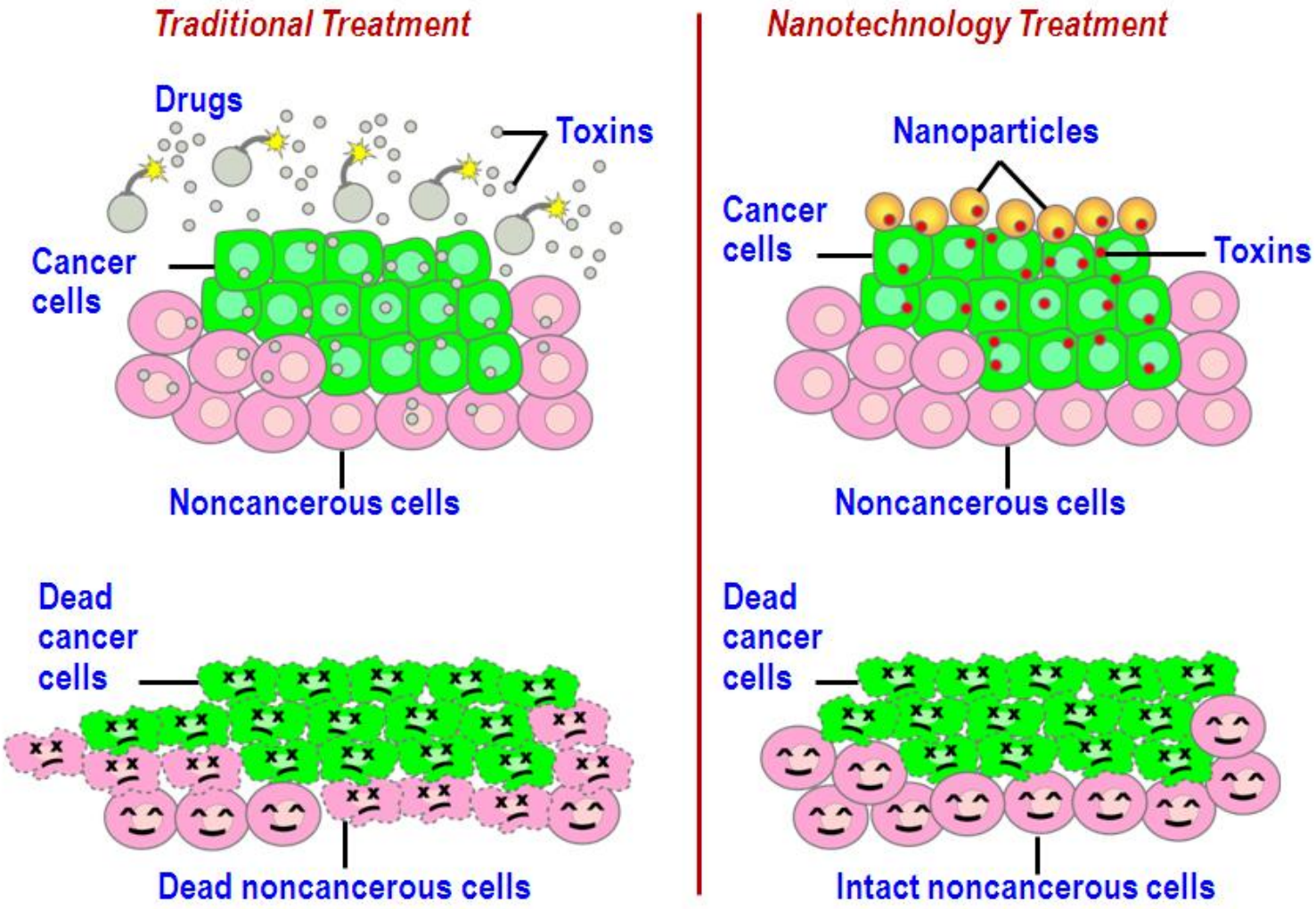
E. The polymer fluorescence is turned off while conjugated to the nanoparticle. Due to the interaction with the cell, the polymeric traces detach from the nanoparticle an emit a fluorescence signal

F. The responses from a NP1, NP2 and NP3 are different due to the different functional group. Thus, the combination of the three signals is characteristic of each cell

PNAS 2009, Vol. 106, pp.10912-10916

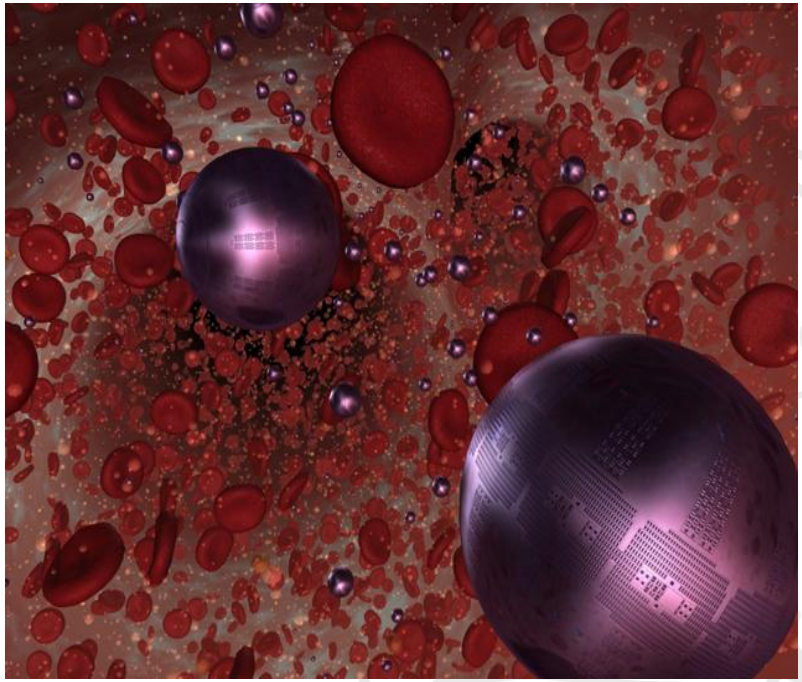
If a **man** takes a **pregnancy test** and gets a **positive result**, it means he most likely has **testicular cancer.**

Improving cancer treatment



https://www.cancer.gov/
https://www.nano.gov/

Nanobots for cancer therapy



Therapy

A. There is a search dual-mode nanoparticle that can detect a tumor (imaging) and destroy it (therapy)

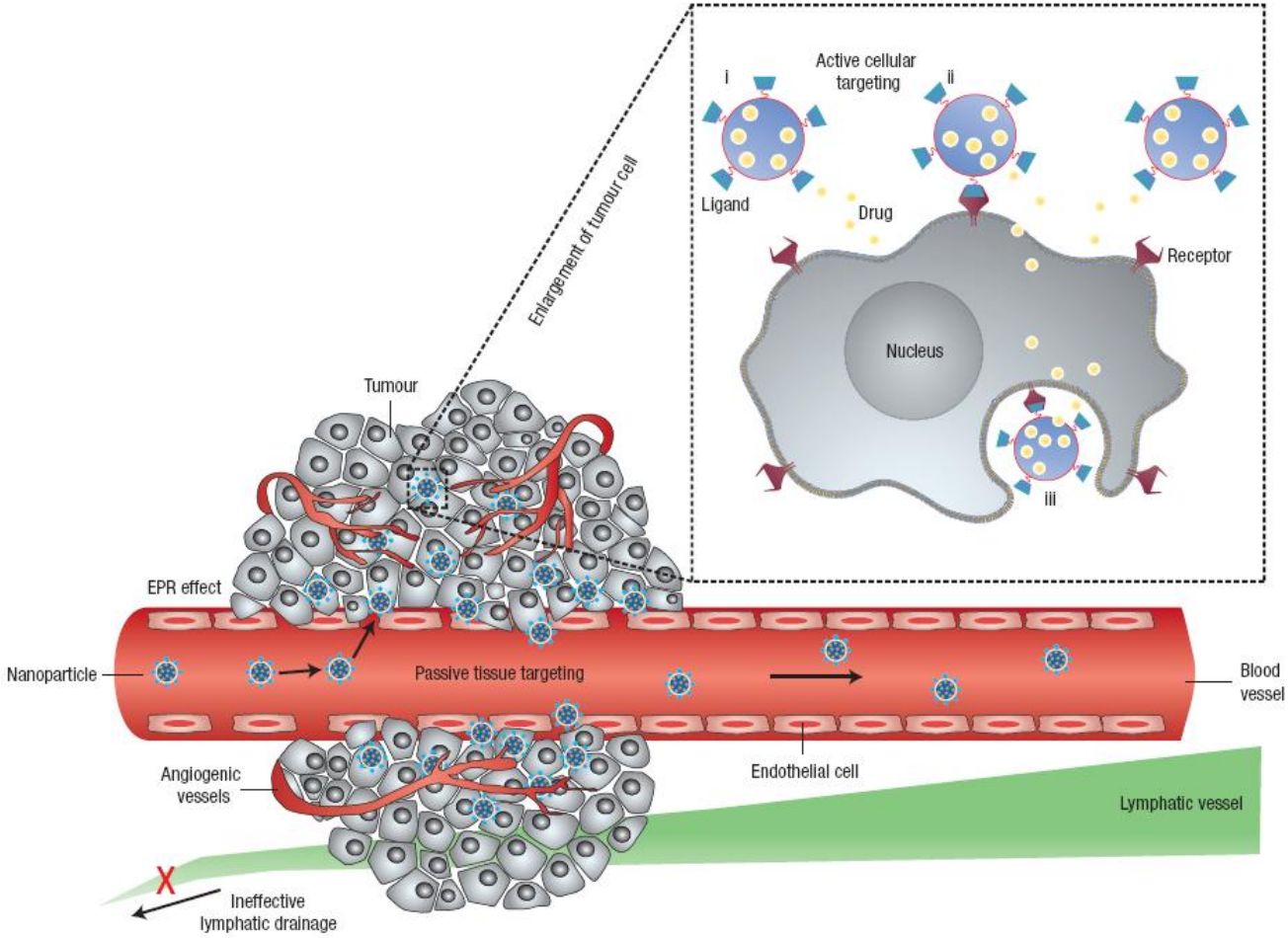
B. There is two action modes for therapeutical nanoparticles

Based on retention effect of particle of certain hydrodynamic size in cancerous tissues

Based on nanoparticle functionalization for specific targeting of cancerous cells

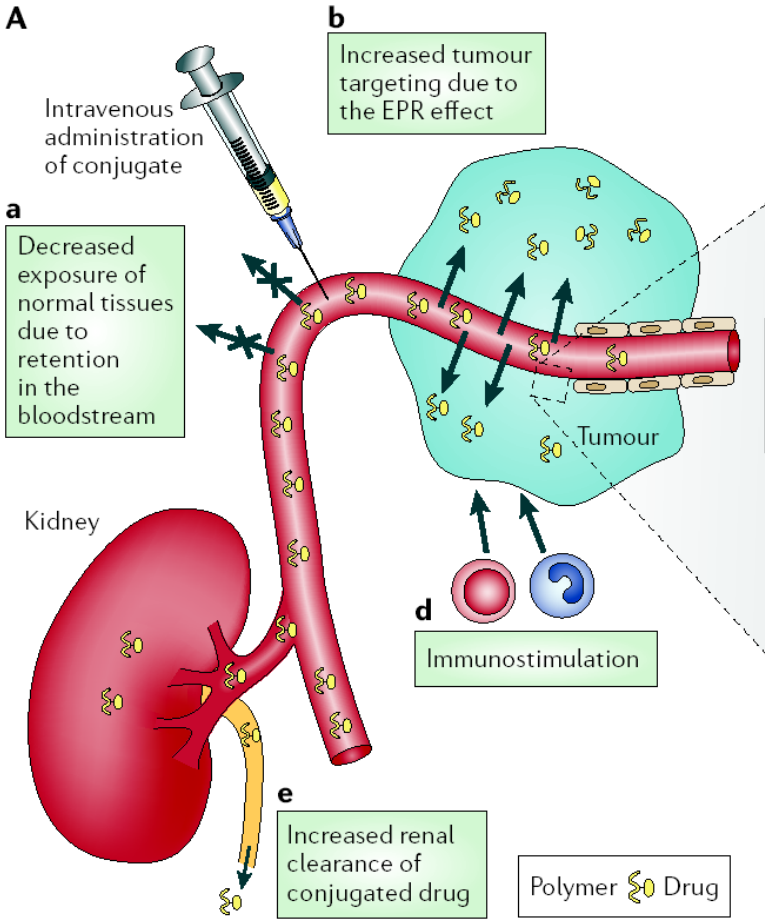
Tumors Grow Blood Vessels

Tumors need blood to grow larger than ~2mm in size



Peer, D, et al. Nature Nanotechnology 2007, 2, 751-760

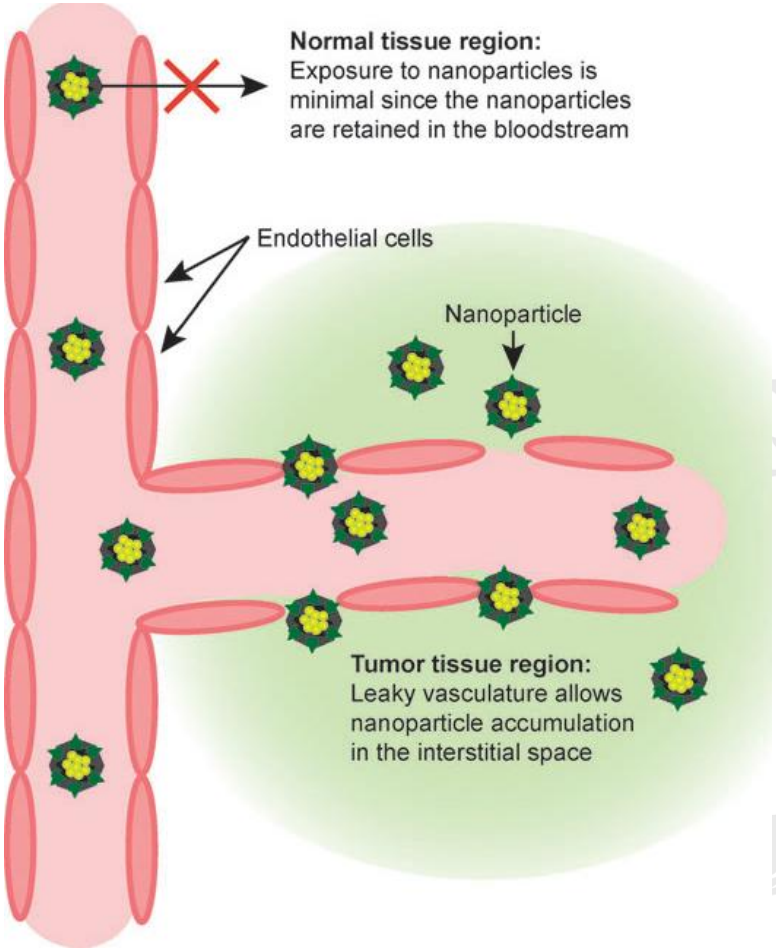
EPR Effect



Tumors have “leaky” blood vessels, which allow relatively large nano-sized “pills” to enter. This is called Enhanced Permeability and Retention (EPR) Effect . Normal blood vessels are not “leaky” and nano-particles are prevented from entering. This allows one to selectively target tumors.

Duncan, R. Nature Reviews Cancer 2006, 6, 688-701

Taking advantage of retention



A. Tumorous tissues suffer of Enhanced Permeability and Retention effect

B. Nanoparticles injected in the blood stream do not permeate through healthy tissues

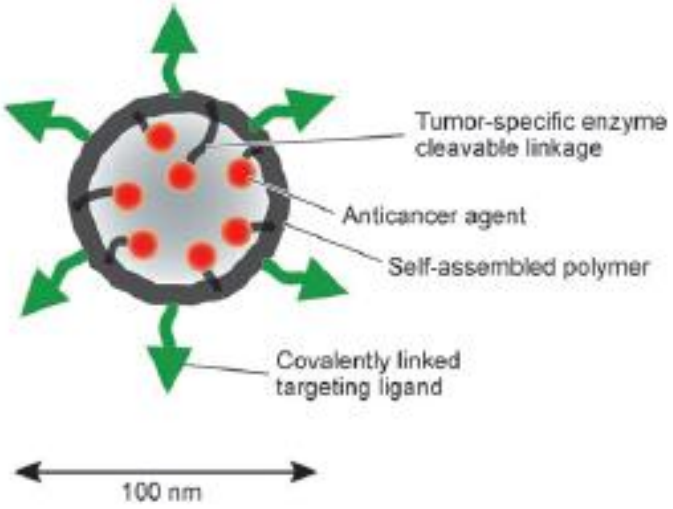
C. Blood vessels in the surrounding of tumorous tissues are defective and porous

D. Nanoparticles injected in the blood permeate through blood vessels toward tumorous tissues, wherein they accumulate

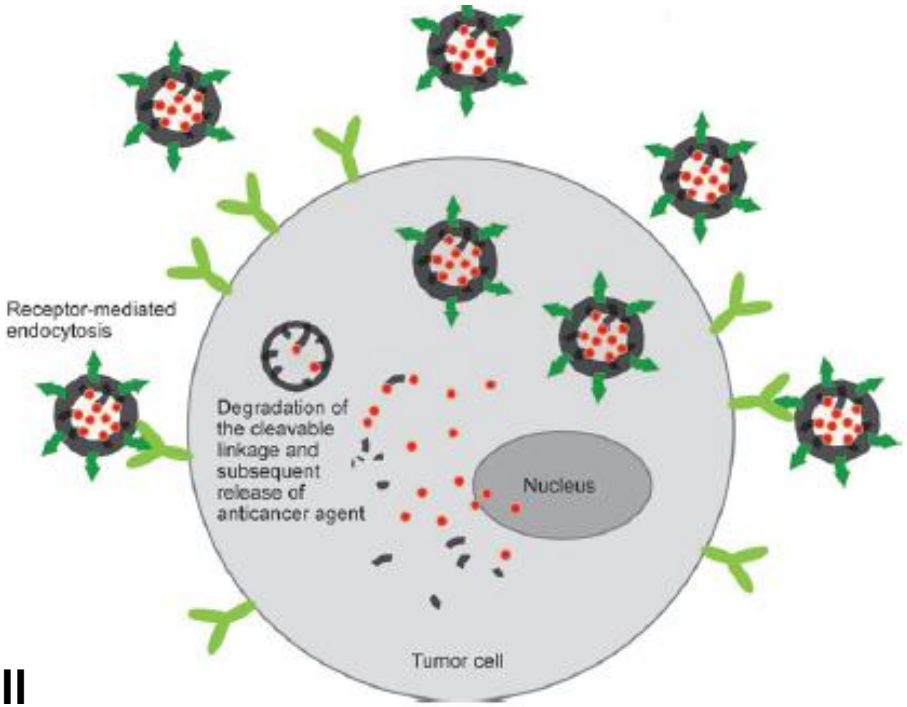
Annu. Rev. Biomed. Eng. 2007. Vol. 9, pp. 257–88

Targeted Polymer Nanoparticle

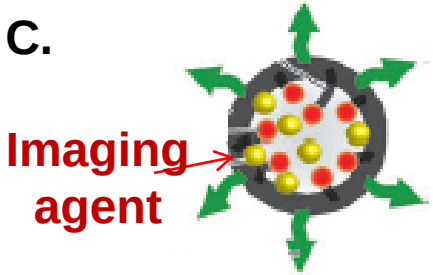
A. A dual Nanoparticle, the targeting ligand allow it to diagnose if a cell is healthy or sick, and bind specifically to the tumorous cell



B. Once inside the cell, the polymeric nanoparticle degrades and the anticancer agent is set free



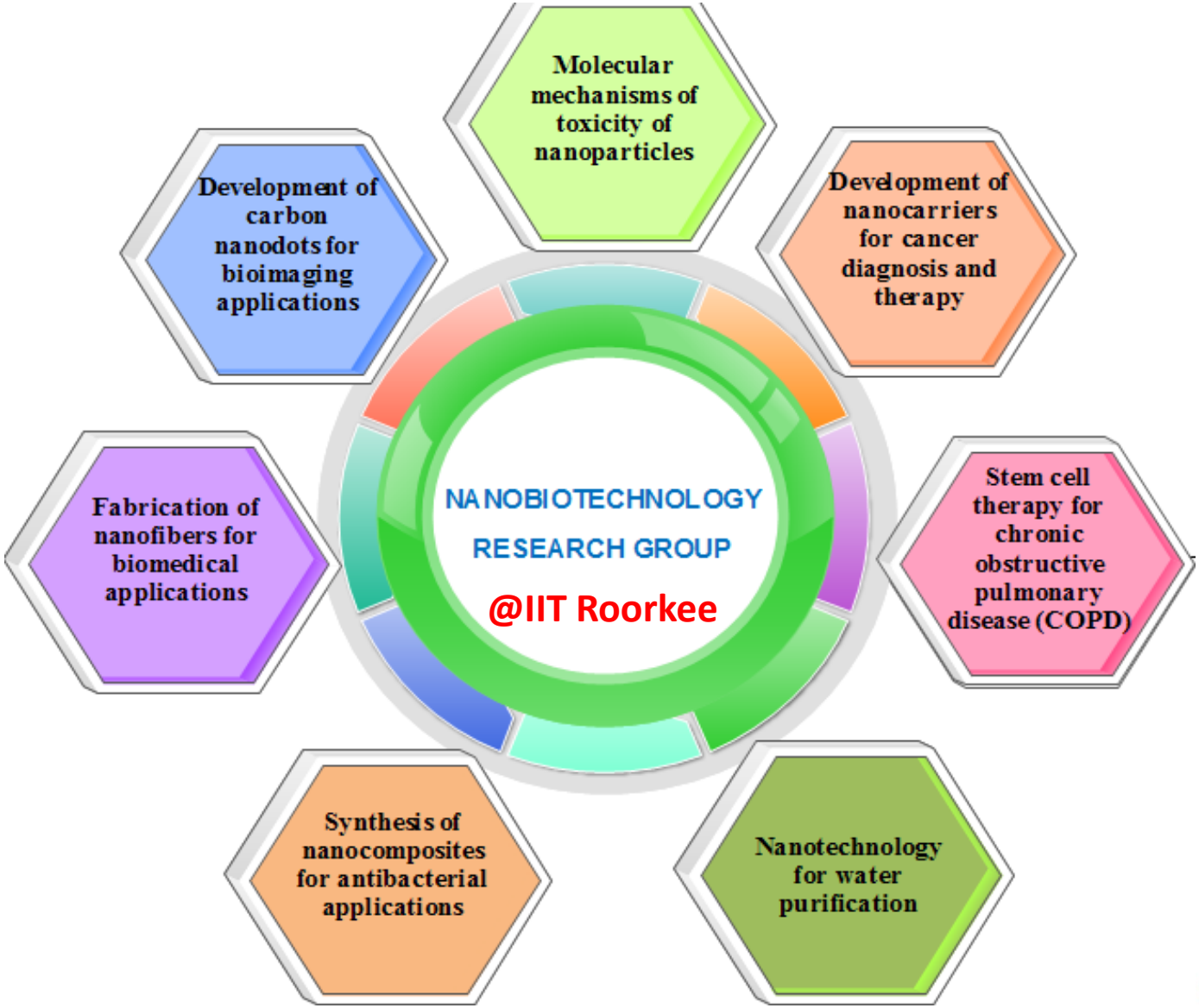
C.



An imaging agent can be added as well

Annu. Rev. Biomed. Eng. 2007. Vol. 9, pp. 257–88

Thrust Area of Our Research



Biolabeling applications

RSC Advances

RSC Publishing

COMMUNICATION

A novel one-step synthesis of PEG passivated multicolour fluorescent carbon dots for potential biolabeling application†

Cite this: *RSC Advances*, 2013, **3**, 16958

Received 15th May 2013,
Accepted 23rd July 2013

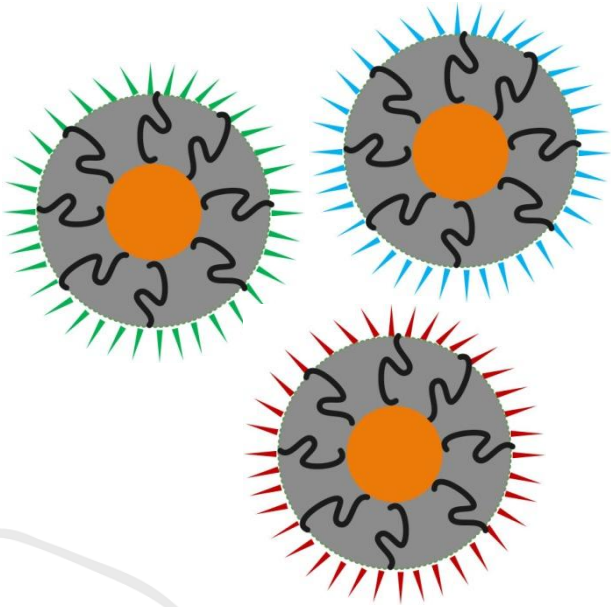
DOI: 10.1039/c3ra42415d

www.rsc.org/advances

Abhay Sachdev, Ishita Matai, S. Uday Kumar, Bharat Bhushan, Poornima Dubey and P. Gopinath*

Carbon dots (C-dots)

- Carbon is generally a black material with low solubility and no fluorescence.
- C-dots are zero dimensional fluorescent nanomaterials with quasispherical shape and sizes below 10 nm.
- The existence of C-dots came to light in 2004 during the purification of single-walled carbon nanotubes (SWCNTs).
- Substantial fractions of oxygen and hydrogen due to which these are also referred to as ‘carbogenic dots’.

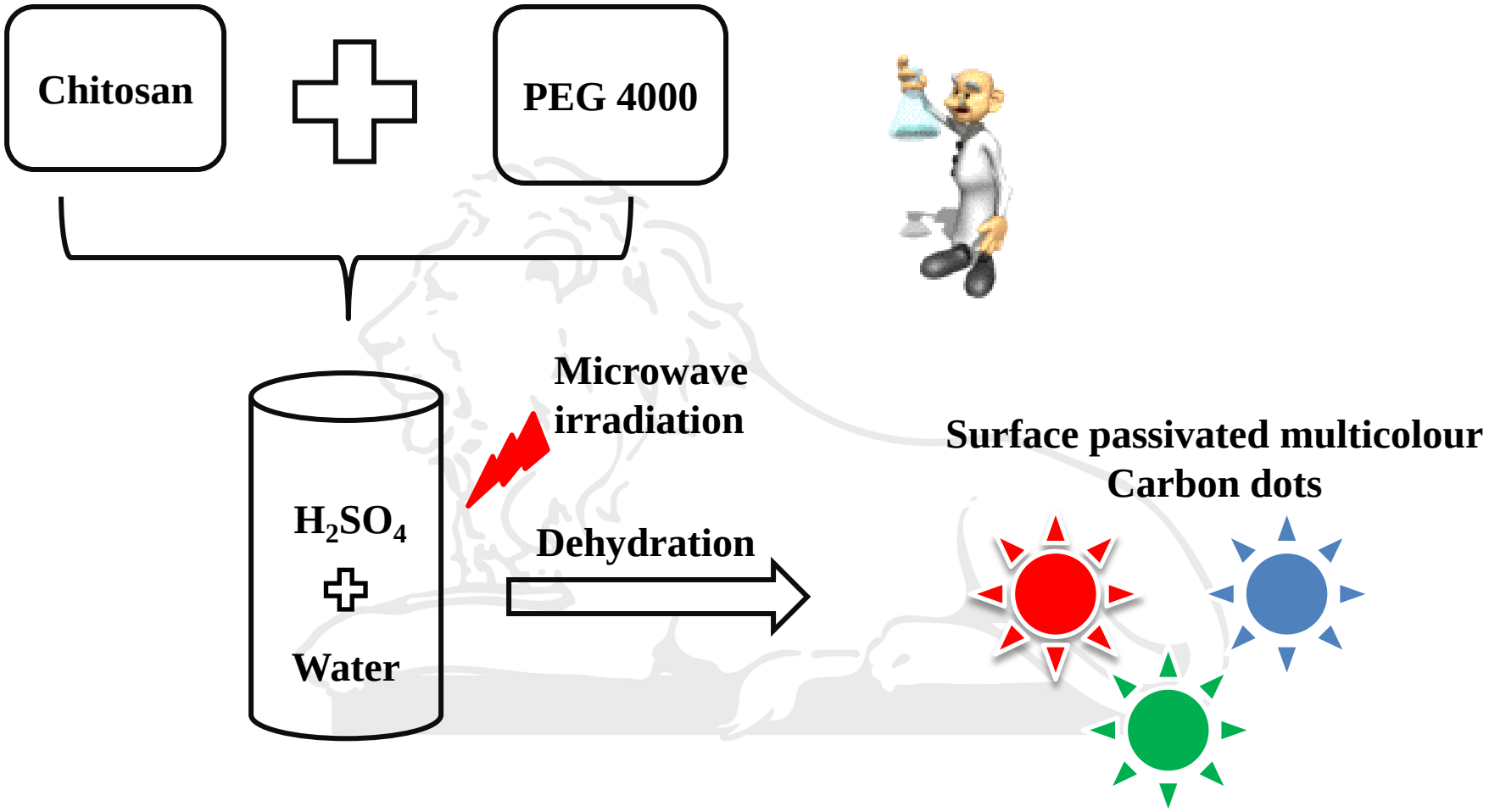


Surface functionalized Fluorescent C-dots

Carbon dots vs Quantum dots

Quantum dots	vs	Carbon dots
✓ Heavy metal core (CdSe, CdTe) associated with **toxicity**.		✓ Most carbon sources are non-toxic. Inherently **biocompatible**.
✓ **Intricate** synthesis.		✓ **Simple** synthesis.
✓ **Difficult** surface functionalization.		✓ **Readily** surface functionalization (-COOH, -NH_2, -OH).
✓ **Poor** aqueous solubility.		✓ **Highly** water soluble.

Synthesis of Carbon dots (C-dots)



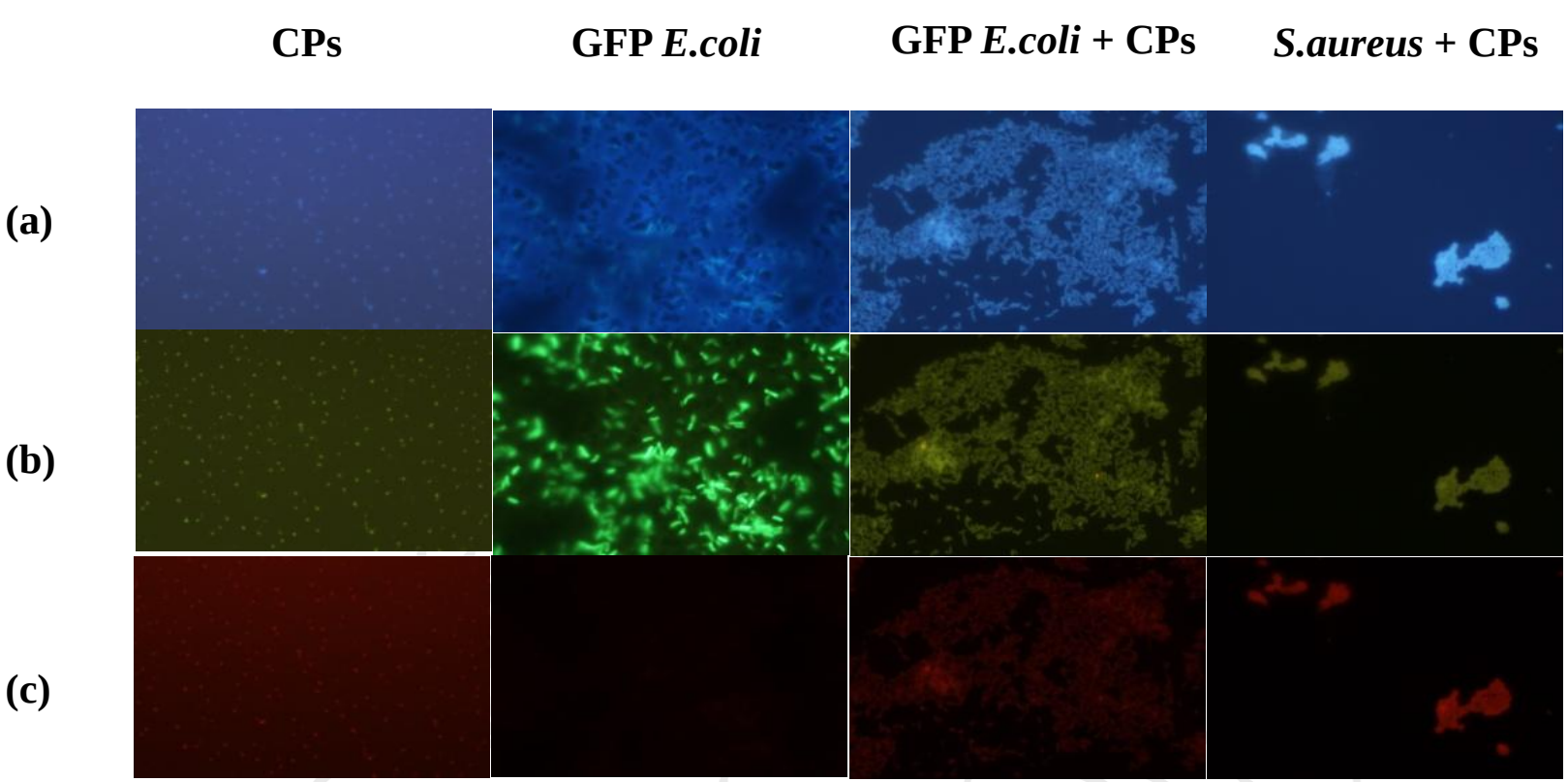
Synthesis of carbon dots (C-dots)

Synthesis of CDs by microwave pyrolysis method:

1. Add 0.2 g of chitosan was added to solution containing 25 mL of water and 4 mL of concentrated H_2SO_4.
2. Then add 0.2 g of PEG-4000 to the above solution and stir at 500 rpm for 15 minutes.
3. Subject the solution to microwave irradiation using a domestic microwave oven (IFB) operating at 100 % power level (700 W) for different cyclic times (20 s on,10 s off).
4. Allow the solution to cool naturally to room temperature.
5. Centrifuge the obtained dark brown solution at 14000 rpm for 15 minutes to separate the less fluorogenic, insoluble black deposit from fluorogenic, yellowish brown supernatant.
6. The yellowish brown supernatant is an indicate of formation of CDs

RSC Advances, **2013**, 3, 16958-16961.

Multicolor fluorescent carbon dots



Fluorescence microscopy images of CP , GFP *E.Coli* and CP labeled bacterial samples under (a) UV-2A (330-380nm), (b) B-2A (450-490nm), (c) G-2A (510-560nm) filter excitation.

Source: A. Sachdev et al., RSC Advances, 2013, 3, 16958-16961.

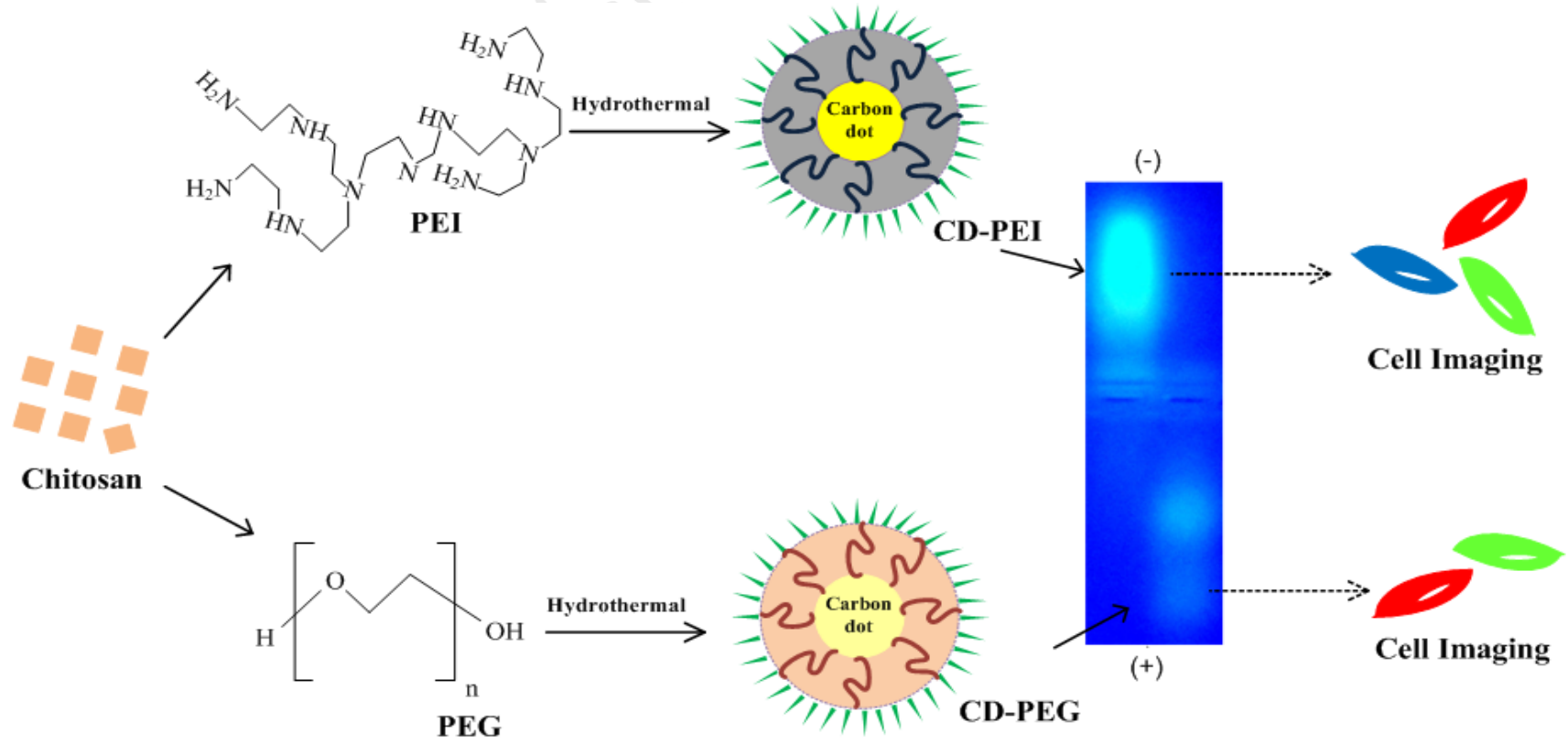
RSC Advances

PAPER

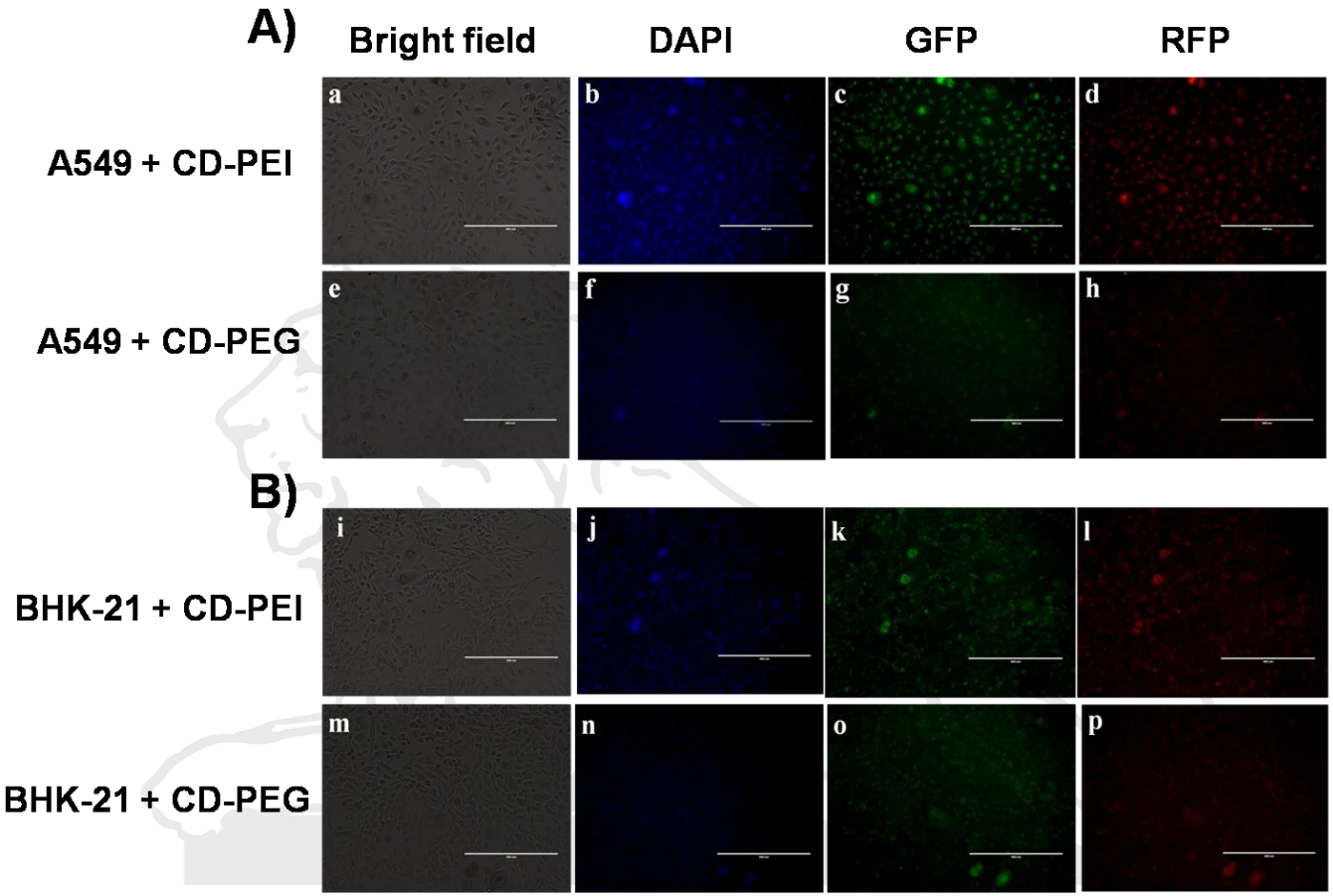
Implications of surface passivation on physicochemical and bioimaging properties of carbon dots†

Cite this: *RSC Adv.*, 2014, **4**, 20915

Abhay Sachdev,[a] Ishita Matai[a] and P. Gopinath*[ab]

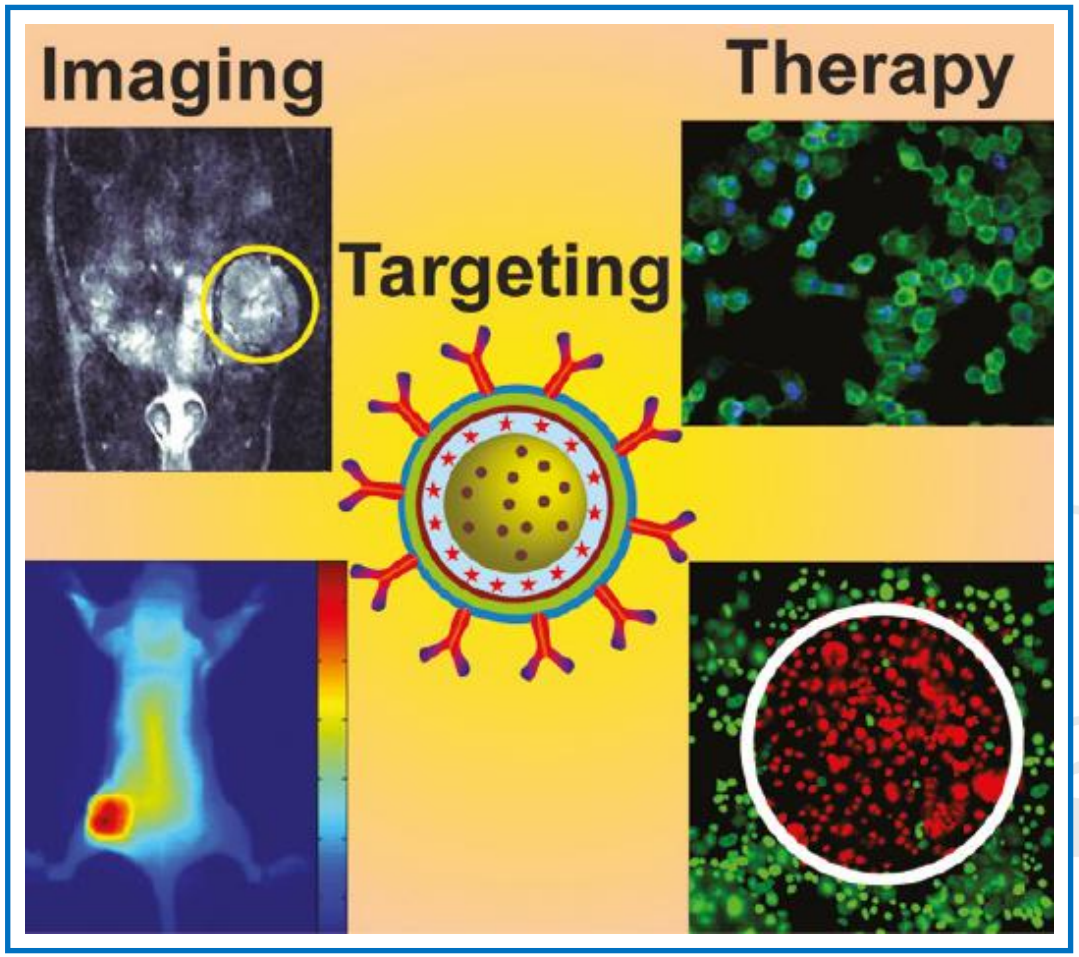


Bioimaging Efficiencies of CDs



(A) Comparison of fluorescence microscopic images of A549 cells incubated with CD-PEI (a-d) and CD-PEG (e-h).(B) Comparison of fluorescence microscopic images of BHK-21 cells incubated with CD-PEI(i-l) and CD-PEG (m-p). Scale bar: 400 µm.

Theranostics



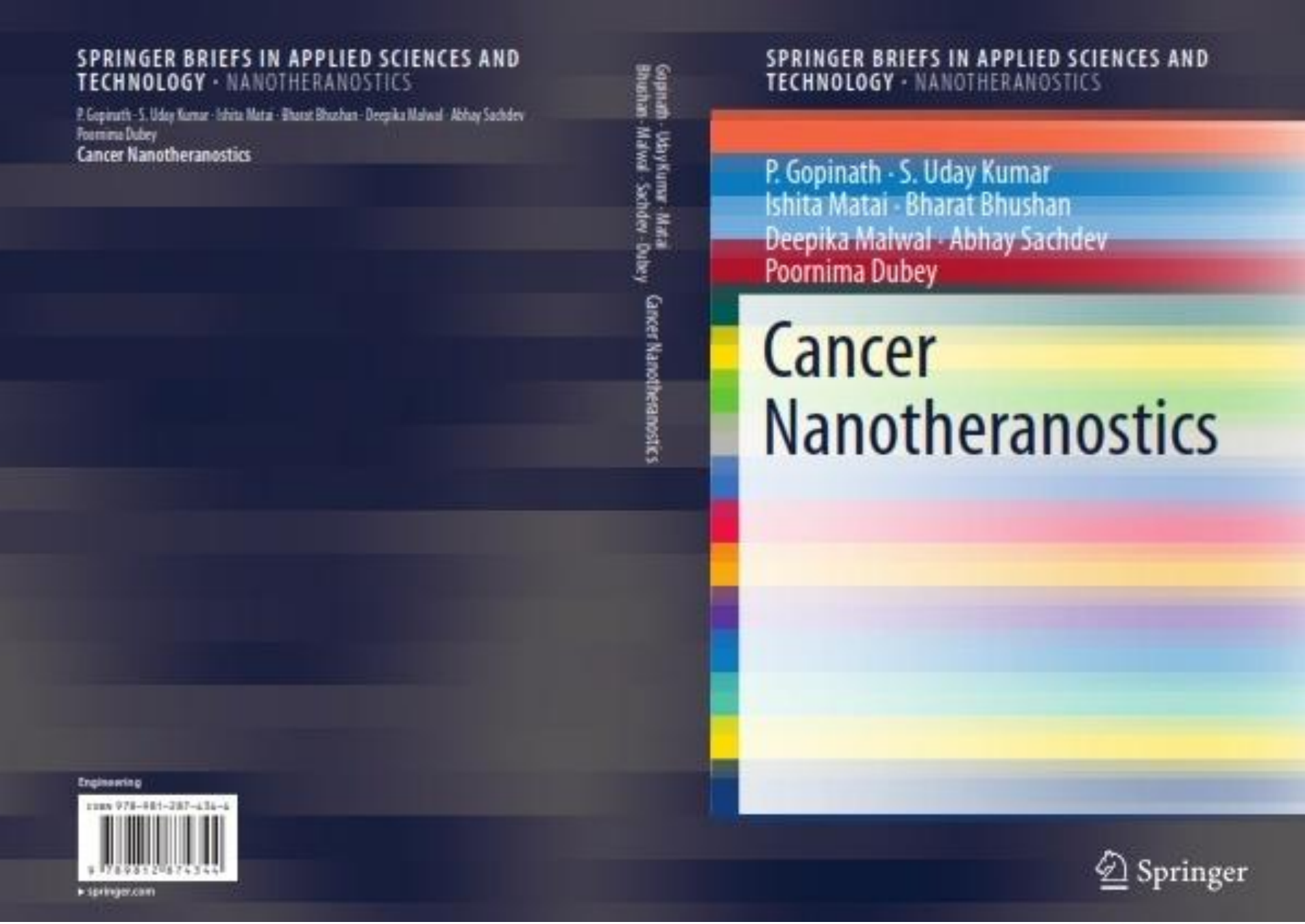
THERAPY

+

DIAGNOSTICS

=

THERANOSTICS


SPRINGER BRIEFS IN APPLIED SCIENCES AND TECHNOLOGY · NANOTHERANOSTICS
P. Gopinath · S. Uday Kumar · Ishita Matai · Bharat Bhushan · Deepika Malwal · Abhay Sachdev
Poornima Dubey
Cancer Nanotheranostics
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Journal of Materials Chemistry B

PAPER

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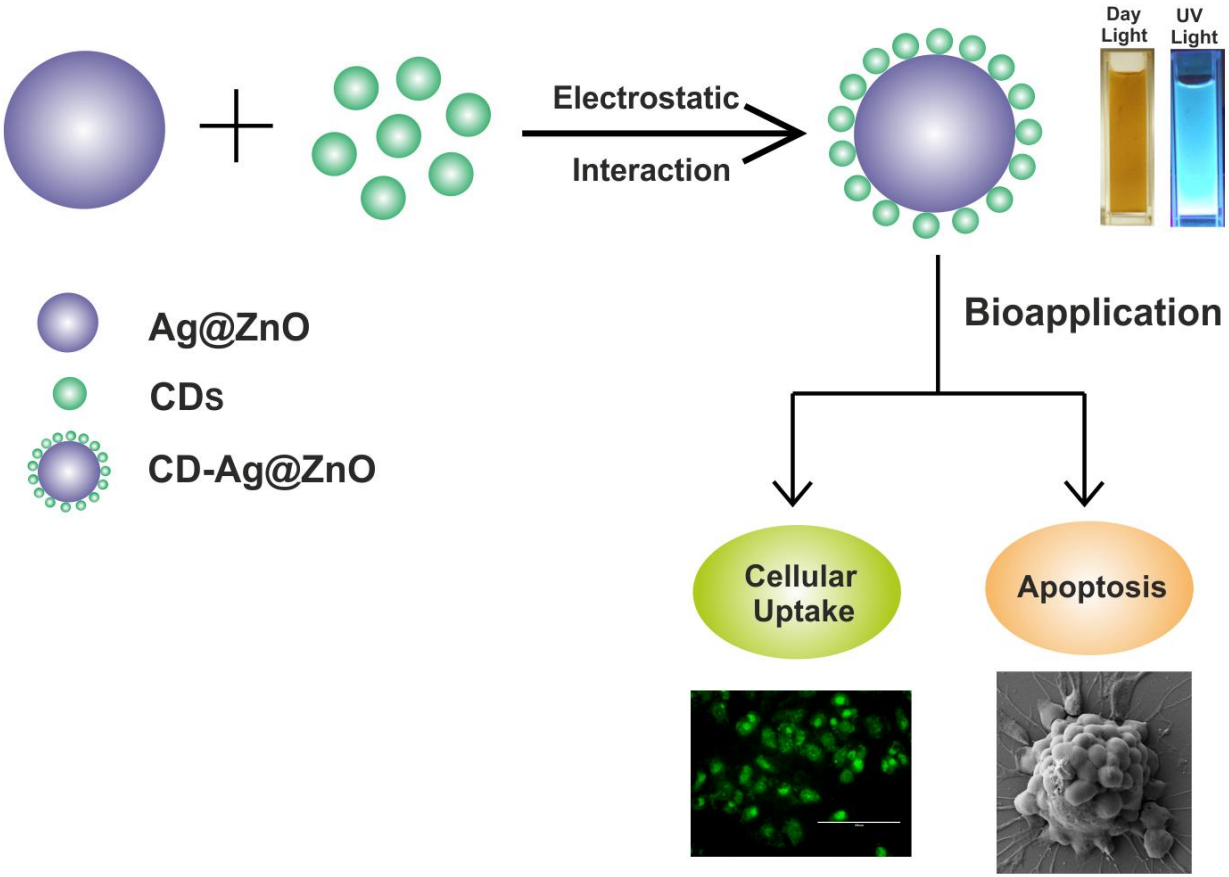
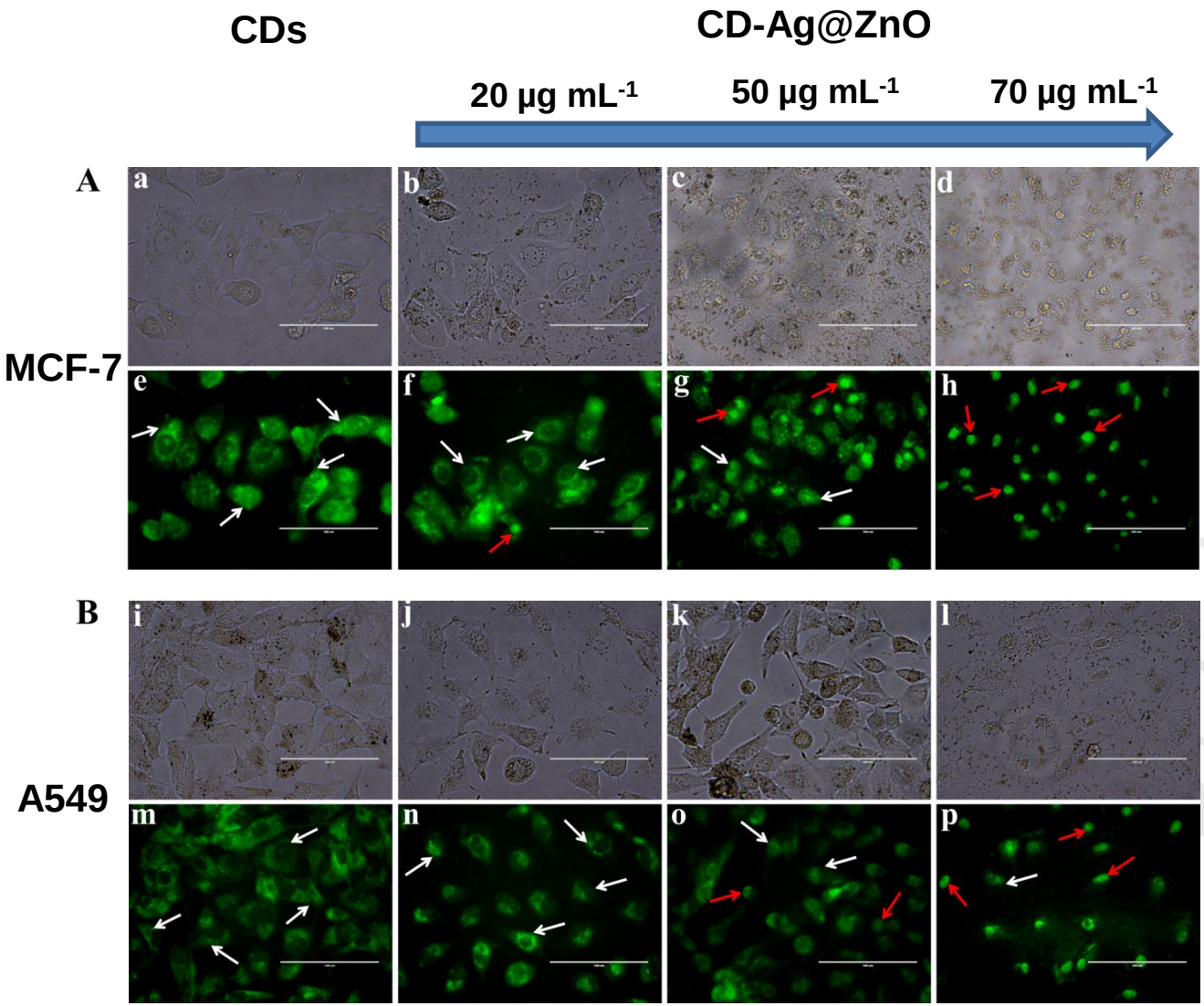
Cite this: DOI: 10.1039/c4tb02043j

Dual-functional carbon dots–silver@zinc oxide nanocomposite: *in vitro* evaluation of cellular uptake and induction of apoptosis†

Abhay Sachdev,[a] Ishita Matai[a] and P. Gopinath*[ab]

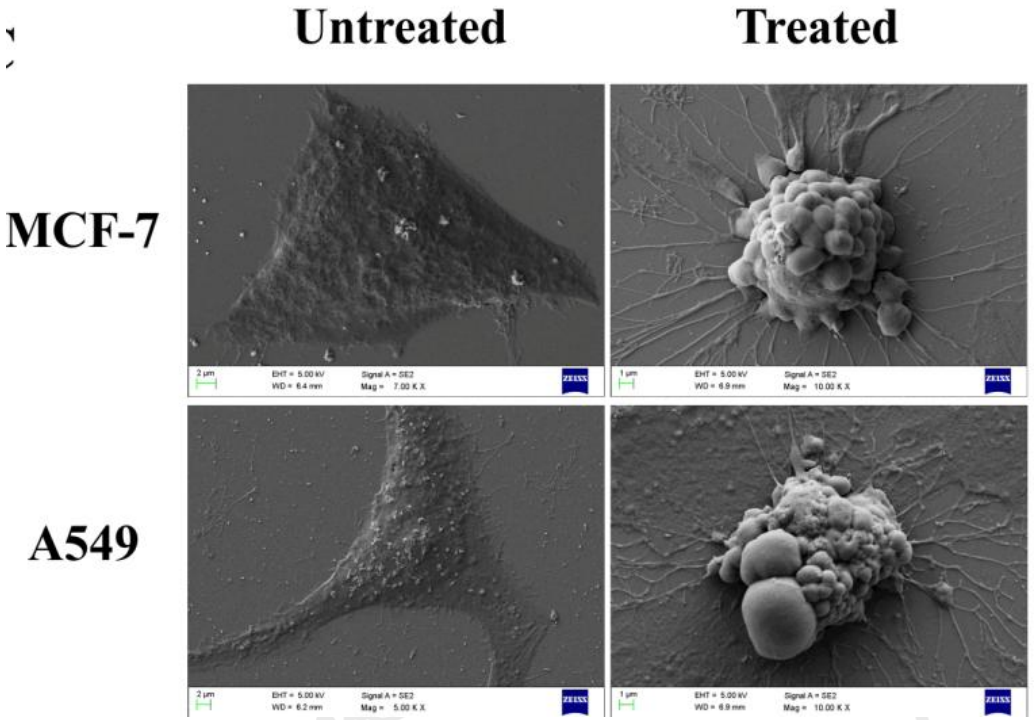


Qualitative Cellular Uptake



- **White** and **red arrows** represent the **cytoplasm** and **nuclear localization**.
- CDs - internalized in the **cytoplasm**.
- CD-Ag@ZnO NC **localization** in the **cytoplasm** as well as in the **nucleus** was observed in a **dose-dependent** manner.
- **Rupturing** of the **nuclear membrane** at **higher** concentrations - **enhanced permeability** of the NC inside **nucleus**.

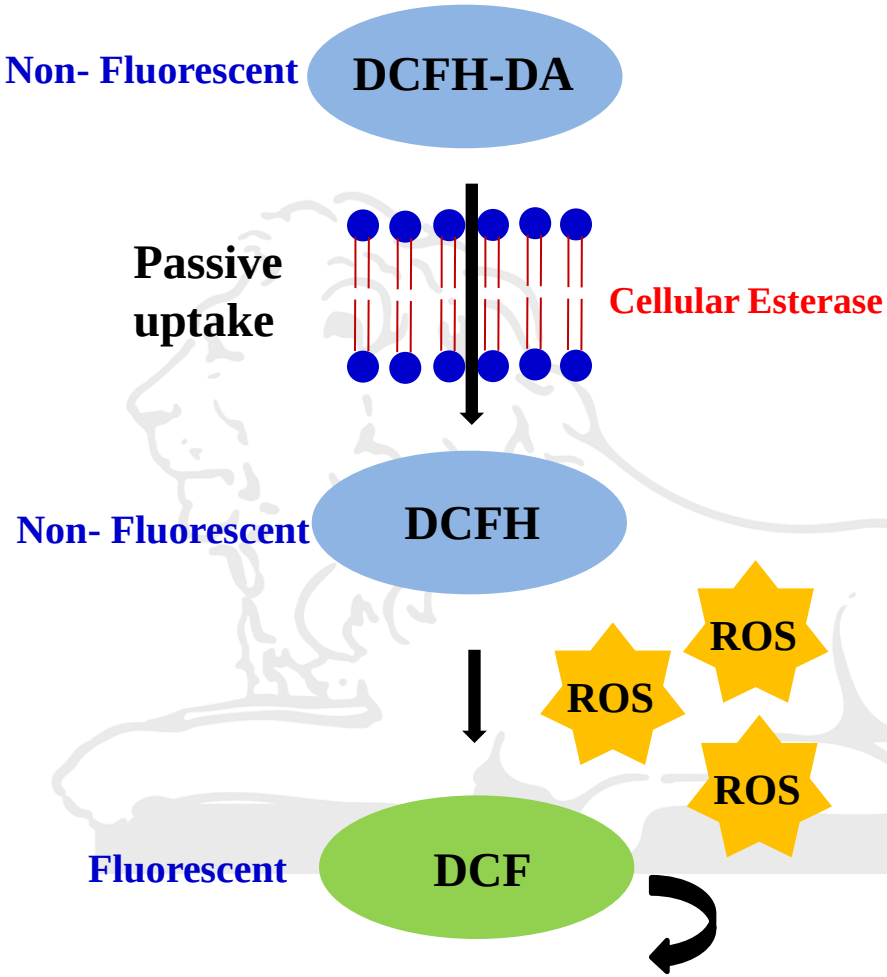
FE-SEM Morphological Examination



Representative FE-SEM images of untreated and CD-Ag@ZnO NC treated cells. Scale bar: 2 µm (untreated) and 1 µm (treated).

- **Untreated** cells- **spindle-shaped**, **well-attached** to the surface and **intact membrane** morphology.
- **IC_{50}** treated cells- **shrunk** in size, **rounded** in shape, **loosely attached** and exhibited **membrane blebbing** which are the hallmarks of **apoptotic cell death**.

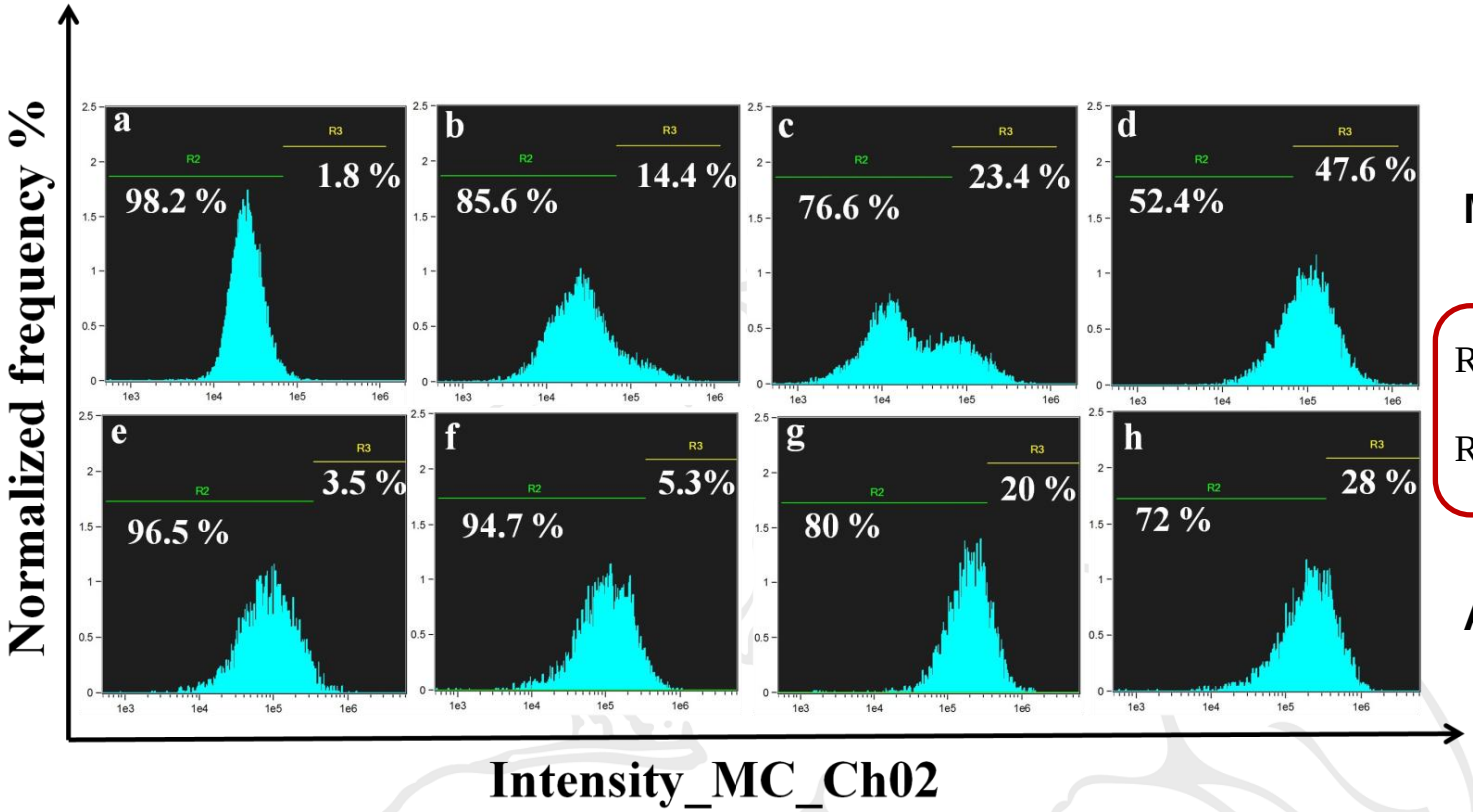
Determination of ROS by 2',7'-dichlorofluorescin diacetate (DCFH-DA) Assay



Quantitation of DCF fluorescence is a measure of intracellular ROS levels

λ_{ex} = 495 nm; λ_{em} = 529 nm

Flow Cytometeric Analysis of ROS Production



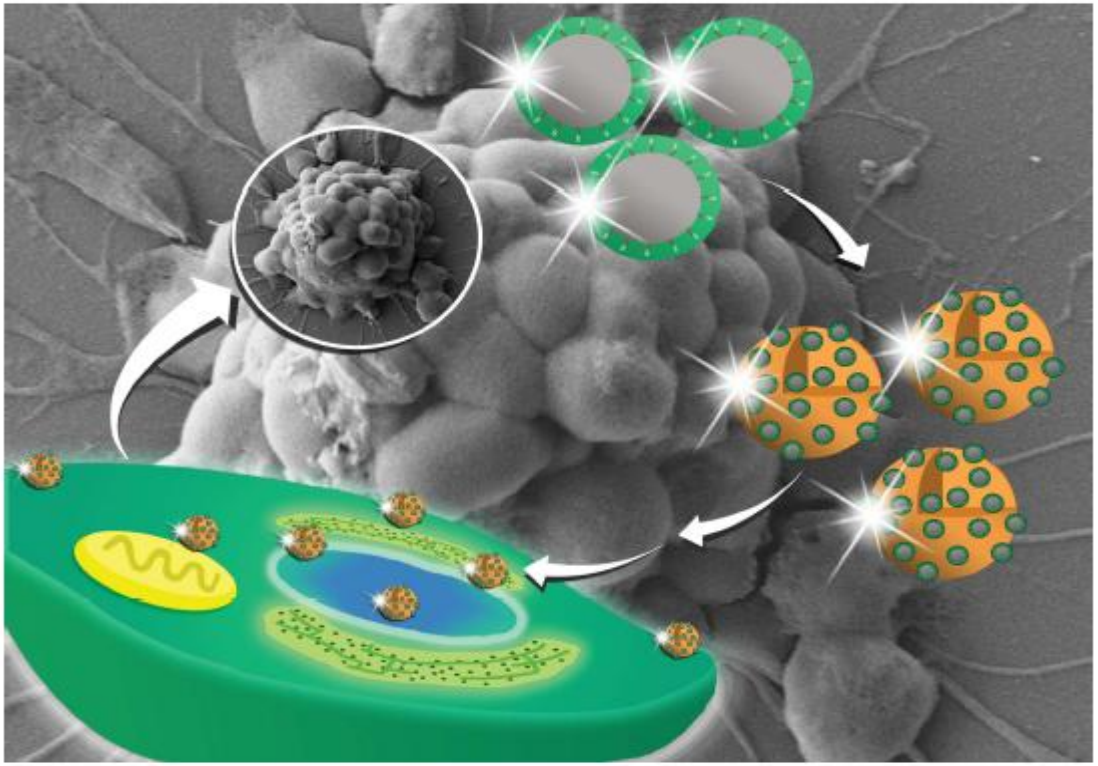
MCF-7

R2: Non-fluorescent

R3: ROS expressing cells

A549

- **CD-Ag@ZnO NC** treated cells showed **increased generation of ROS** in a **dose-dependent** manner.
- **ROS production** in **MCF-7 > A549 cells**.

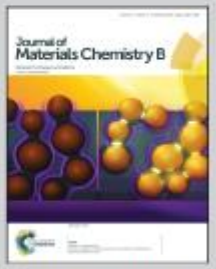


A dual-functional carbon dots–silver@ zinc oxide nanocomposite is developed by the Nanobiotechnology lab of Dr. P. Gopinath at Indian Institute of Technology Roorkee, Roorkee, India.

Title: Dual-functional carbon dots–silver@ zinc oxide nanocomposite: *in vitro* evaluation of cellular uptake and induction of apoptosis

This work demonstrates the development of novel carbon dots decorated silver–zinc oxide (CD–Ag@ZnO) nanocomposite (NC) consisting of highly fluorescent CDs and silver–zinc oxide (Ag@ZnO). This multifunctional CD–Ag@ZnO NC has the ability to evoke apoptosis while allowing real-time intracellular trafficking, which may be of great relevance for cancer theranostic applications.

As featured in:



See P. Gopinath *et al.*, *J. Mater. Chem. B*, 2015, 3, 1208.

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/MaterialsB

Registered charity number: 207890

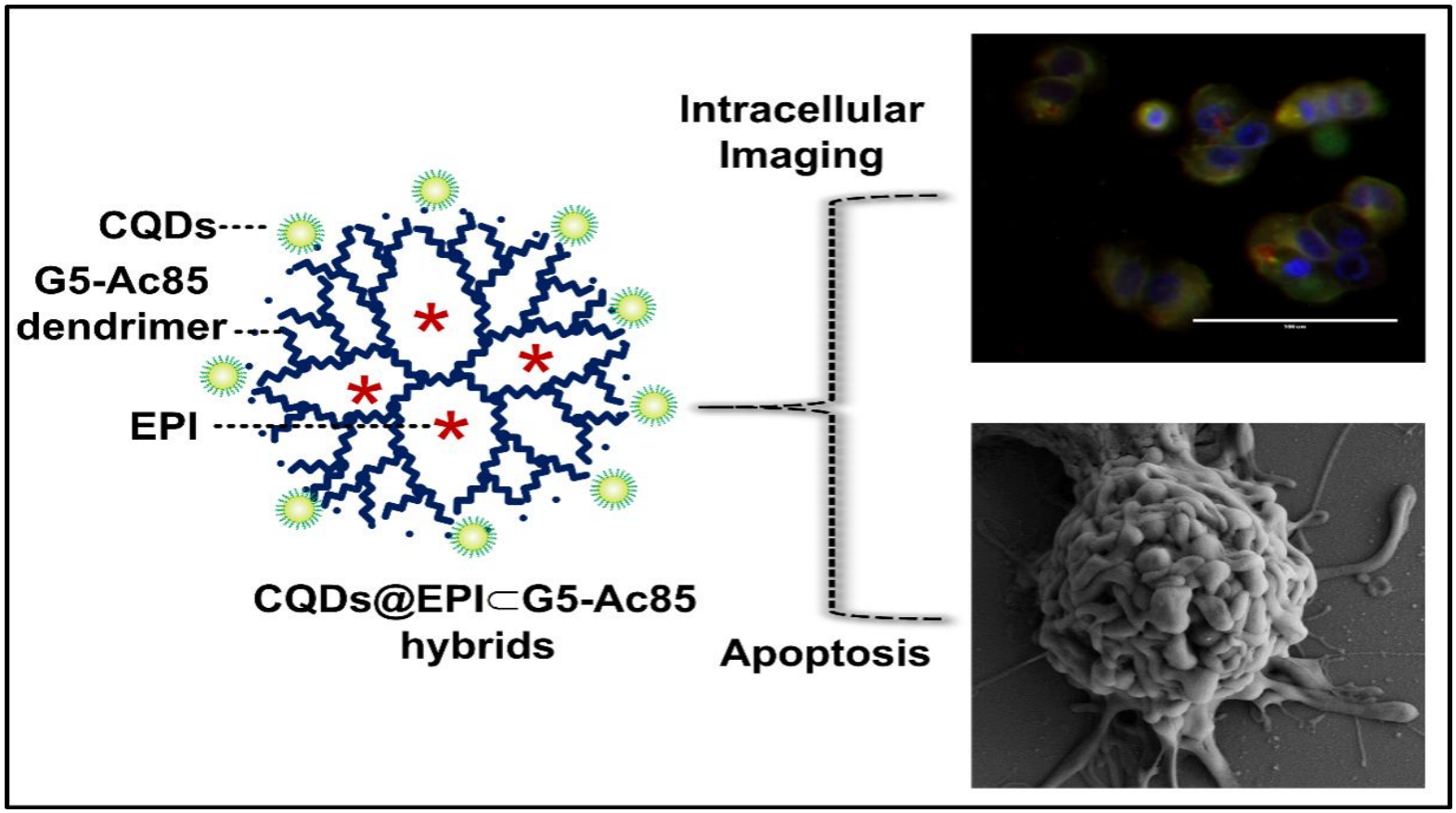
Dendrimers: “Polymers of the 21st century”

- The word dendrimer comes from the Greek word ”DENDRON” meaning tree and “MEROS” meaning part.
- First reports published in the late 1970s and early 1980s by the groups of Tomalia, Vogtle, Denkewalter, Newkome.
- Macromolecule, which is characterized by its highly branched 3D structure that provides a high degree of surface functionality, versatility and multivalency.
- Approximate diameter of 2-10 nm.
- Graphically, molecular architecture and dimensions resemble closely to small proteins & sometimes referred to as ‘artificial proteins’.

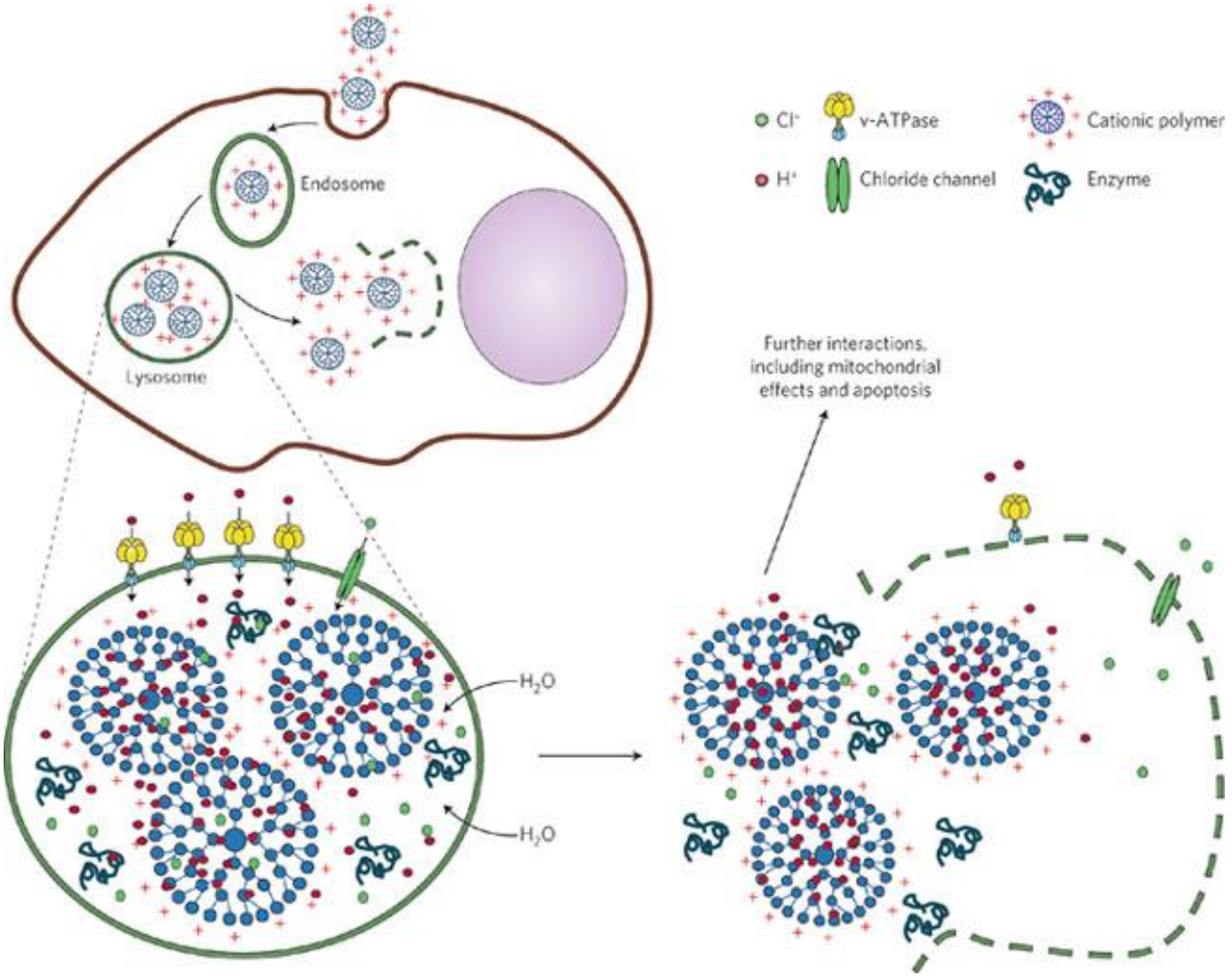
ACS APPLIED MATERIALS & INTERFACES
Research Article
www.acsami.org

Self-Assembled Hybrids of Fluorescent Carbon Dots and PAMAM Dendrimers for Epirubicin Delivery and Intracellular Imaging

Ishita Matai,[†] Abhay Sachdev,[†] and P. Gopinath*[,†,‡]



Possible "proton sponge " effect

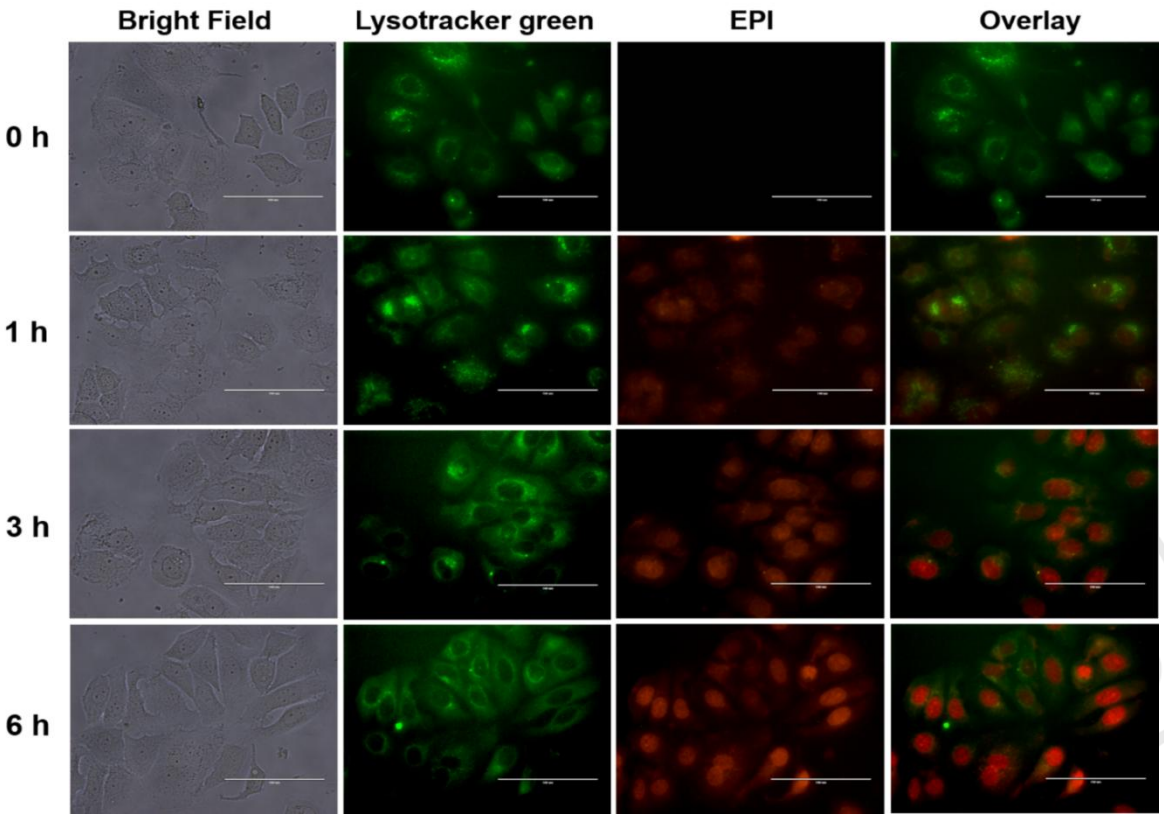


Source: Nature Materials **8**, 543 - 557 (2009)

ACS Biomaterials SCIENCE & ENGINEERING
Article
pubs.acs.org/journal/abseba

Chemically Cross-Linked Hybrid Nanogels of Alginate and PAMAM Dendrimers as Efficient Anticancer Drug Delivery Vehicles

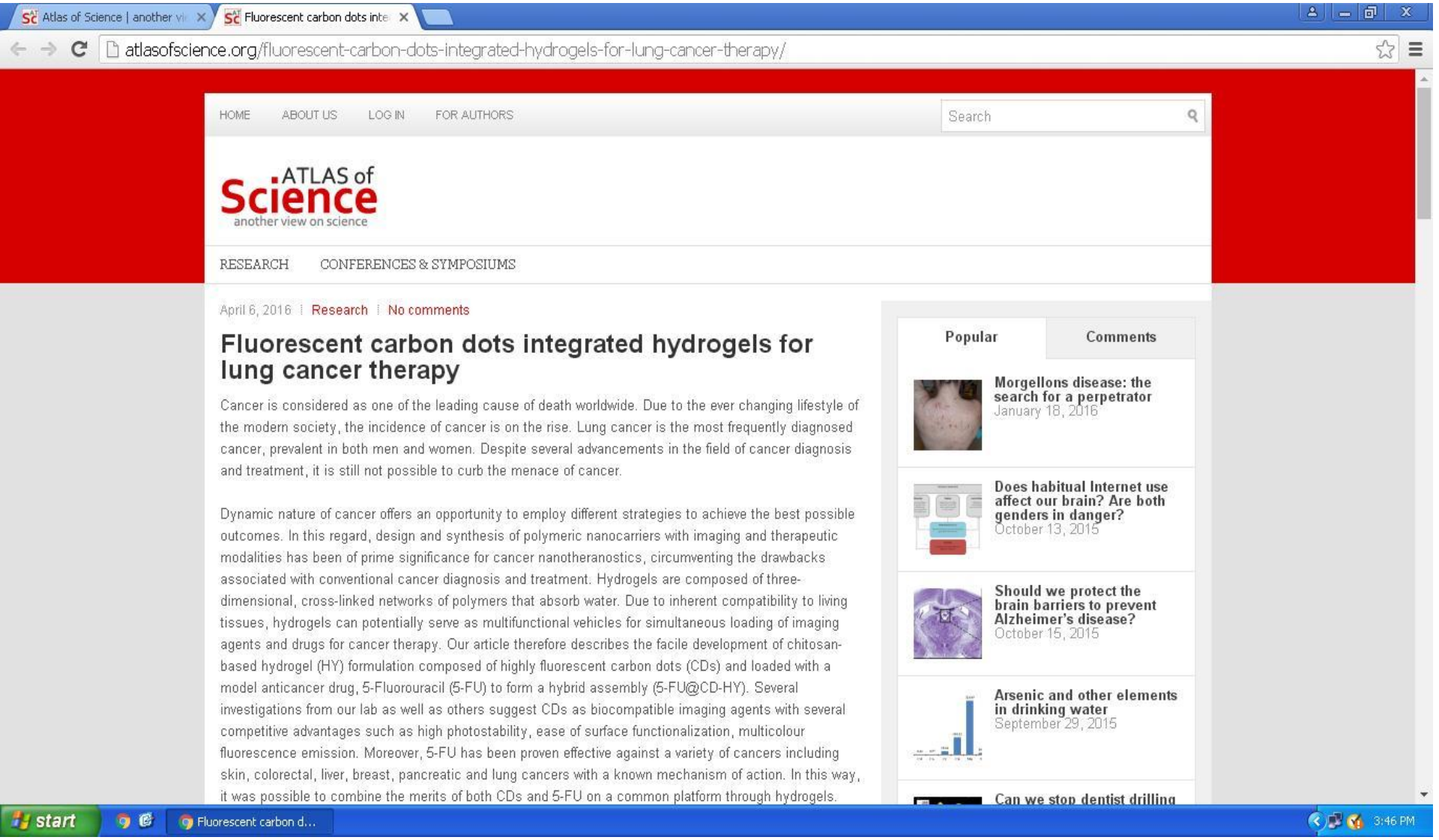
Ishita Matai[†] and P. Gopinath*[,†,‡]



The red fluorescent signals were mostly distributed in the nuclear region and didn't merge with the green fluorescent signals of lysotracker

Fluorescence microscopic images of MCF-7 cells incubated with EPI⊂AG nanogels captured after different time intervals. The red fluorescence of EPI (under RFP filter) indicative of its intracellular distribution increased in a time-dependent manner. (Scale bar = 100 μm).

Our article featured in



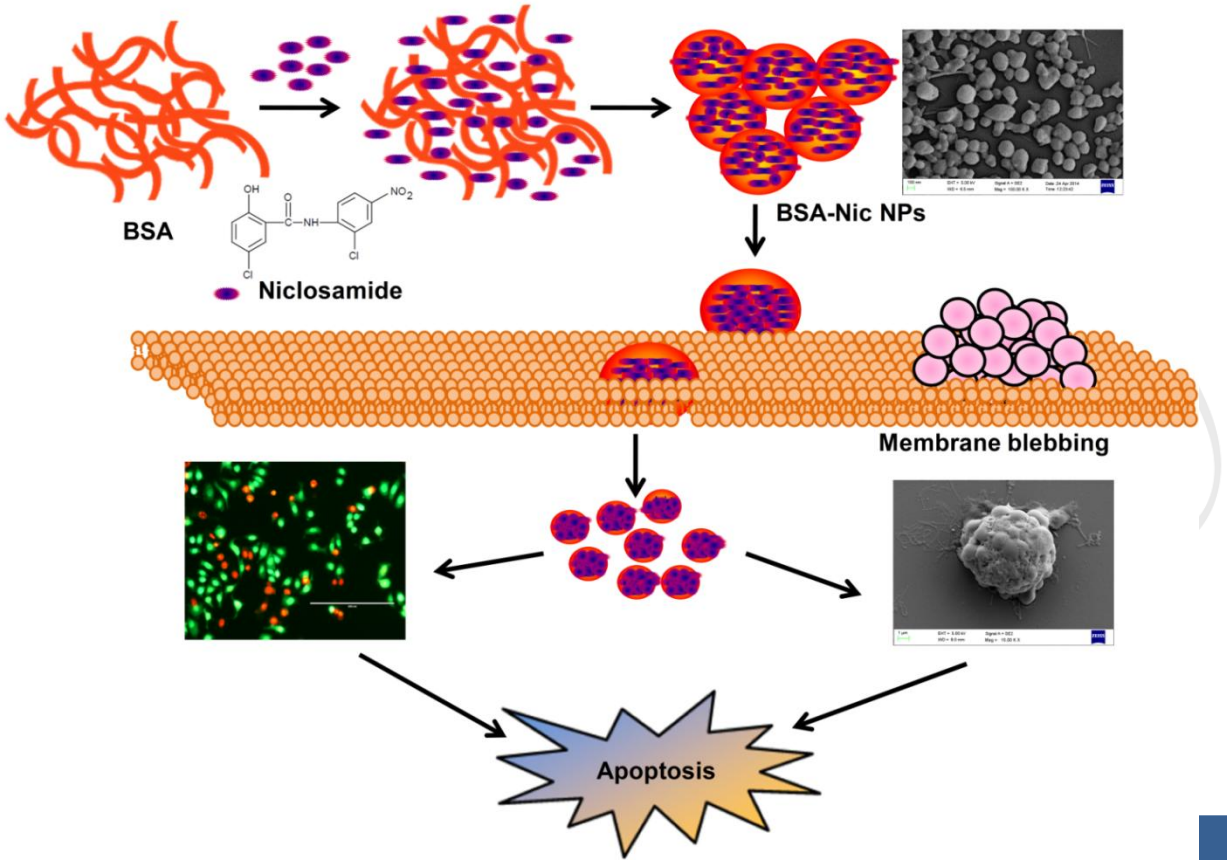
RSC Advances

PAPER

Cite this: *RSC Adv.*, 2015, 5, 12078

Bionanotherapeutics: niclosamide encapsulated albumin nanoparticles as a novel drug delivery system for cancer therapy†

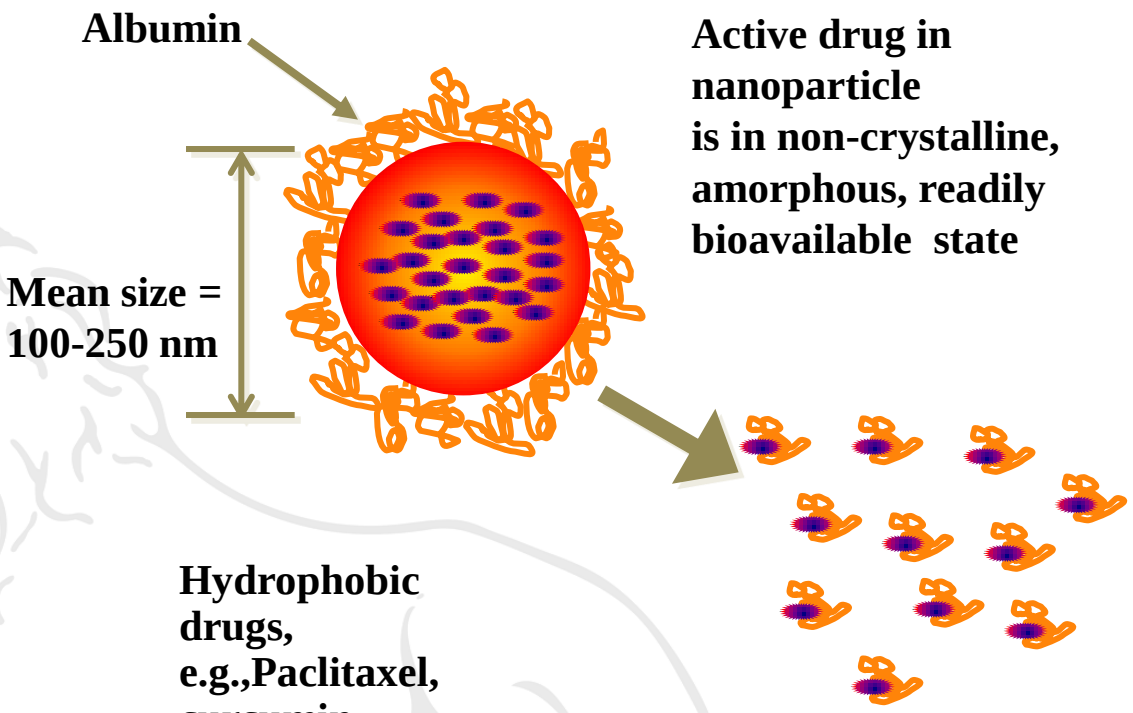
Bharat Bhushan,[a] Poornima Dubey,[a] S. Uday Kumar,[a] Abhay Sachdev,[a] Ishita Matai[a]



Albumin nanoparticles

- The presence of functional charged groups including amino and carboxylic groups offer albumin with various possibilities for surface modification and interaction with various nanoparticles and drug molecules

- Around seven albumin based drugs or imaging agents are in market and around ten such products are under clinical trials for various applications including: oncology, diabetes, hepatitis C and rheumatoid arthritis.



P. Gopinath et al., *Cancer Nanothernostics (2015).*

Albumin nanoparticles

Product	Drug	indication	Current status
ABI-007 (Abraxane®)	Albumin-paclitaxel nanoparticle	Oncology	Marketed
^{99m}Tc-Albures	^{99m}Tc –aggregated albumin	Oncology	Marketed
^{99m}Tc-Nanocoll	^{99m}Tc –aggregated albumin	Oncology	Marketed
Vasovist®	Albumin-binding Gadolinium (III) complex	Oncology	Marketed
B-22956/1	Albumin-binding Gadolinium (III) complex	Oncology	Marketed
Levenir®	Albumin-binding fatty acid derivative of insulin	Diabetes	Marketed
Liraglutide (Victoza®)	Albumin-binding fatty acid derivative of GLP-1	Diabetes	Marketed
Albuferon®	Albumin-fusion protein of interferon-α-2b	Hepatitis C	Phase III
AT-103 (Ozoralizumab)	Albumin-binding nanobody directed against human TNF-α	Rheumatology	Phase II
INNO-206	Albumin binding prodrug of doxorubicin	Oncology	Phase II
ABI-008	Albumin-docetaxel nanoparticle	Oncology	Phase II
MTX-HSA	Methotrexate albumin conjugate	Oncology	Phase I/II
MM-111	Albumin fusion protein directed against ErbB2 and ErbB3	Oncology	Phase I/II
AFL-HSA	Albumin conjugate of aminofluorescein	Oncology	Phase I/II
CjC-1134-PC	Albumin conjugate of exendin-4	Diabetes	Phase I/II
ABI-009	Albumin-rapamycin nanoparticle	Oncology	Phase I
ABI-010	Albumin nanoparticle with a HSP90 inhibitor	Oncology	Phase I

Albumin based drugs and imaging agents in market and under clinical trials

Ren et al., J. Nanomed. Nanotechol. (2013).

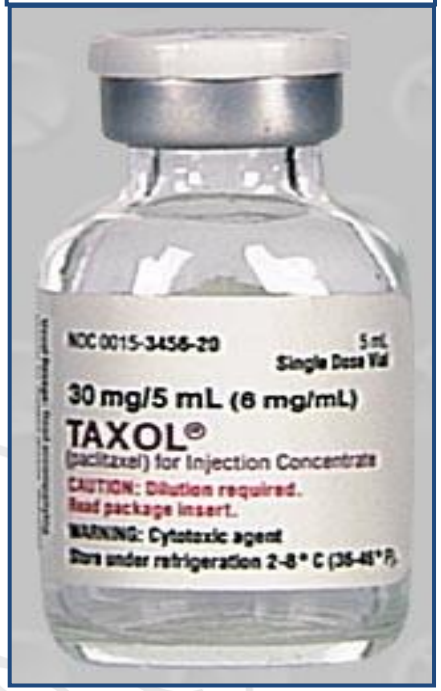
Abraxane an example of nab™ [nanoparticle albumin-bound] technology

Abraxane

Contents:
100 mg paclitaxel
900 mg albumin
No Surfactants/Solvents

- Abraxane is solvent free "nano" version of taxol (cremophor-based paclitaxel).
- Abraxane received FDA Approval January, 2005 for metastatic breast cancer.

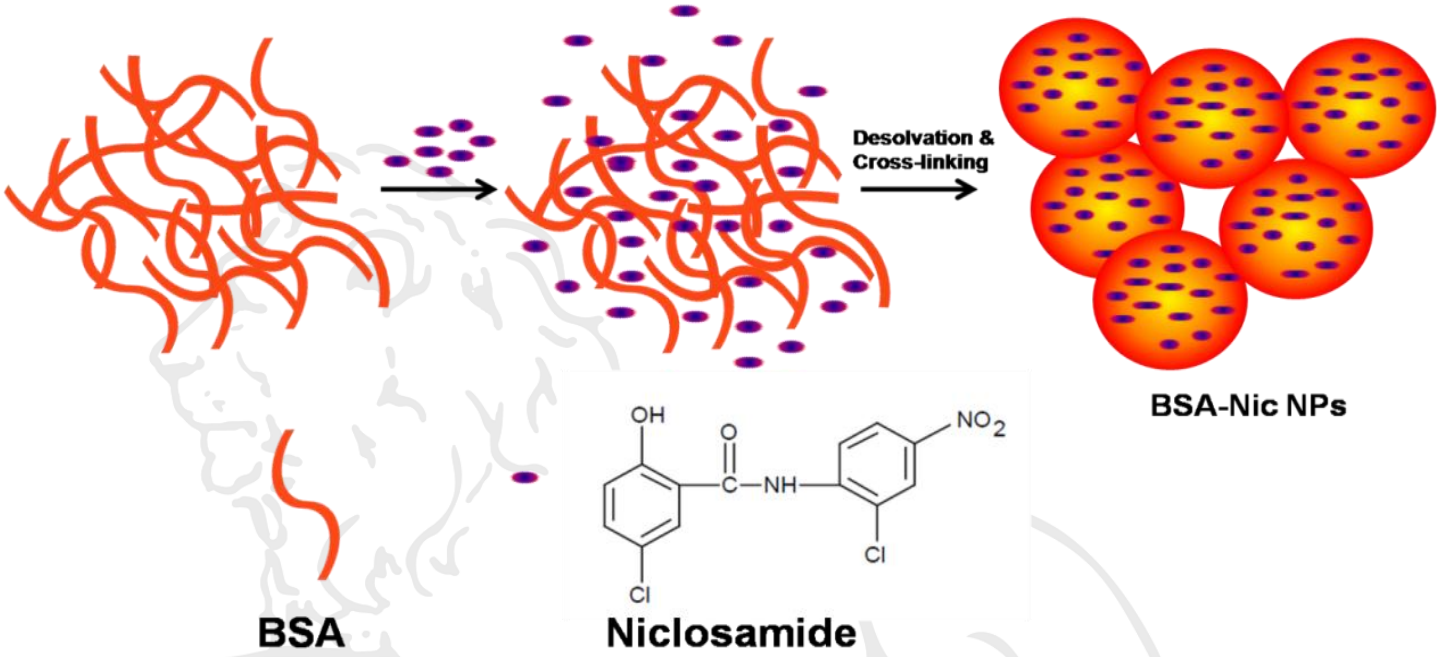
Taxol



Contents:
Paclitaxel 6 mg/ml
Cremophor 537 mg/ml
Ethanol 396 mg/ml

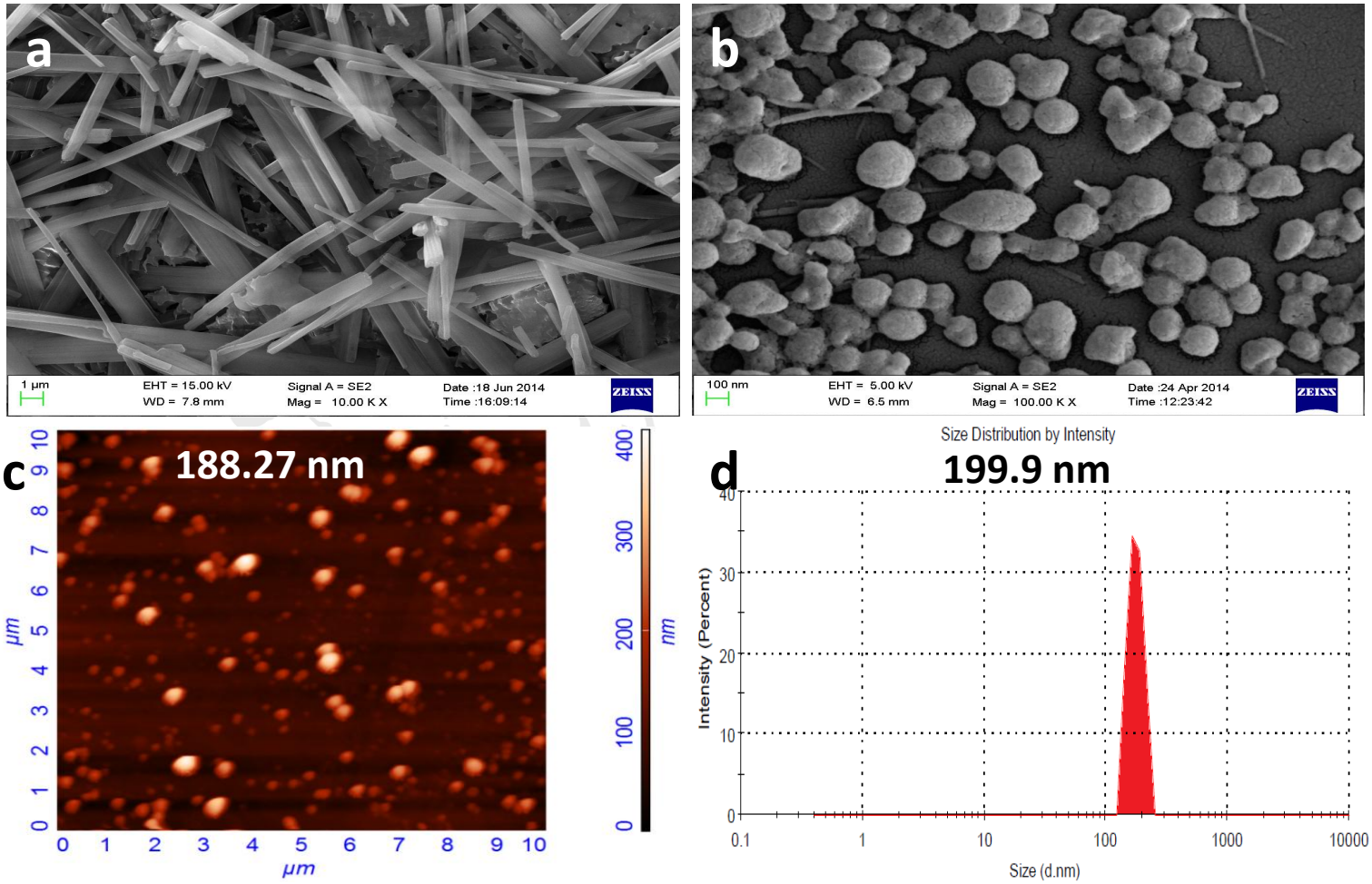
www.pharmafile.com/news/181988/cancer-treatment-abraxane-gets-eu-nod
www.indiamart.com /ikonbiopharma/ anti-cancer-injectables

Preparation of niclosamide encapsulated bovine serum albumin (BSA) nanoparticles



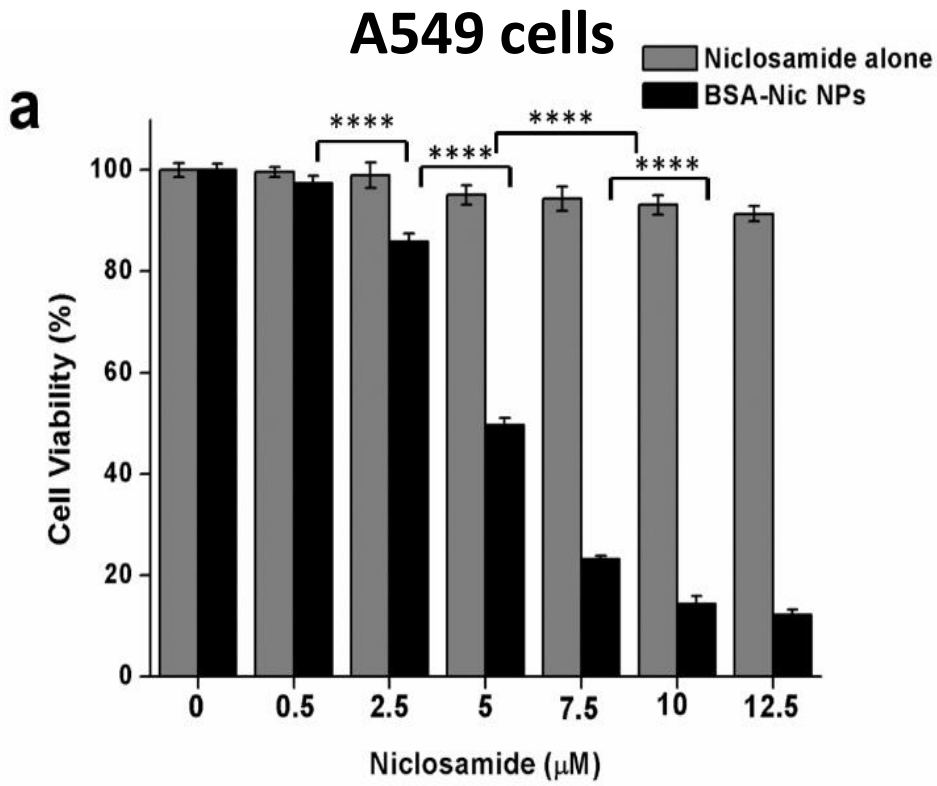
Schematic outline of niclosamide encapsulated BSA nanoparticles (BSA-Nic NPs) fabrication by desolvation technique .

Characterization: surface morphology, particle size analysis

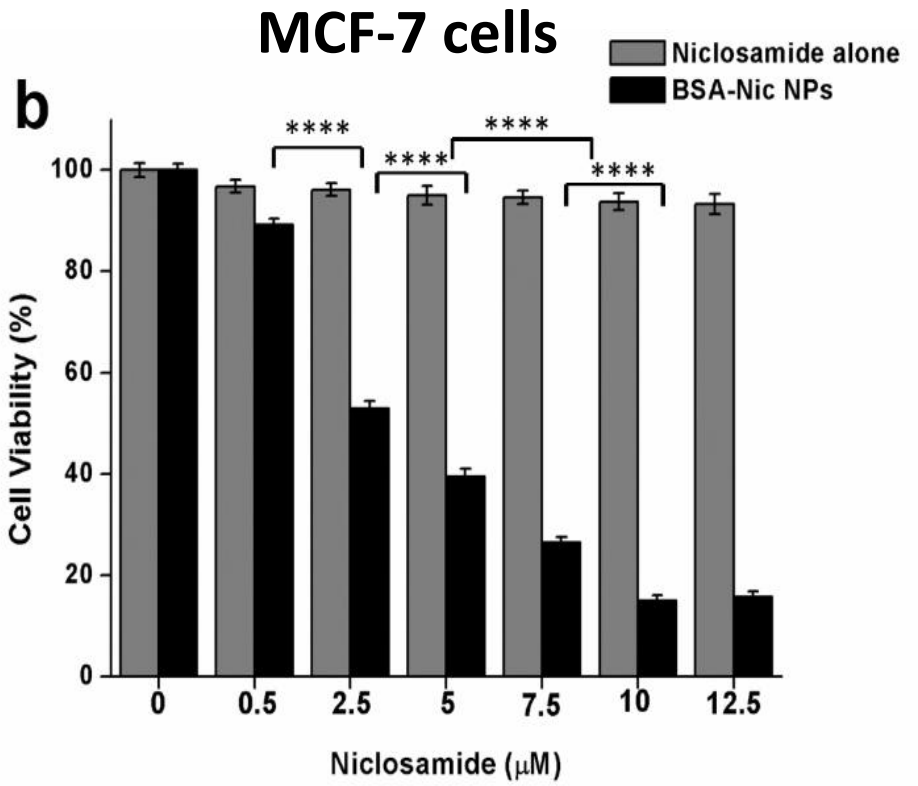


Field emision scanning electron microscopy (FE-SEM) images of (a) raw niclosamide powder and (b) BSA–Nic NPs (c) Atomic force microscopy (AFM) and (d) dynamic light scattering (DLS) images of BSA–Nic NPs.

Cell viability assay



IC_{50} **-5 μM**



IC_{50} **-2.6 μM**

Bare niclosamide (in water) showed a nontoxic effect due to its practical insoluble nature in aqueous medium

Nanofibers

- A nanofiber is a continuous fiber which has diameter in the range of billionths of a meter.

Unique Properties of Nanofibers :

- Size: nanofibers are very small which gives them unique physical and chemical properties and allows them to be used in diverse applications.
- Surface-to-volume ratio: nanofibers have a huge surface area compared to their volume.

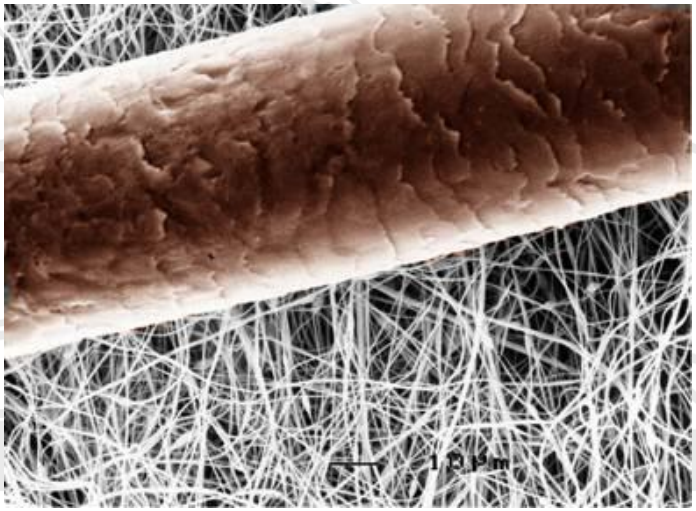


Fig Comparison of size of nanofiber with human hair.

Ref. Burger, Christian, et. al. 2006

Making Nanofibers

“Melt” Fibers: some nanofibers can be made by melting polymers and spinning or shooting them through very small holes. As the fiber spins out it stretches smaller and smaller…

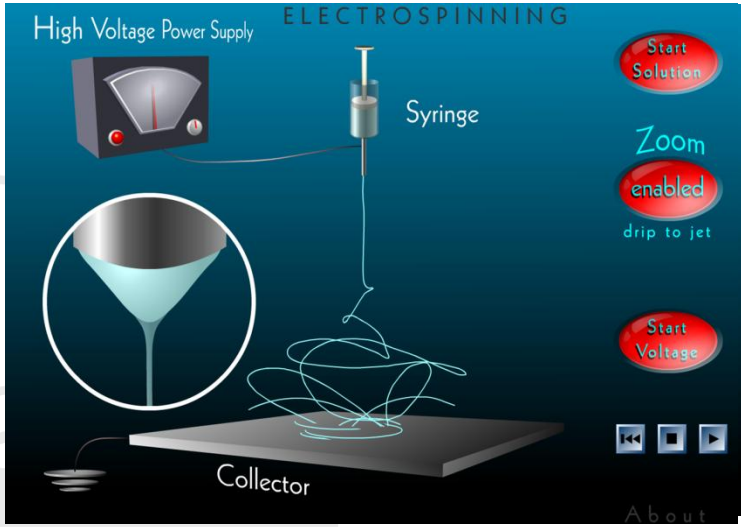
Cotton candy is made by heating syrup to a high temperature and then the liquid is spun out through tiny holes. As the fiber spins it is pulled thinner and thinner. It cools, hardens and, presto! Cotton Candy!!

Electrospinning

- Electrospinning: A versatile method to produce fibers with diameters in the **nano range.**

Electrospinning Procedure:

- An **electrostatic potential** is applied between a spinneret and a collector
- A **polymer** fluid is slowly **pumped** through the spinneret.
- The **droplet** is held by its own surface tension at the spinneret tip, until it gets **electrostatically charged**.
- After threshold accumulation of charges polymer fluid assumes a **conical shape** and thin stream of **fiber elutes** from the droplet.



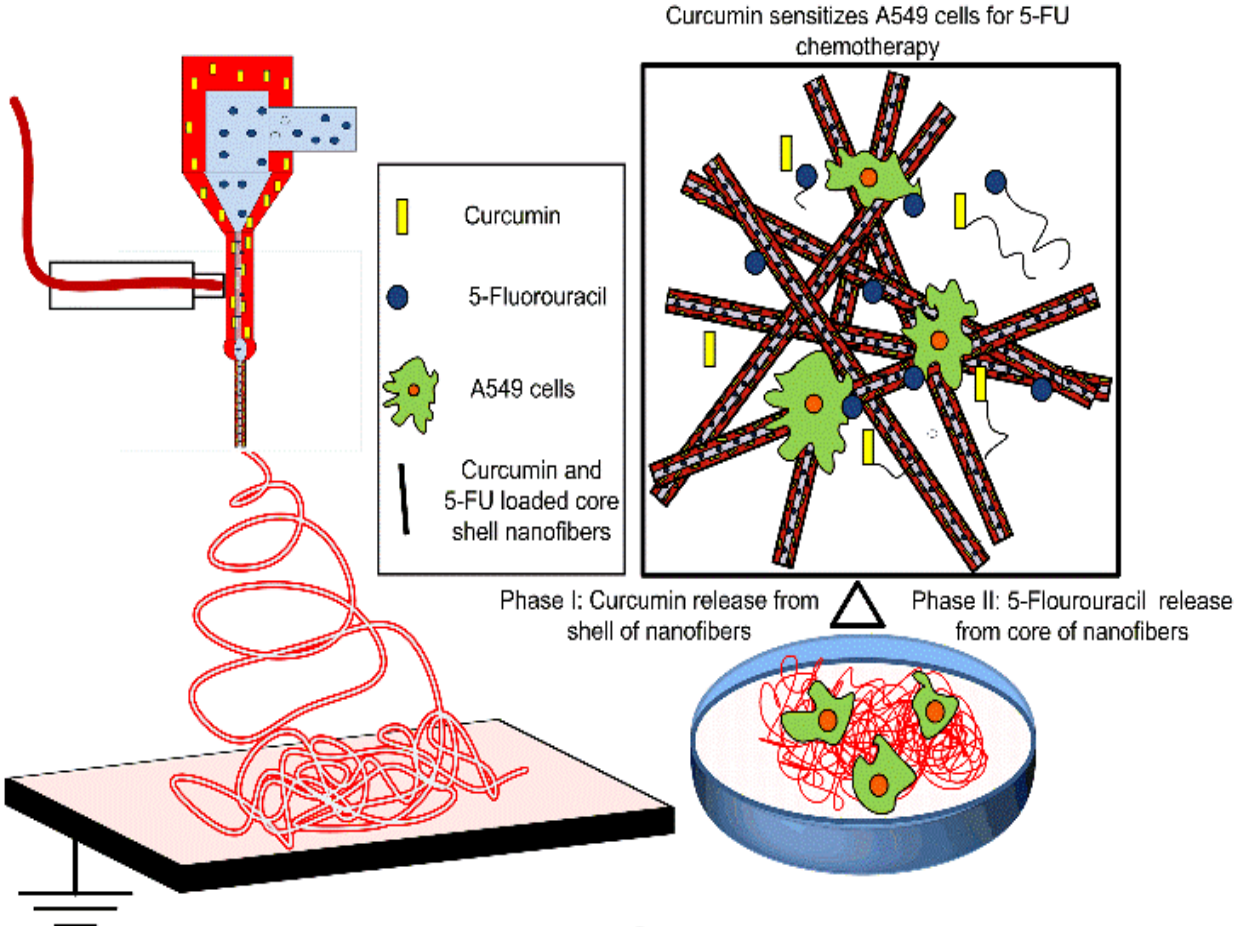
Electrospinning set up

Source: Burger, Christian, et. al. 2006.

ANTICANCER DRUG LOADED NANOFIBERS FOR POTENTIAL POSTSURGICAL CANCER TREATMENT

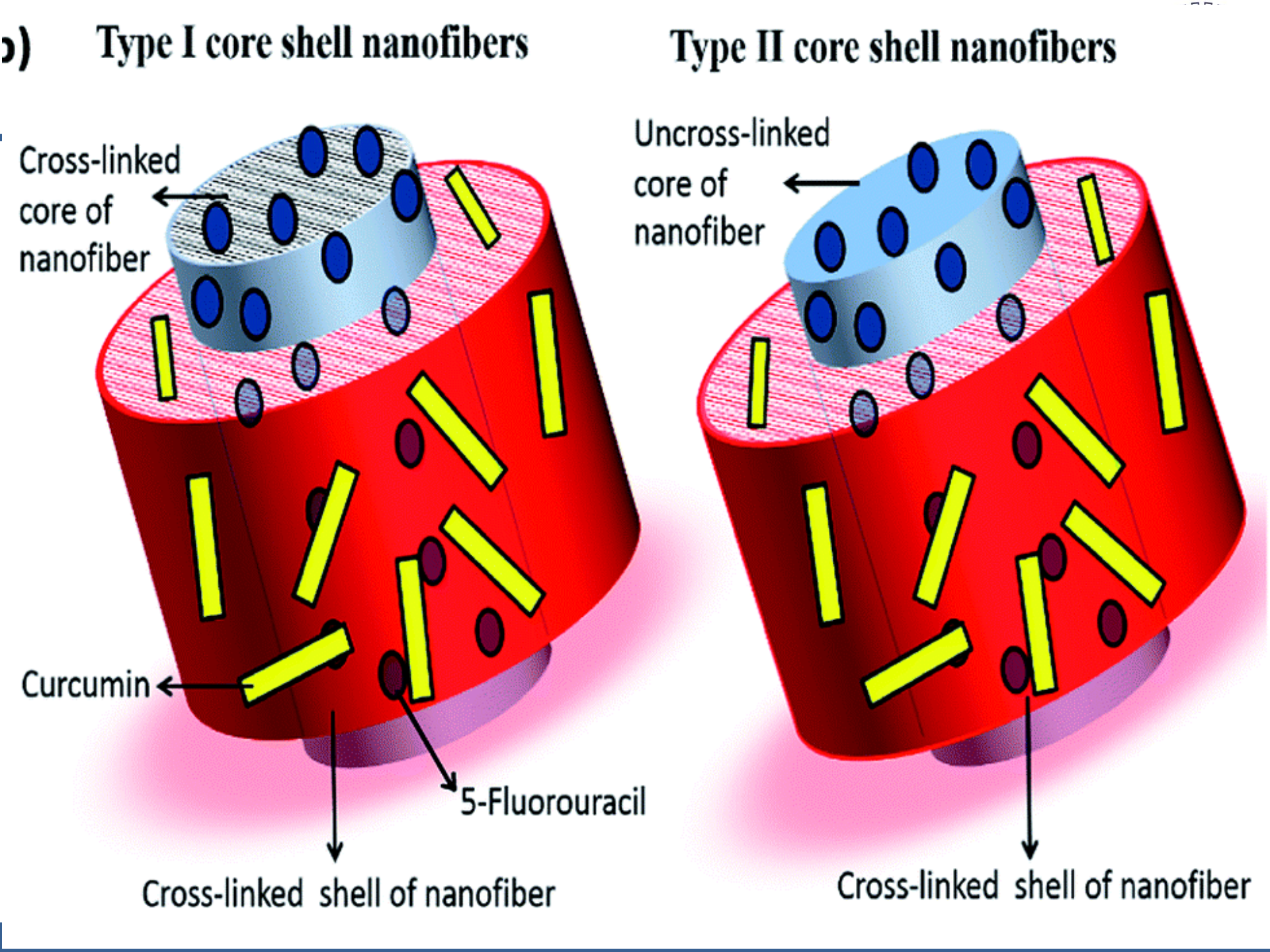
Core-shell nanofibers provide a controlled and sustained release of anticancer drugs for preventing local tumor recurrence after surgery.

Core-shell nanofibers for dual drug delivery

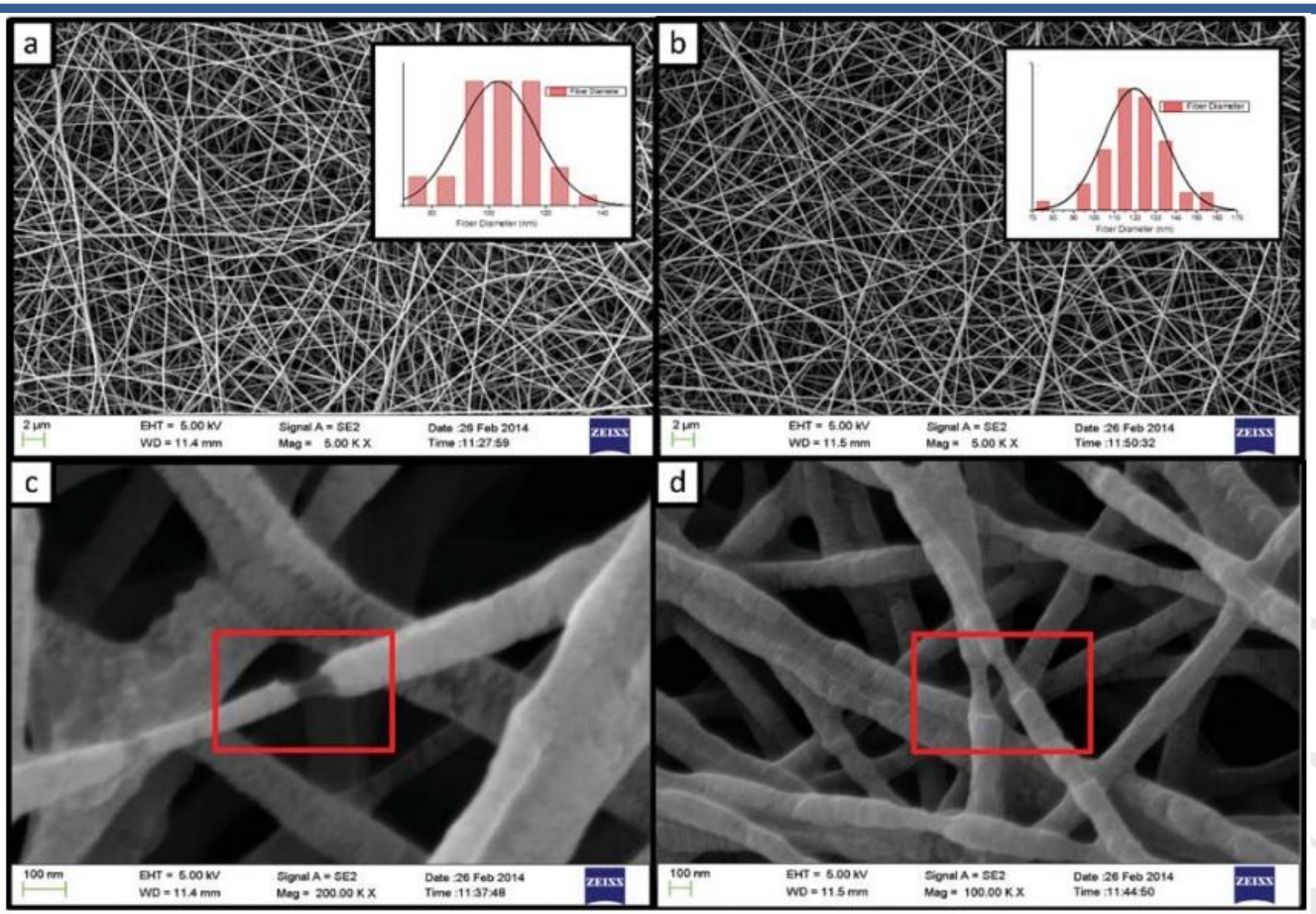


- In order to harness the **synergistic anticancer potential of 5-FU and curcumin** core-shell nanofibers have been fabricated in this work.

- **5-FU** is loaded in **nanofiber core** and **curcumin** is loaded in **nanofiber shell.**


Type I core shell nanofibers
Type II core shell nanofibers
Cross-linked core of nanofiber
Uncross-linked core of nanofiber
Curcumin
5-Fluorouracil
Cross-linked shell of nanofiber
Cross-linked shell of nanofiber

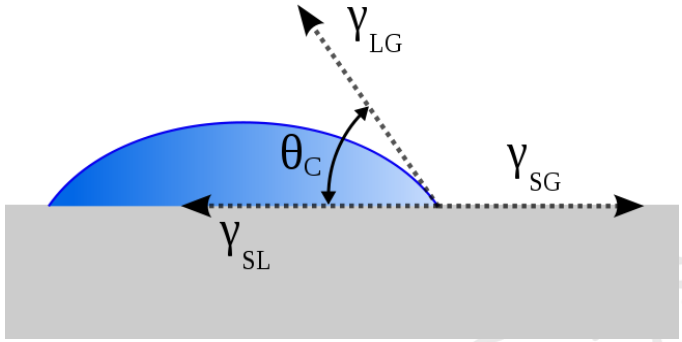
Core-shell nanofibers morphology



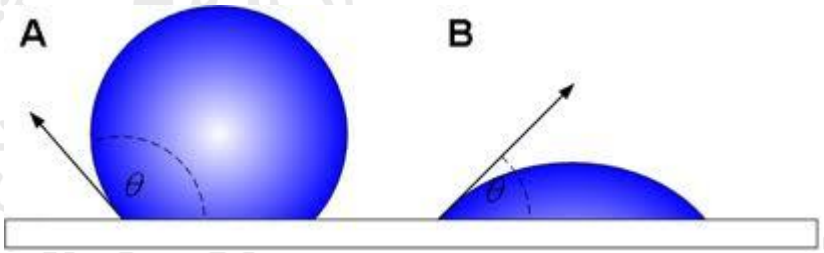
- The FE-SEM revealed uniform diameter of **type I and type II** core–shell nanofibers i.e. **103±13 nm and 119±14.97 nm**, respectively.
- The **core** of the nanofibers was **intact and uniform** throughout i.e. ~ 45 nm for type II and ~58 nm for type I nanofibers.

FE-SEM images of type II core-shell nanofibers (a), (c) and type I core-shell nanofibers (b), (d) with insets showing mean fiber diameter and fiber diameter distribution.

Contact angle



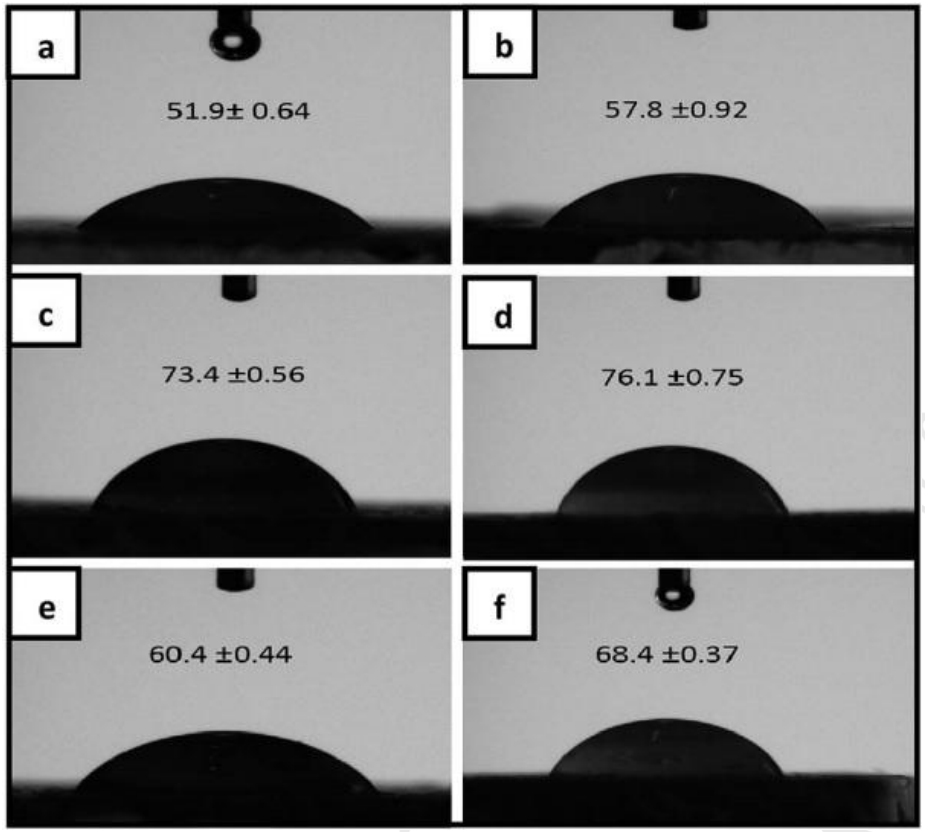
When we rest a small droplet of water on the solid surface, **tangential outline** of the droplet on the solid forms the **contact angle.**



A – $\theta_C > 90^\circ$ - Hydrophobic surface **B – $\theta_C < 90^\circ$ – Hydrophilic surface**

Condition	Nature of surface
$\theta_C<90^\circ$	Hydrophilic
$\theta_C> 90^\circ$ $(90^\circ$ -$120^\circ)$	Hydrophobic
$\theta_C>150^\circ$	Super-hydrophobic

Contact angle analysis



Contact angle measurement for (a) type I and (b) type II bare PEO–PEI core–shell nanofibers; (c) type I and (d) type II 5-FU and curcumin loaded PEO–PEI core–shell nanofibers; (e) type I and (f) type II crosslinked 5-FU and curcumin loaded PEO–PEI core–shell nanofibers

- The type I and type II nanofibers were hydrophilic due to inherent **hydrophilic nature** of base polymers i.e.PEO and bPEI. (i.e. **51.9±0.64 and 57.8 ±0.92**)
- After **drug loading** a considerable **increase in contact angle** was observed due to inclusion of curcumin in shell of nanofibers. (i.e. **73.4±0.56 and 76..1±0.75**)
- In the case of their **crosslinked** counterparts a small **decline in contact angle (i.e. 60.4and 68.4,** respectively) was observed owing to glutaraldehyde mediated surface modification

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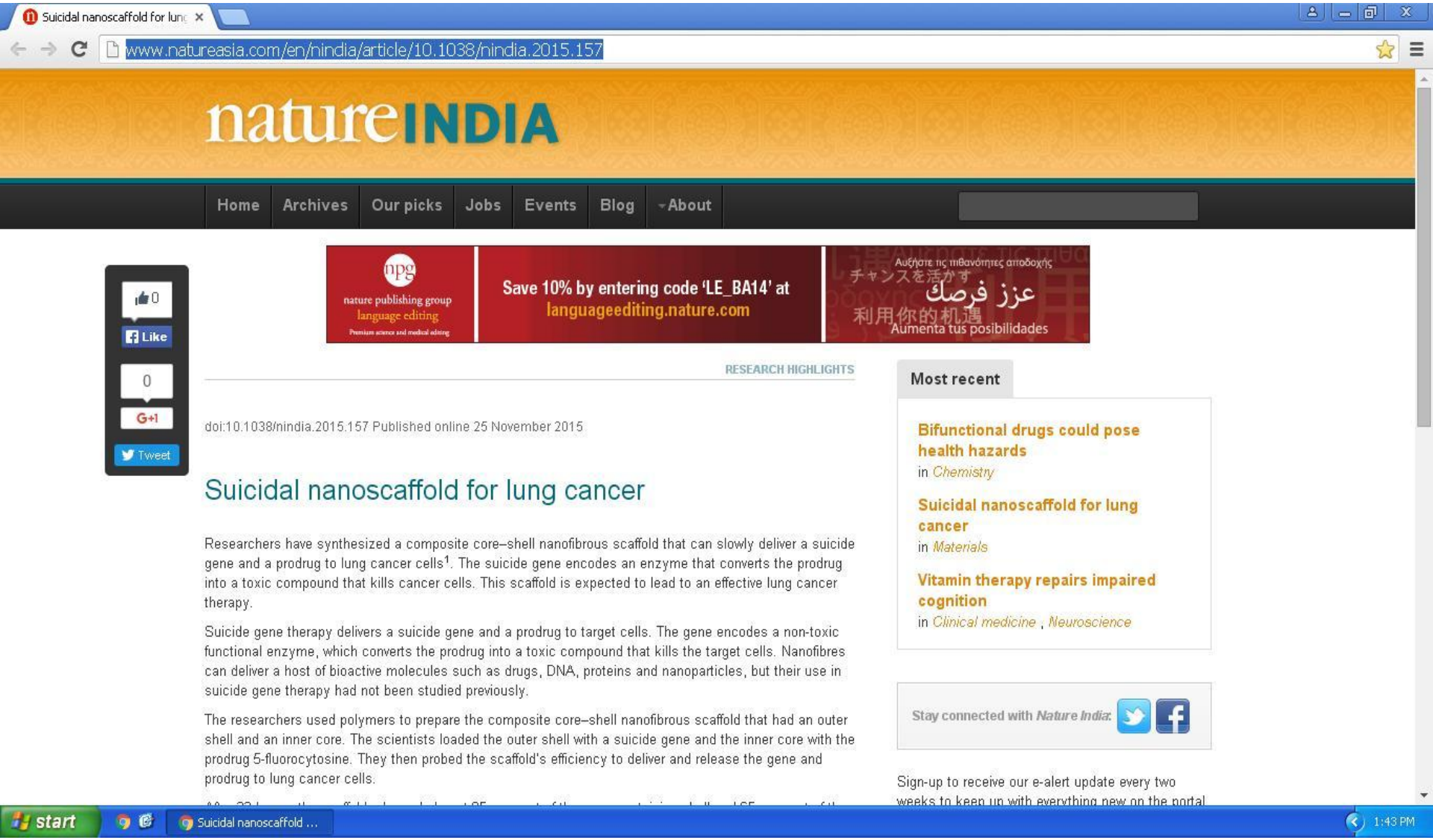

Suicidal nanoscaffold for lung

www.natureasia.com/en/nindia/article/10.1038/nindia.2015.157

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RESEARCH HIGHLIGHTS

doi:10.1038/nindia.2015.157 Published online 25 November 2015

Suicidal nanoscaffold for lung cancer

Researchers have synthesized a composite core–shell nanofibrous scaffold that can slowly deliver a suicide gene and a prodrug to lung cancer cells[1]. The suicide gene encodes an enzyme that converts the prodrug into a toxic compound that kills cancer cells. This scaffold is expected to lead to an effective lung cancer therapy.

Suicide gene therapy delivers a suicide gene and a prodrug to target cells. The gene encodes a non-toxic functional enzyme, which converts the prodrug into a toxic compound that kills the target cells. Nanofibres can deliver a host of bioactive molecules such as drugs, DNA, proteins and nanoparticles, but their use in suicide gene therapy had not been studied previously.

The researchers used polymers to prepare the composite core–shell nanofibrous scaffold that had an outer shell and an inner core. The scientists loaded the outer shell with a suicide gene and the inner core with the prodrug 5-fluorocytosine. They then probed the scaffold's efficiency to deliver and release the gene and prodrug to lung cancer cells.

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Bioactive carbon dots lights up microtubules and destabilises cell cytoskeletal framework – A robust imaging agent with therapeutic activity

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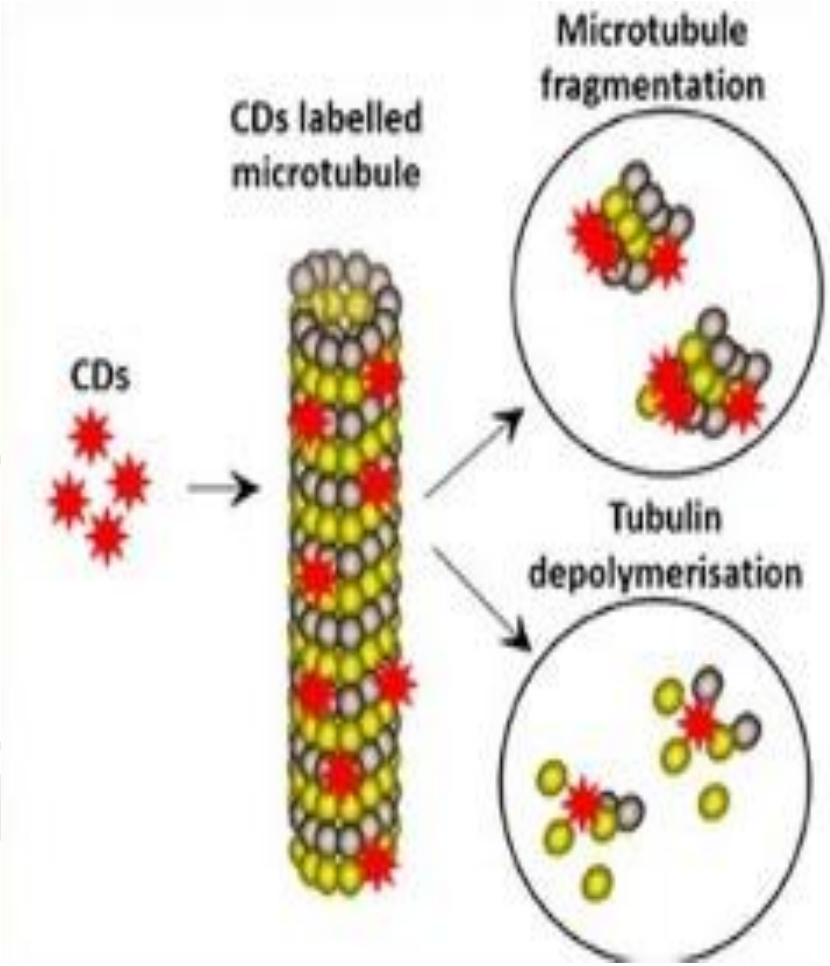
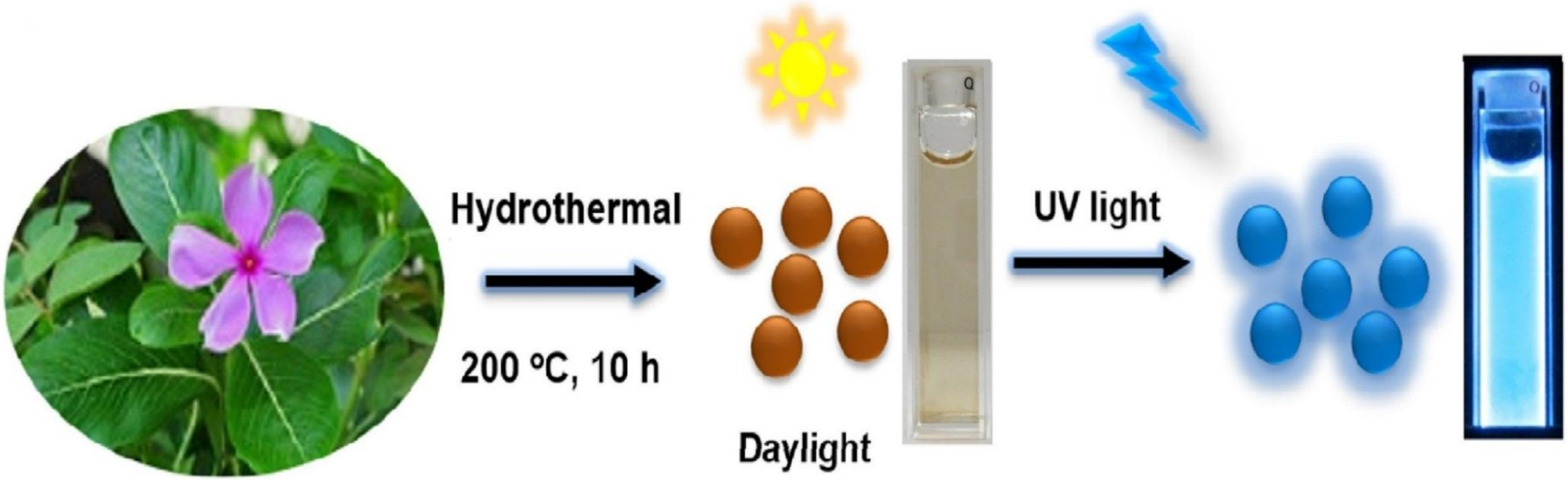
Theranostic C-dots from *Catharanthus roseus*

- **Used as a carbonaceous precursor.**
- **Traditional medicinal plant.**
- **Used in various disease .**
- **Vinca alkaloid present, have high affinity toward tubulin.**

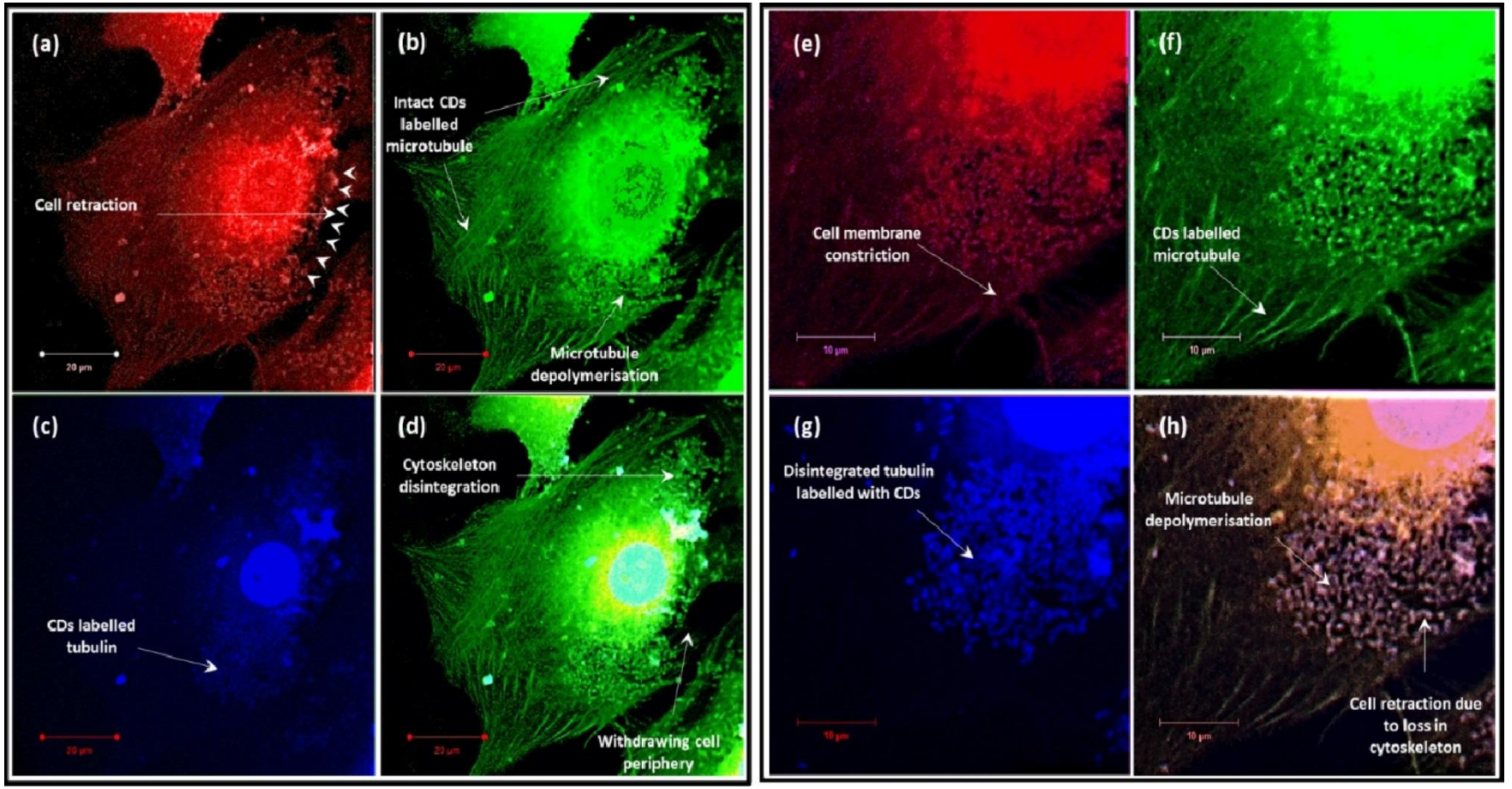


Synthesis of CD

- Hydrothermal method used.
- Simple equipment setup ,low cost , one step synthesis.
- Pyrolysis of carbonaceous precursor.



Morphological changes observed by Confocal microscope



Confocal microscopy images of fluorescent CDs labelled NIH 3T3 cells under (a, e) red filter(663 to 738nm), (b, f) green filter(510 and 560nm) and (c, g) DAPI filter(478-495nm), (d, h) overlay of images acquired under all three filters

RESEARCH HIGHLIGHTS

Fluoroscent nanotags seek out, kill cancer cells

doi:10.1038/nindia.2017.142 Published online 20 November 2017

Researchers have synthesised fluorescent carbon dots from rosy periwinkle plant leaves that can be used as nanotags for detecting and killing cancer cells[1].

Current cancer-detecting techniques use quantum dots that use toxic metals. They are expensive to produce and easily break down when exposed to light.

To develop a safe way to detect cancer cells, scientists from the Indian Institute of Technology, Roorkee, heated a solution of finely chopped periwinkle plant leaves under controlled conditions and then cooled it down to room temperature. This process yielded nanosized carbon dots.

When incubated with specific mice cells, the carbon dots entered the cells. These cells showed enhanced fluorescence, indicating that the dots reached inside the cells. The dots selectively bound to microtubules, filamentous intracellular structures that support cell division and help transport various molecules inside the cells.

The dots destabilised the structure of the microtubules, converting them into fragments that accumulated inside the cells. This, in turn, inhibited the normal activity of the microtubules arresting cell division – a key property that makes the dots potentially useful for stopping the proliferation of cancer cells.

This is an economical and green way to produce fluorescent carbon dots from the leaves of a common medicinal plant, says lead researcher Gopinath Packirisamy.

References

1. Kumar, S. U. *et al.* Bioactive carbon dots lights up microtubules and destabilises cell cytoskeletal framework – A robust imaging agent with therapeutic activity. *Colloids and Surfaces B: Biointerfaces.* 159, 662-672 (2017)

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