Nanotechnology for Medical Applications

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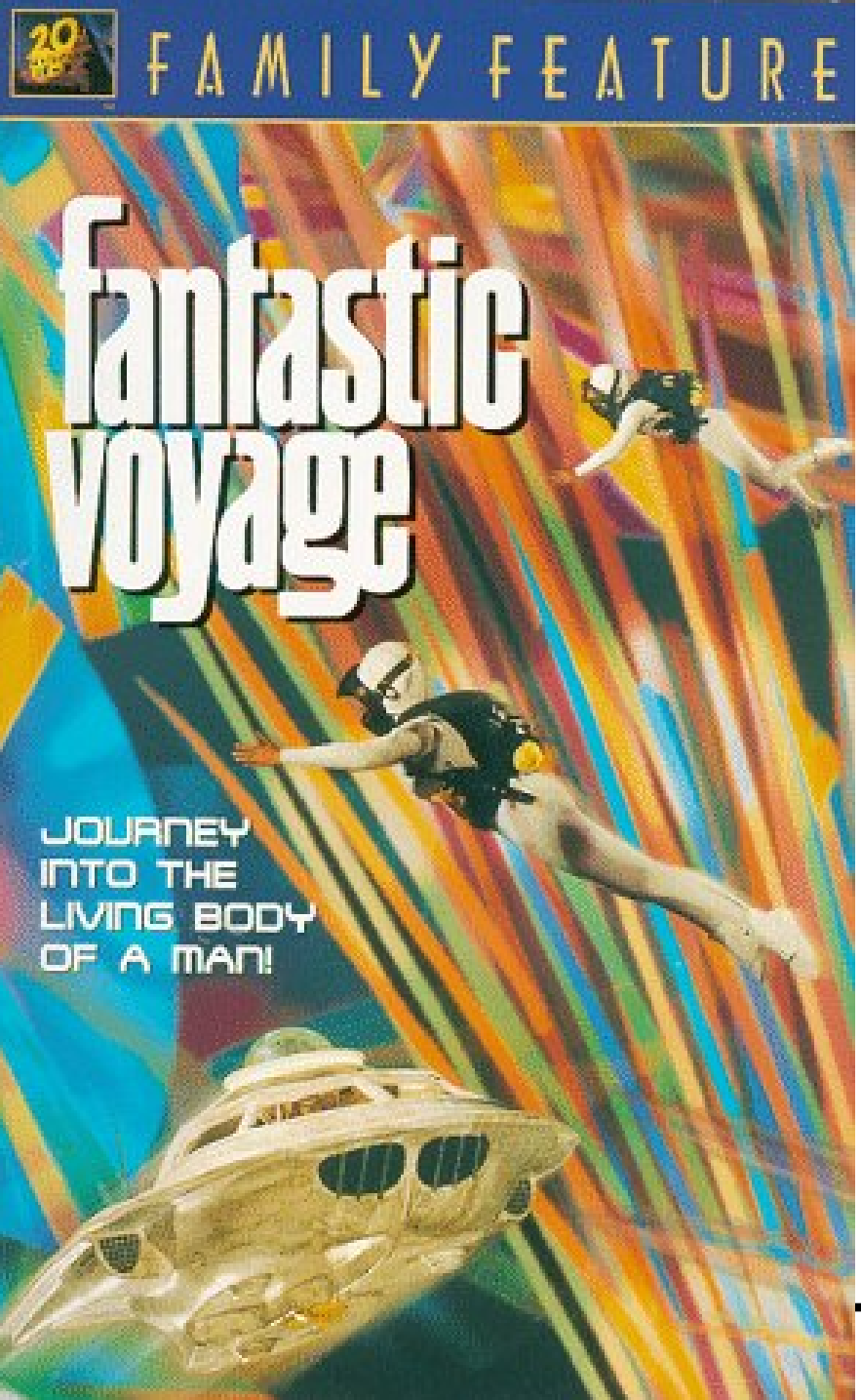
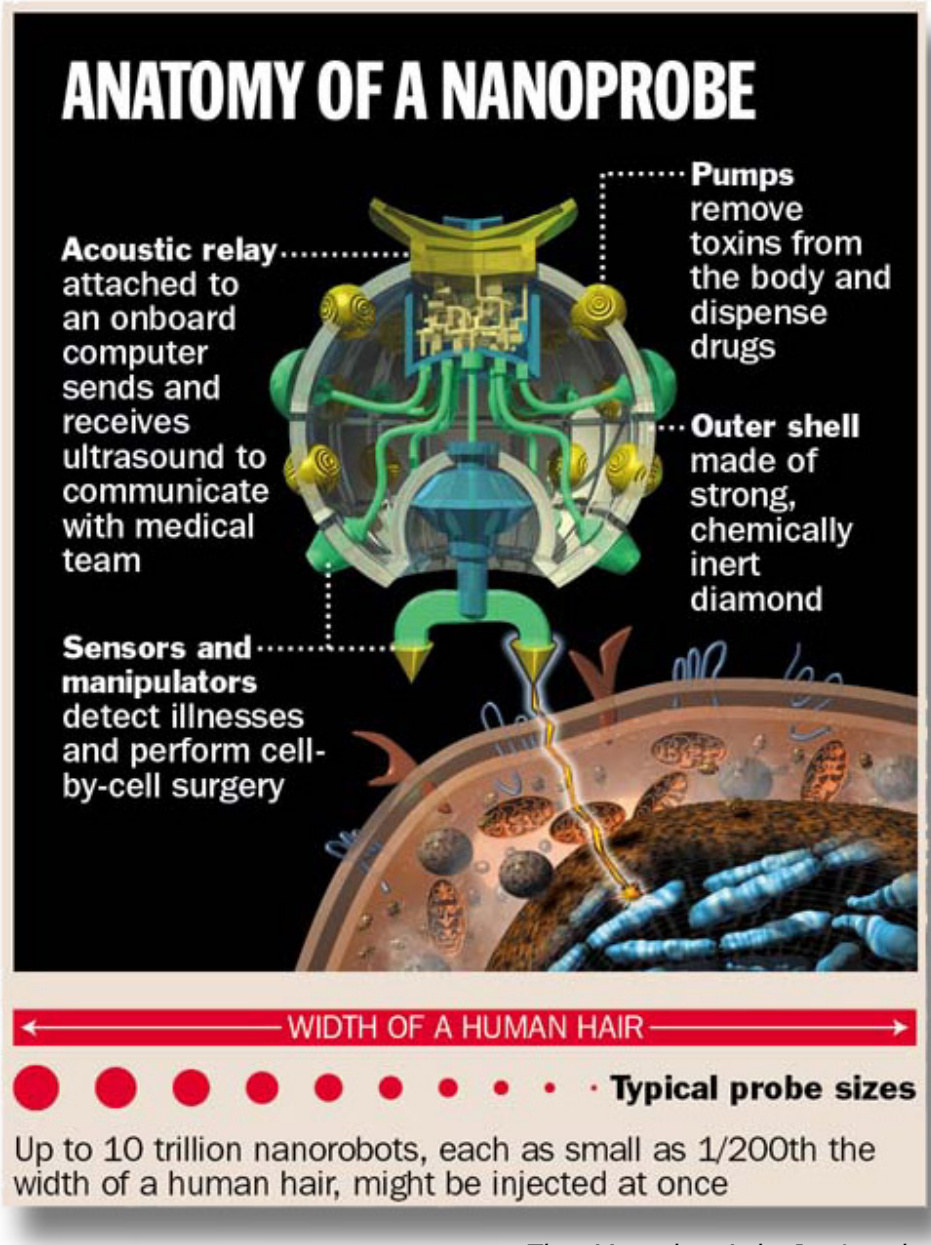
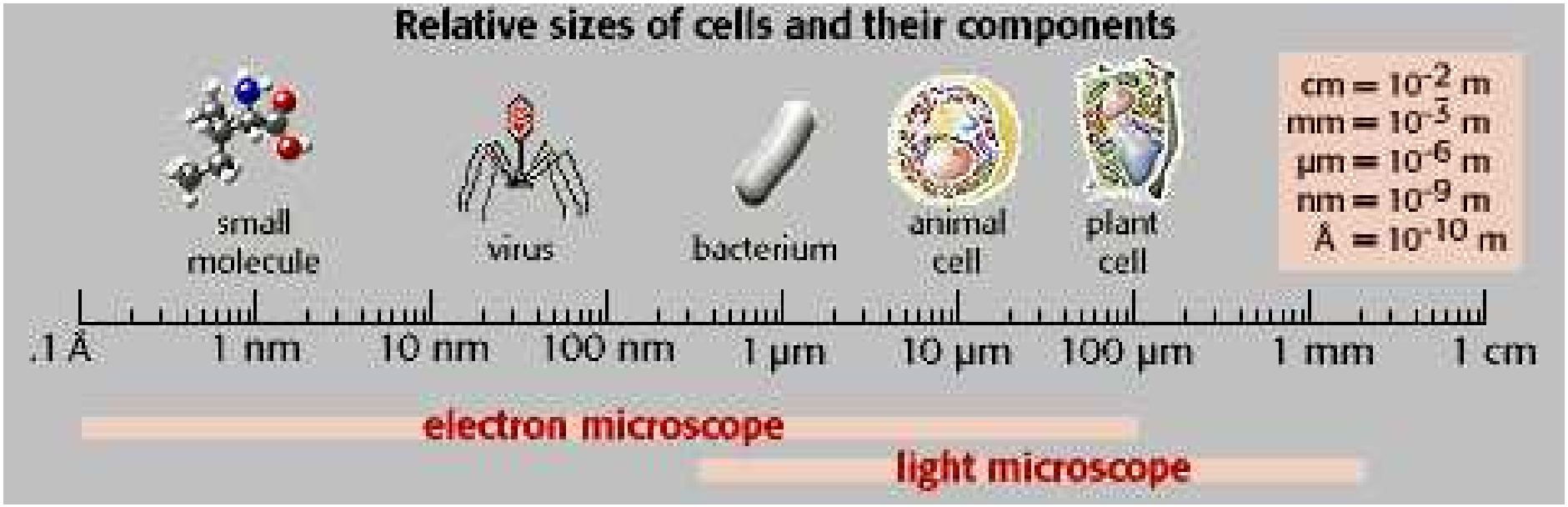
www.nano.med.umich.edu

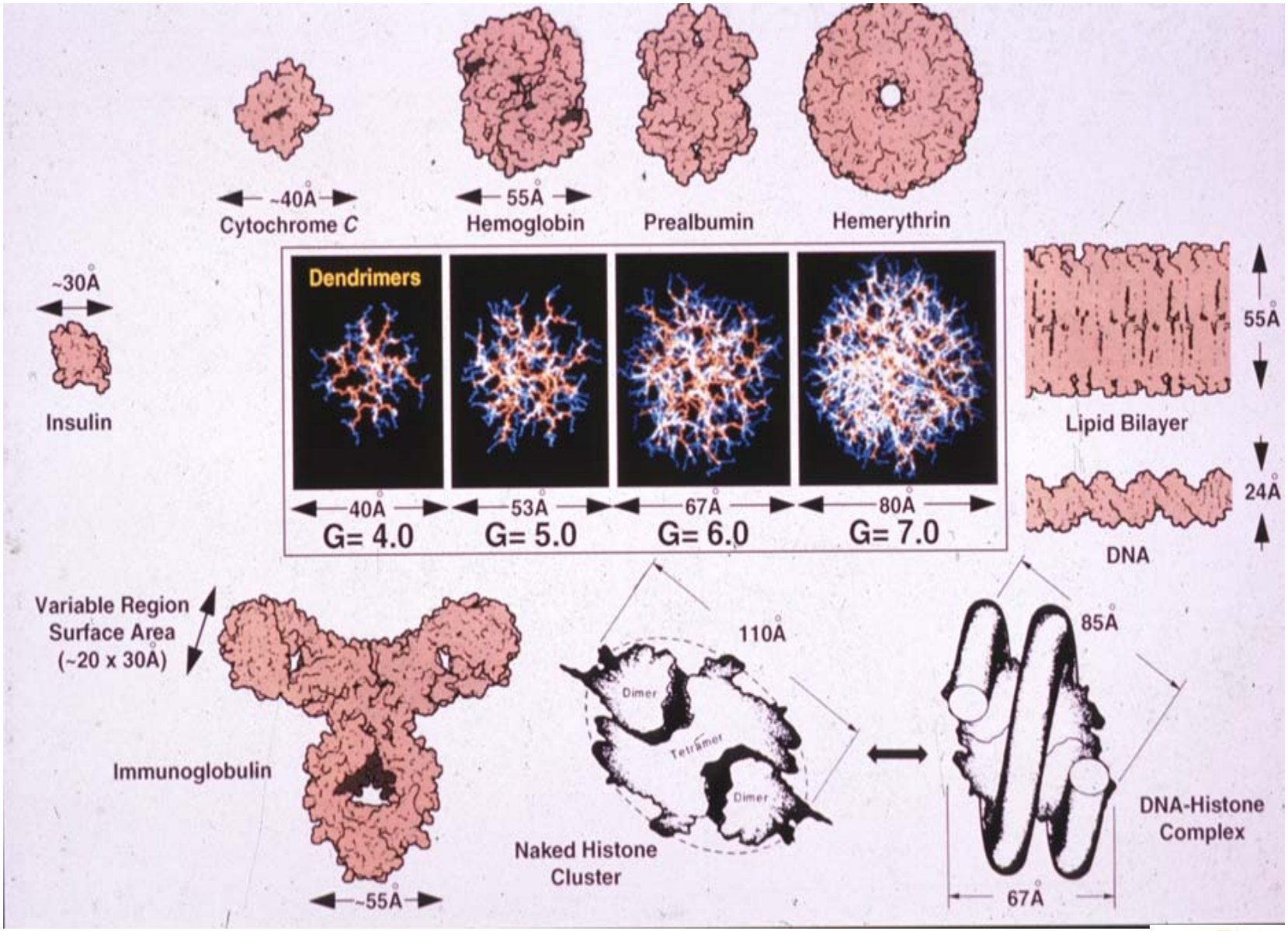

FAMILY FEATURE
fantastic voyage
JOURNEY INTO THE LIVING BODY OF A MAN!



Time Magazine, Artist Joe Lertola

Friend or Foe?


Relative sizes of cells and their components
small molecule
virus
bacterium
animal cell
plant cell
cm = 10-2 m
mm = 10-3 m
µm = 10-6 m
nm = 10-9 m
Å = 10-10 m
.1 Å
1 nm
10 nm
100 nm
1 µm
10 µm
100 µm
1 mm
1 cm
electron microscope
light microscope


~40Å
Cytochrome C
55Å
Hemoglobin
Prealbumin
Hemerythrin
~30Å
Insulin
Dendrimers
40Å
G= 4.0
53Å
G= 5.0
67Å
G= 6.0
80Å
G= 7.0
55Å
Lipid Bilayer
24Å
DNA
Variable Region
Surface Area
(~20 x 30Å)
Immunoglobulin
~55Å
110Å
Dimer
Tetramer
Dimer
Naked Histone
Cluster
85Å
67Å
DNA-Histone
Complex

What is “Nanomedicine”?

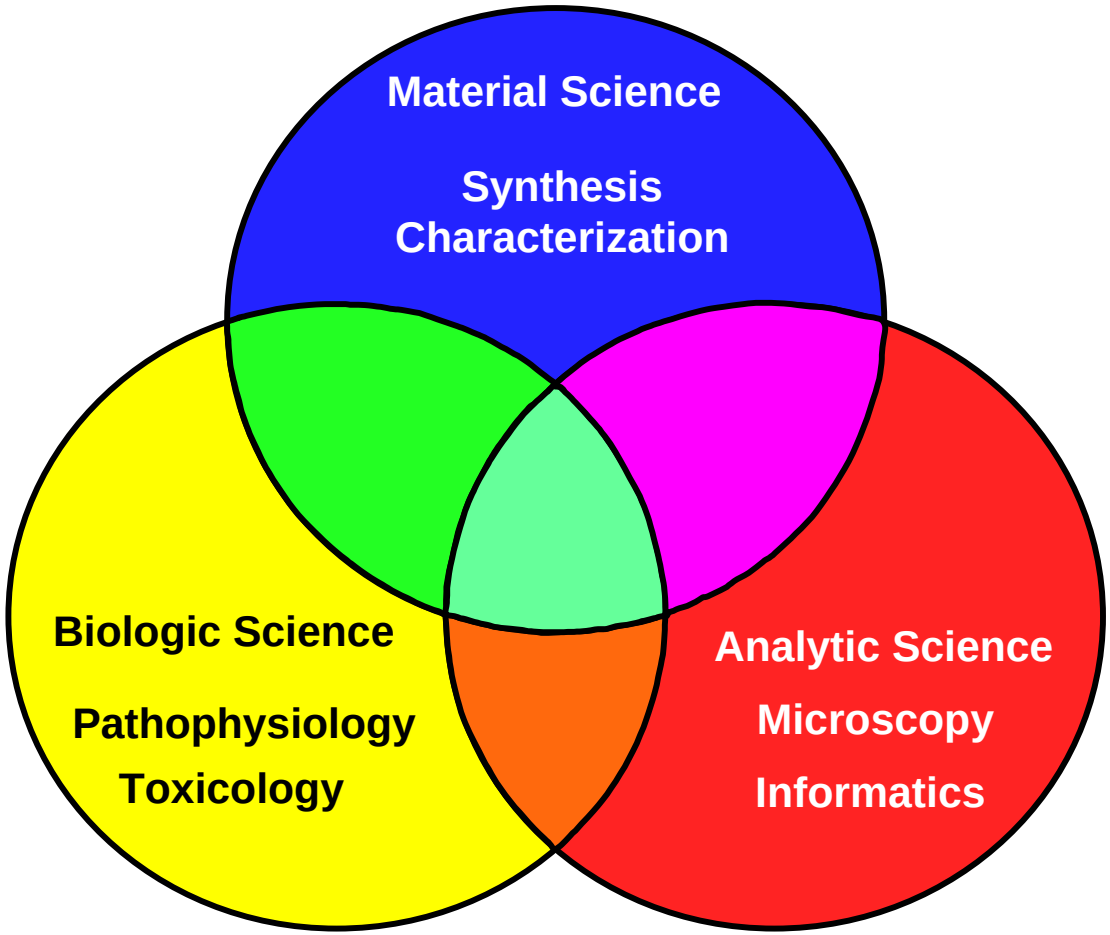
Nano-structures yield → “Nanomedicines”

- Designed, defined synthetic/biosynthetic structure where nanometer size is necessary for function *in vivo*.
- Self assembling or directed synthesis of *uniform* nano-structures.
- Material functions in biologic environment.
- Caveat: the complexity of nature often prevails.

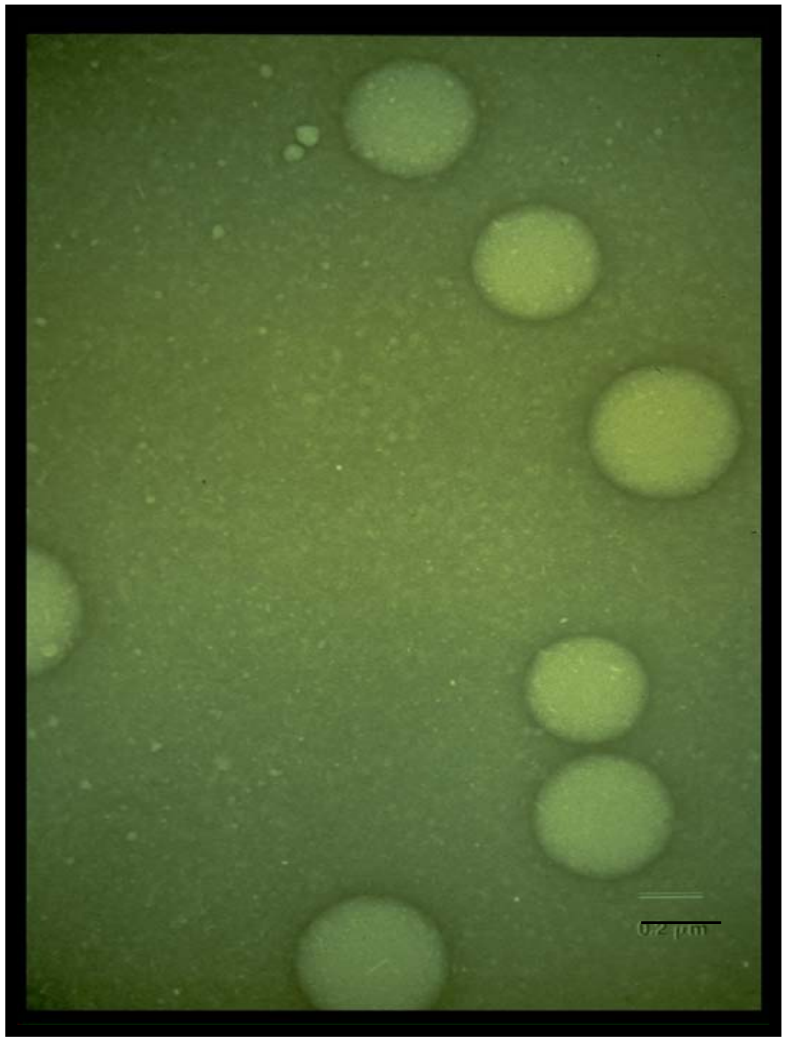
Examples of “Nanomedicines”

- Self assembling nano-structures with unique attributes owing to size.
- Designed, defined nano-device where size is necessary for function *in vivo*.
- Nano-structures designed to defeat viruses where nature prevails.

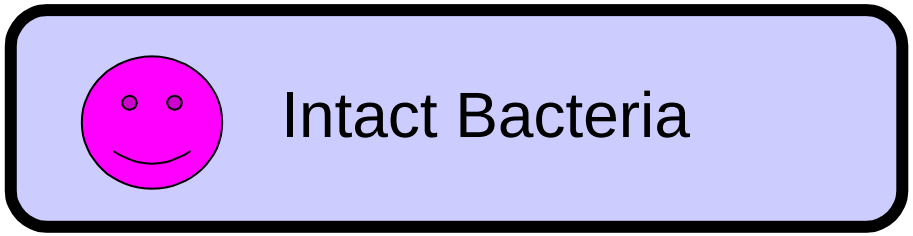
The Center for Biologic Nanotechnology: Scientific Organization

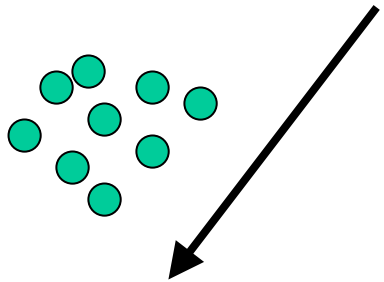


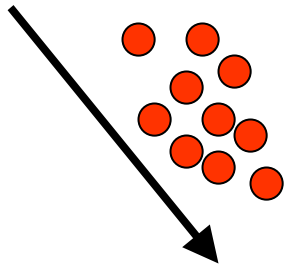
Nanoemulsion Technology

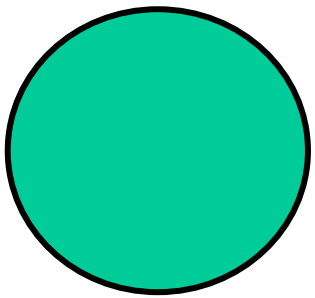


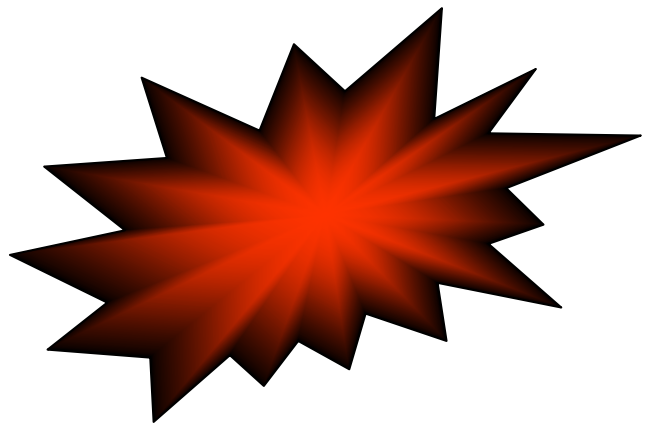
- Nanoemulsion consisting of:
  - -vegetable oil
  - -non-ionic detergent
  - -solvent
  - -water
- Nontoxic: Oral, Mucosal, Tissue Injection & Irrigation
- Cidal Activity: Bacteria, Spores, Enveloped Viruses, Fungi, Mycobacteria







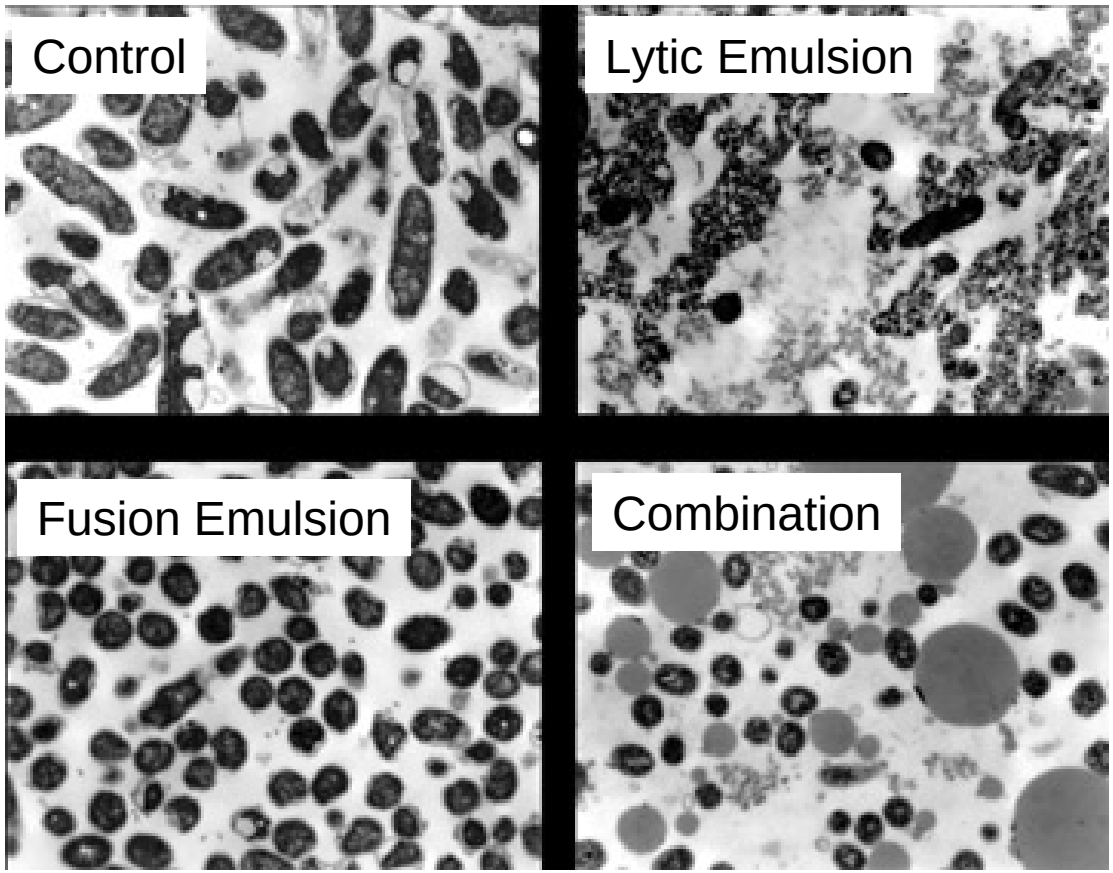




Fusogenic Emulsion Disrupts Ultrastructure of the Organism

Lysogenic Emulsion Disrupts Membrane of the Organism Causing Lysis

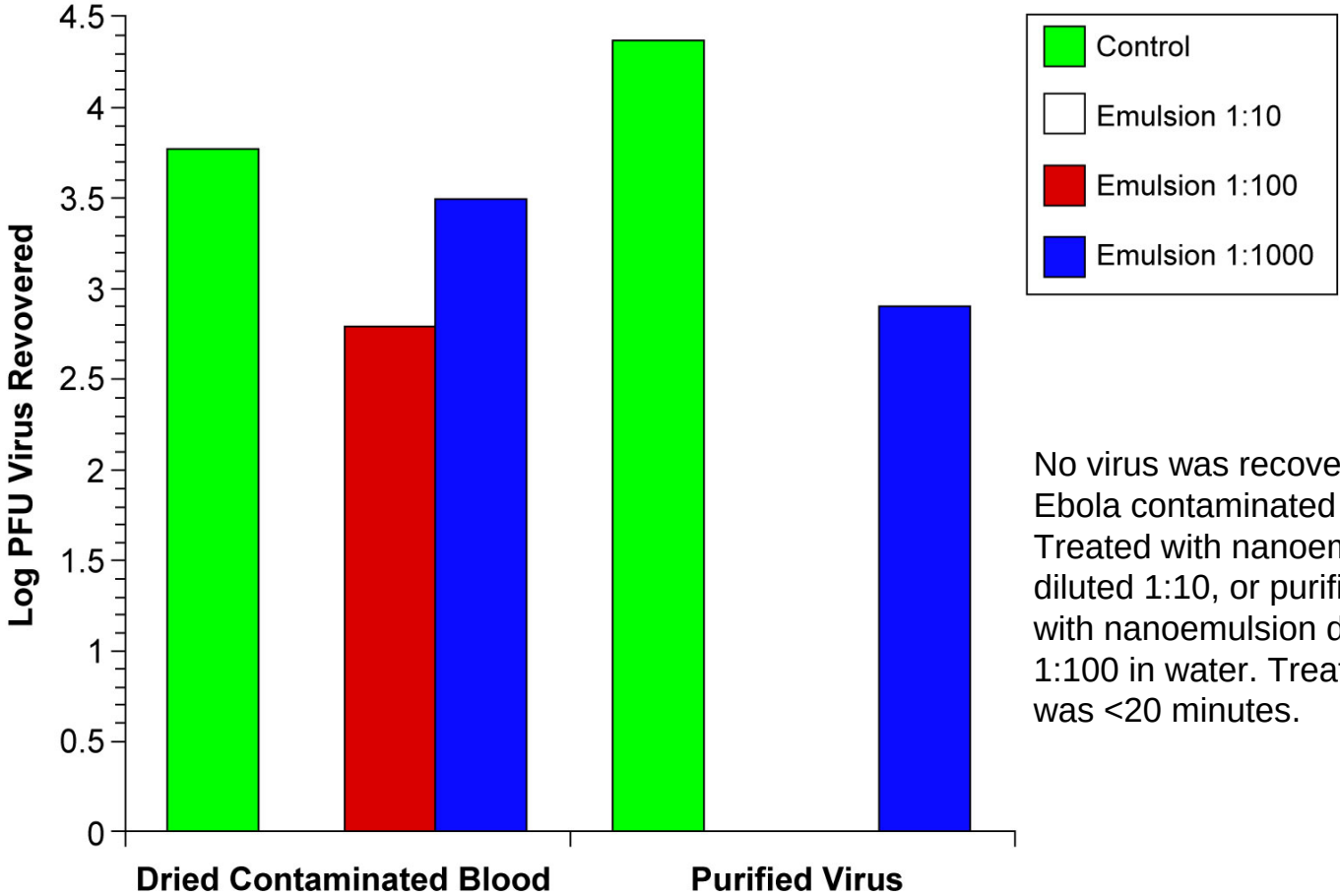
Effect of Nanoemulsions on *Vibrio* Cholerae (El Tor Strain)



Inactivation of Ebola Virus

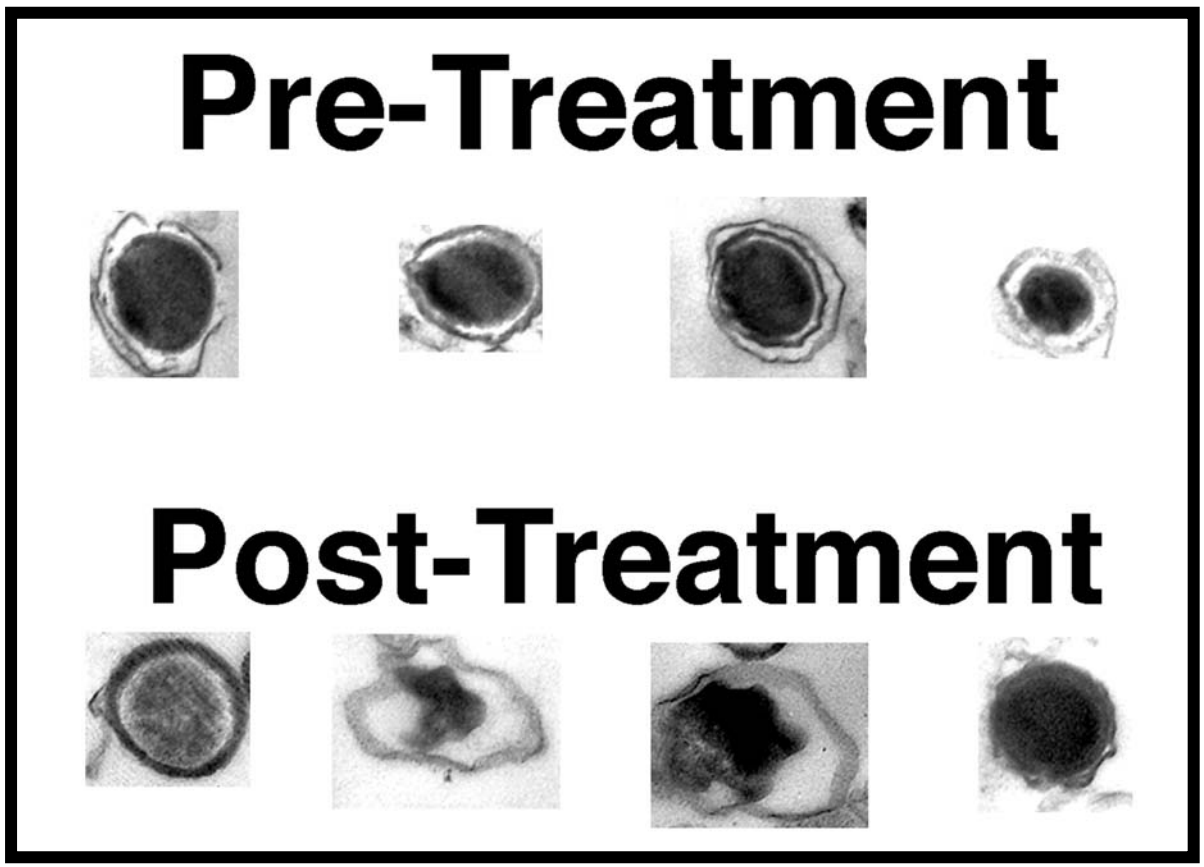
Recovery of Ebola Virus After Treatment with Nanoemulsion

Source: Dr. A. Chepurnov, Vector, NS, Russia

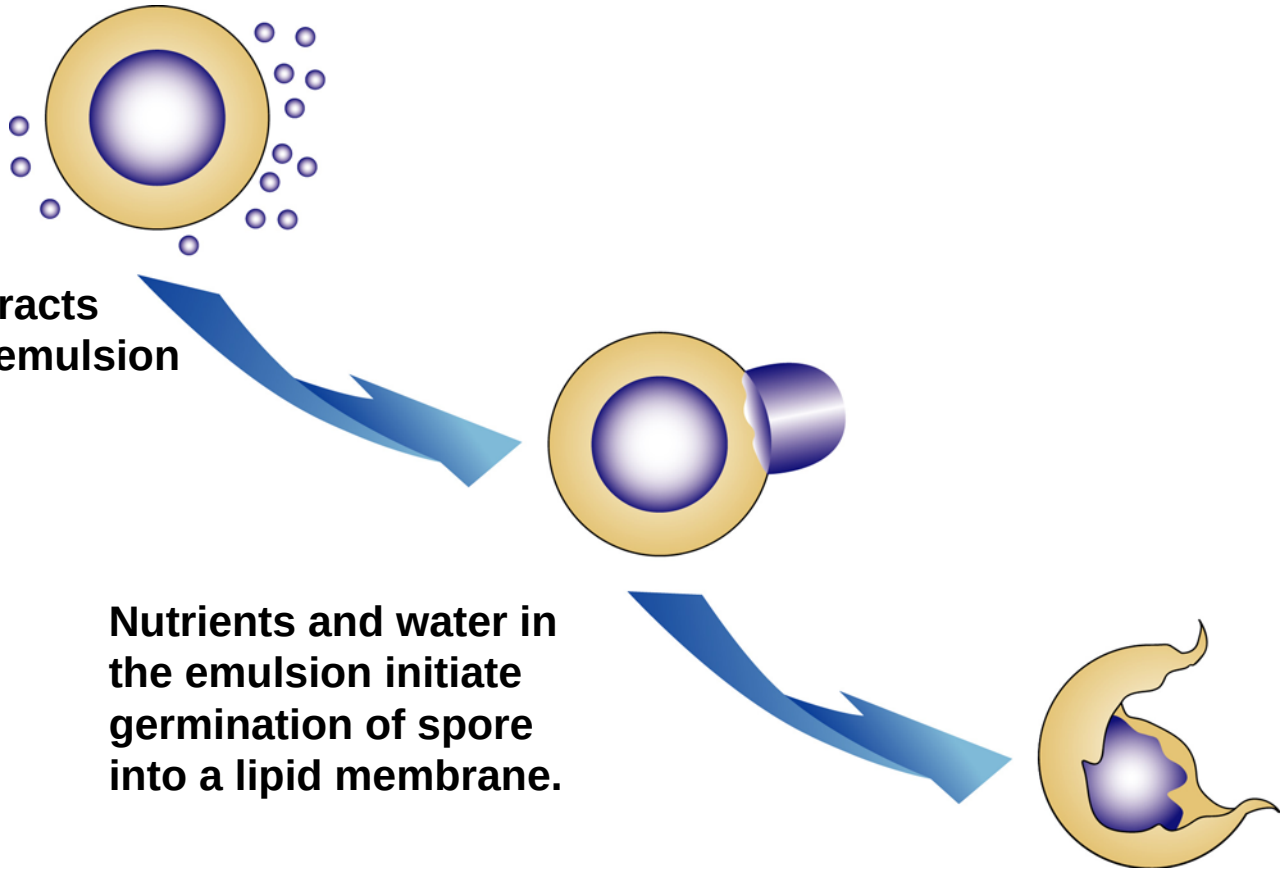


No virus was recovered from Ebola contaminated dried blood Treated with nanoemulsion diluted 1:10, or purified virus treated with nanoemulsion diluted 1:10 or 1:100 in water. Treatment time was <20 minutes.

Alterations of *Bacillus* cereus spores Induced by Nanoemulsions



Sporicidal Activity of Nanoemulsion

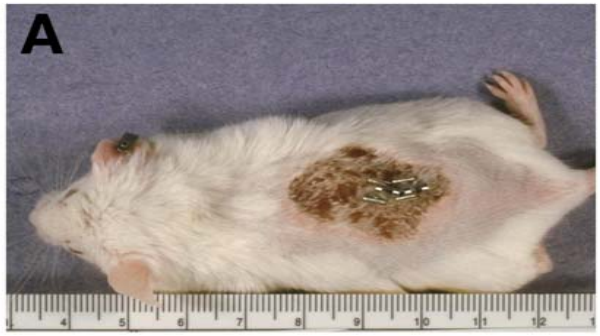


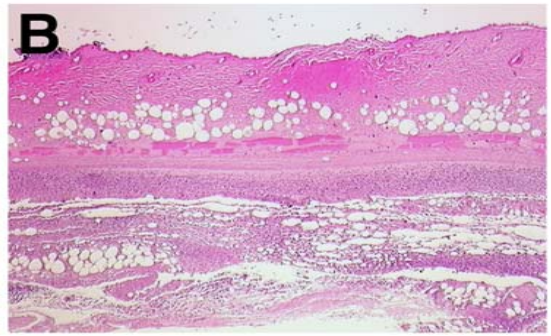
Spore interacts with Nanoemulsion droplets.

Nutrients and water in the emulsion initiate germination of spore into a lipid membrane.

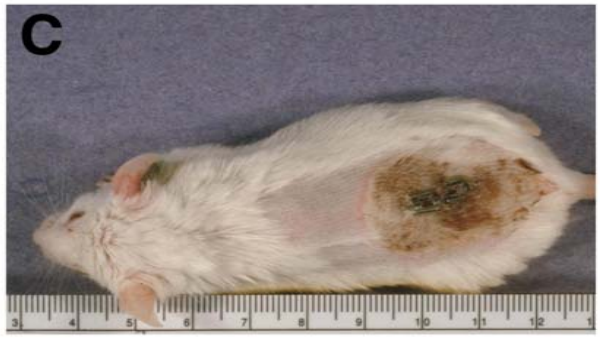
Nanoemulsion disrupts spore as it germinates

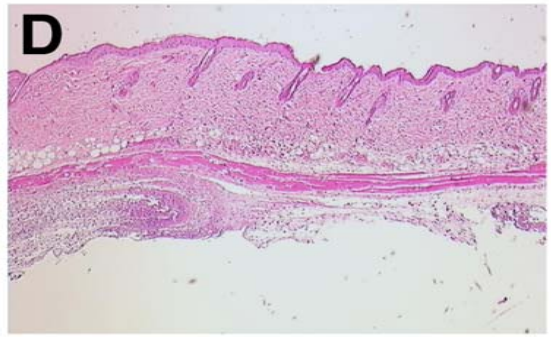
Spores in Wound Alone



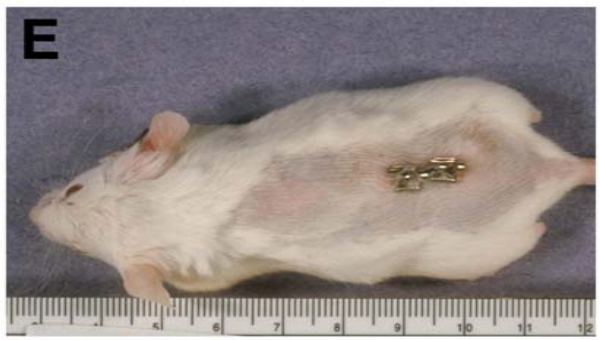


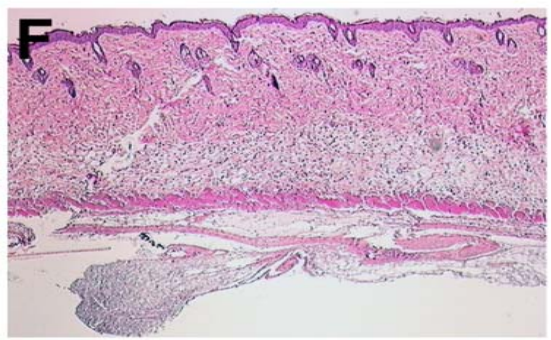
Spores in Wound Irrigated With Saline





Spores in Wound Irrigated With Emulsion





The Road to Dugway

Bang Box 2

Results of Decontamination Trial at Dugway, UT December 1999

1) University of Michigan	Antimicrobial Emulsion
2) Sandia National Laboratory	Concentrated Liquid Peroxide
3) Lawrence Livermore Laboratory	Liquid Peroxidant
4) Dugway Standard Technique	Neutralized Bleach

4 other technologies failed to kill spores

Result of Decontamination Trial at Dugway, UT

Although your product is a good bio-killer, the question is what is its ability to destroy/neutralize chemical agents. Most armed services want a magic pixie dust - "kills bio and chem, not toxic to humans, environmentally safe".

William G. Davis, SBCCOM, Dugway UT


NanoBio®
Corporation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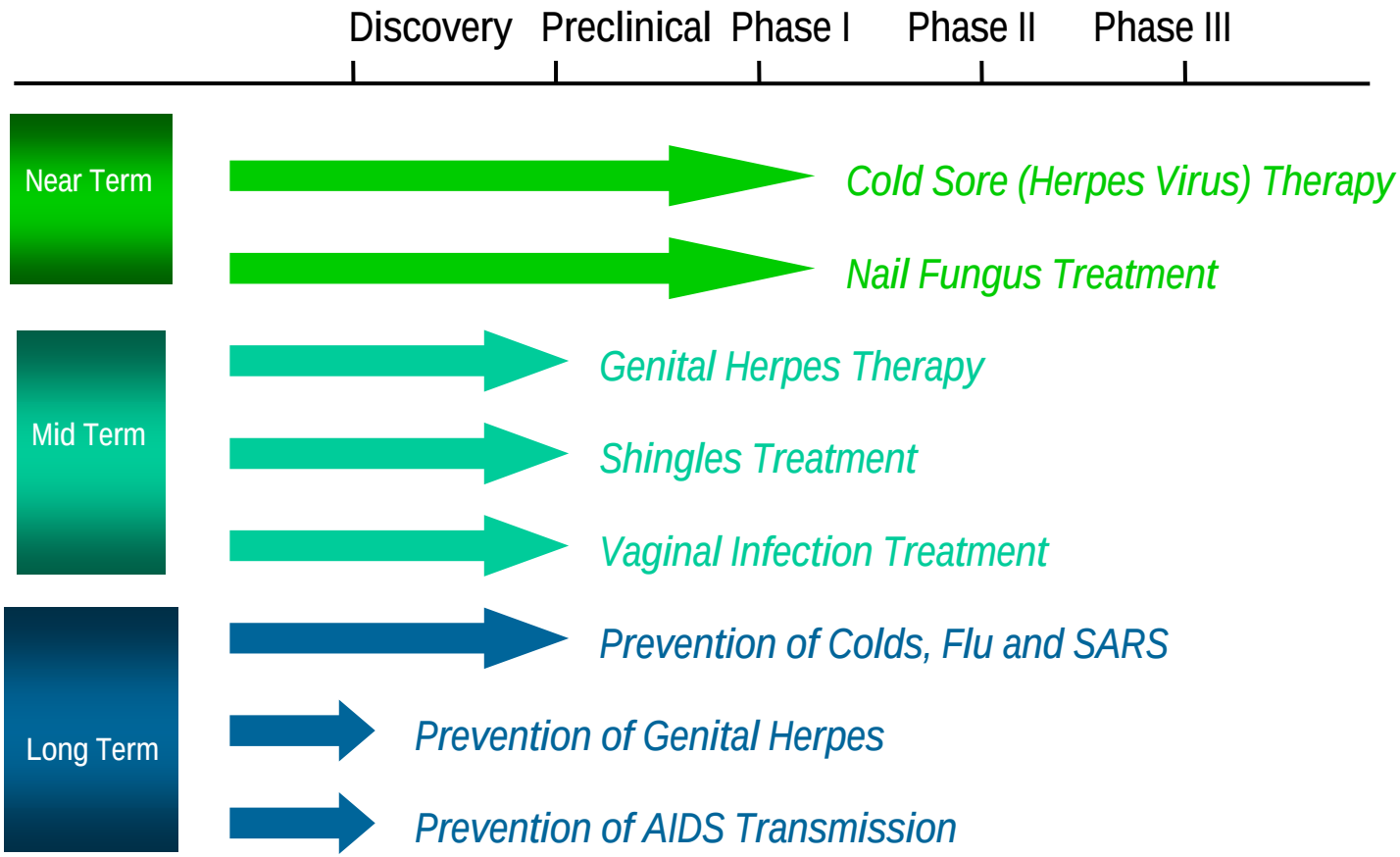
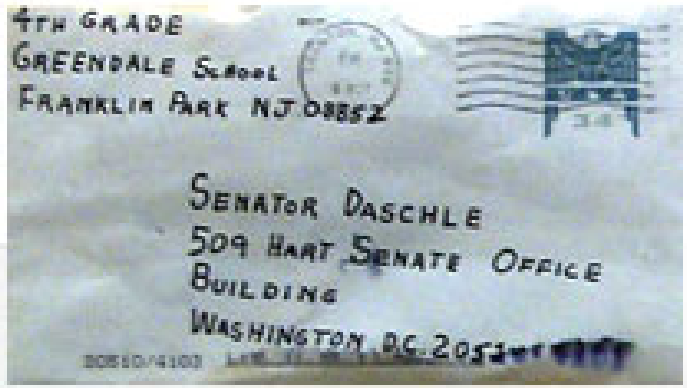
NanoBio® Product Pipeline



NanoBio Corporation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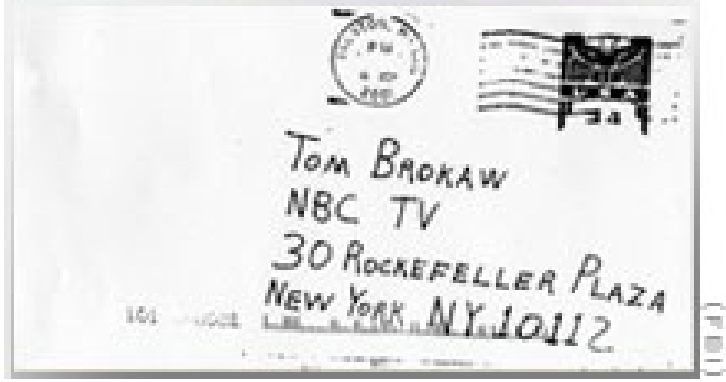
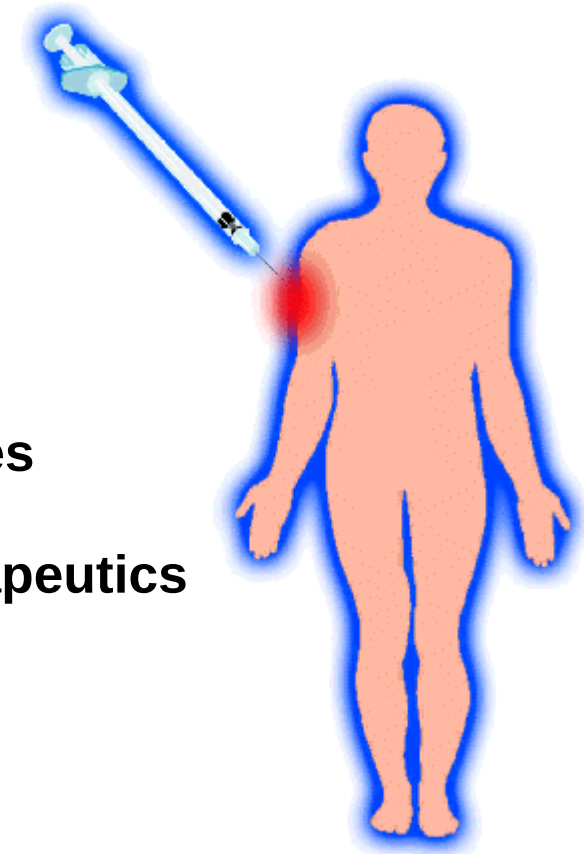
GREENDALE SCHOOL
FRANKLIN PARK NJ 08852
SENATOR DASCHLE
509 HART SENATE OFFICE
BUILDING
WASHINGTON DC 205

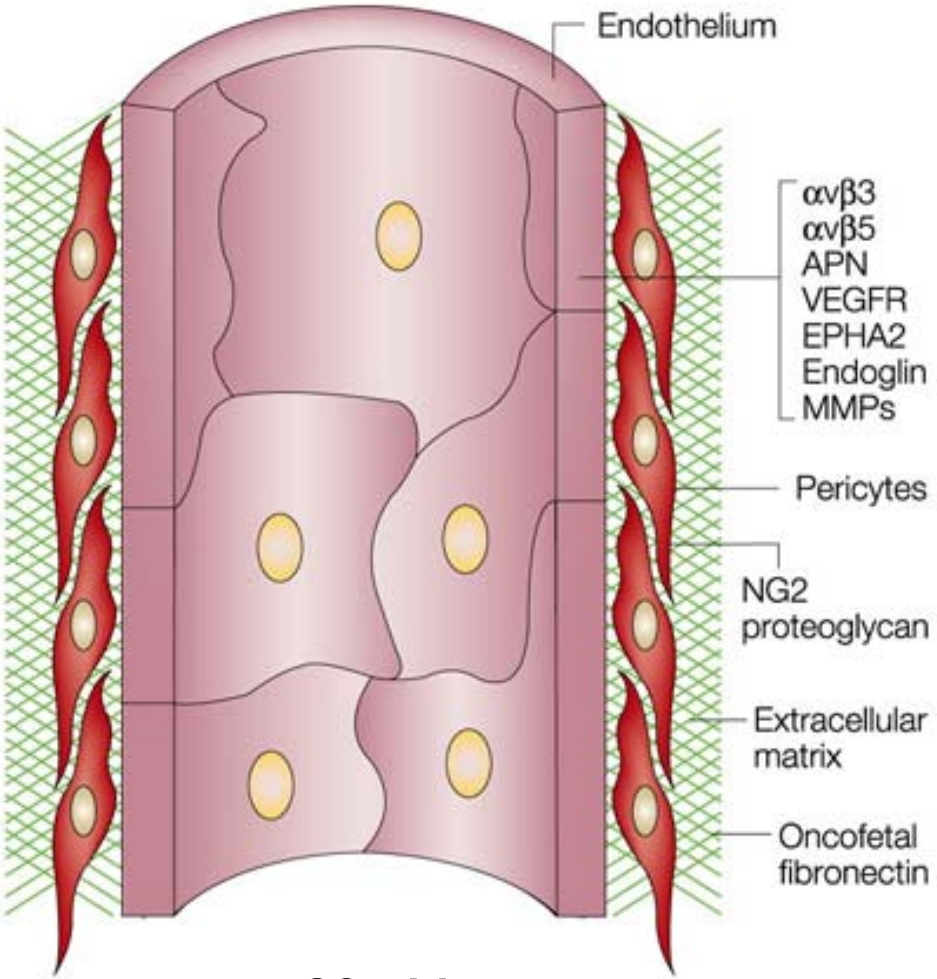

TOM BROKAW
NBC TV
30 ROCKEFELLER PLAZA
NEW YORK NY 10112

Smart Cancer Sensor/Therapeutic

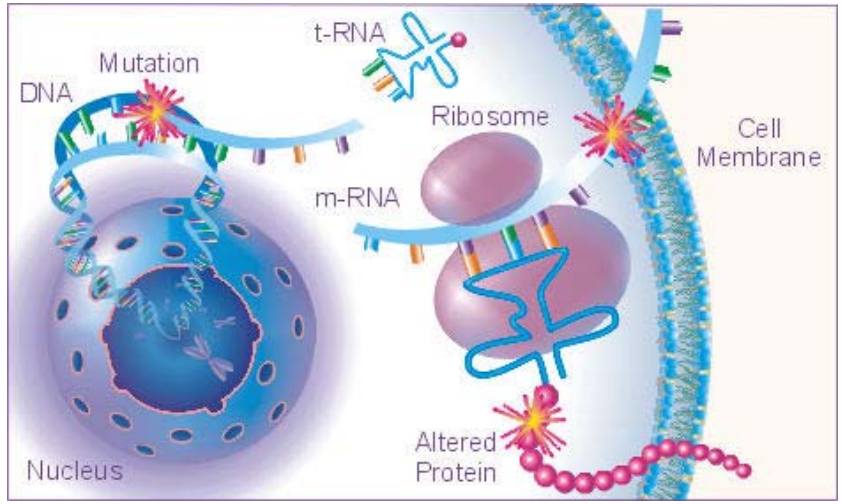
- Targets to Site and Into Cells
- Imaging Capability to Document Presence
- Senses for Pathophysiologic Changes
- Selects Therapeutic Agents Based on Changes
- Non-invasive External Trigger Releases Therapeutics
- Documents Response to Therapeutic

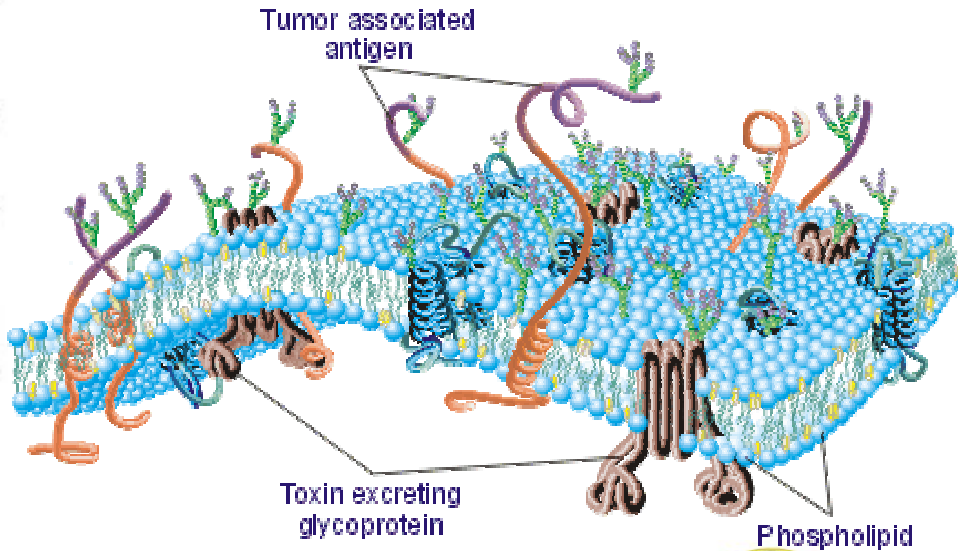


Barriers to Targeted Therapeutics



<20 nM





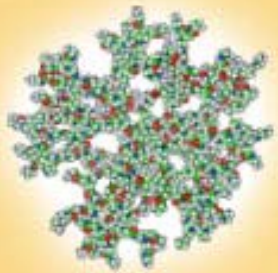
<150 nM

Nature Reviews | Cancer

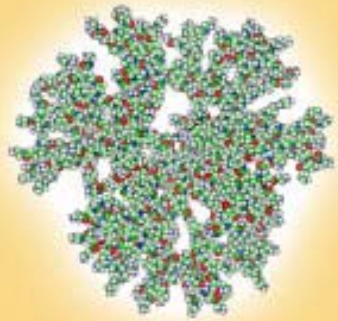
Dendrimer Size Comparison

G3 Dendrimer

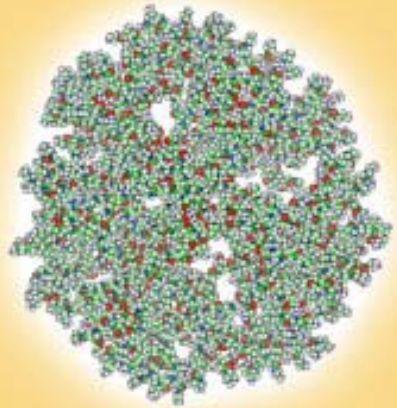
G4 Dendrimer



G5 Dendrimer



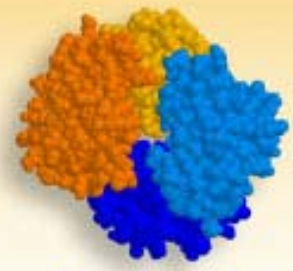
G6 Dendrimer



G7 Dendrimer

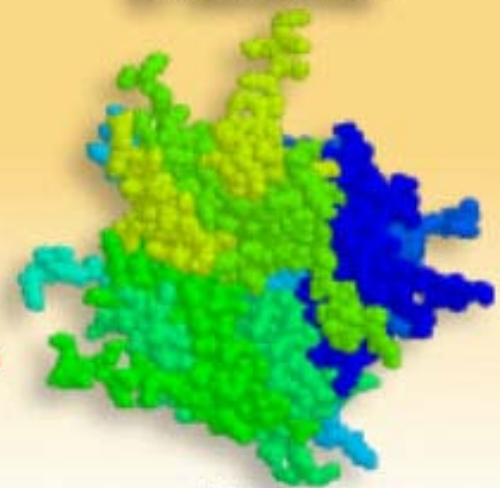
Insulin

Cytochrome C



Hemoglobin

Transthyretin



Histone

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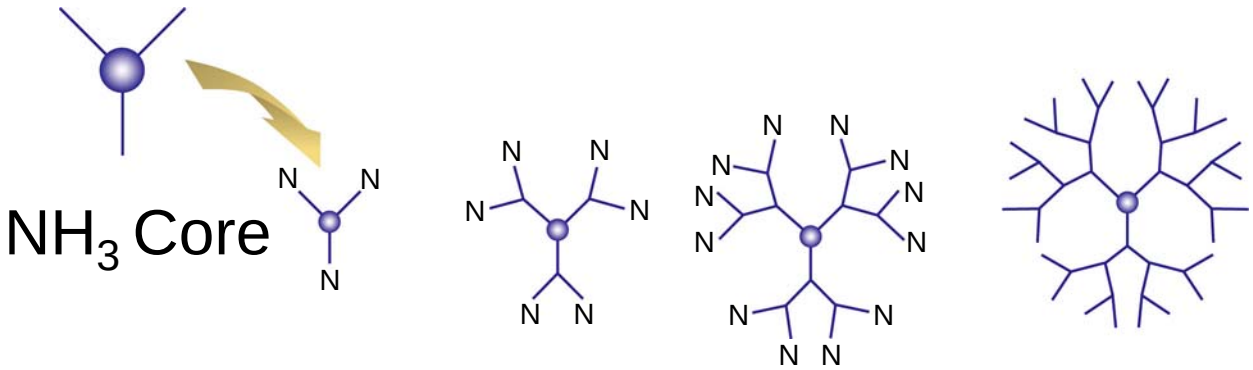
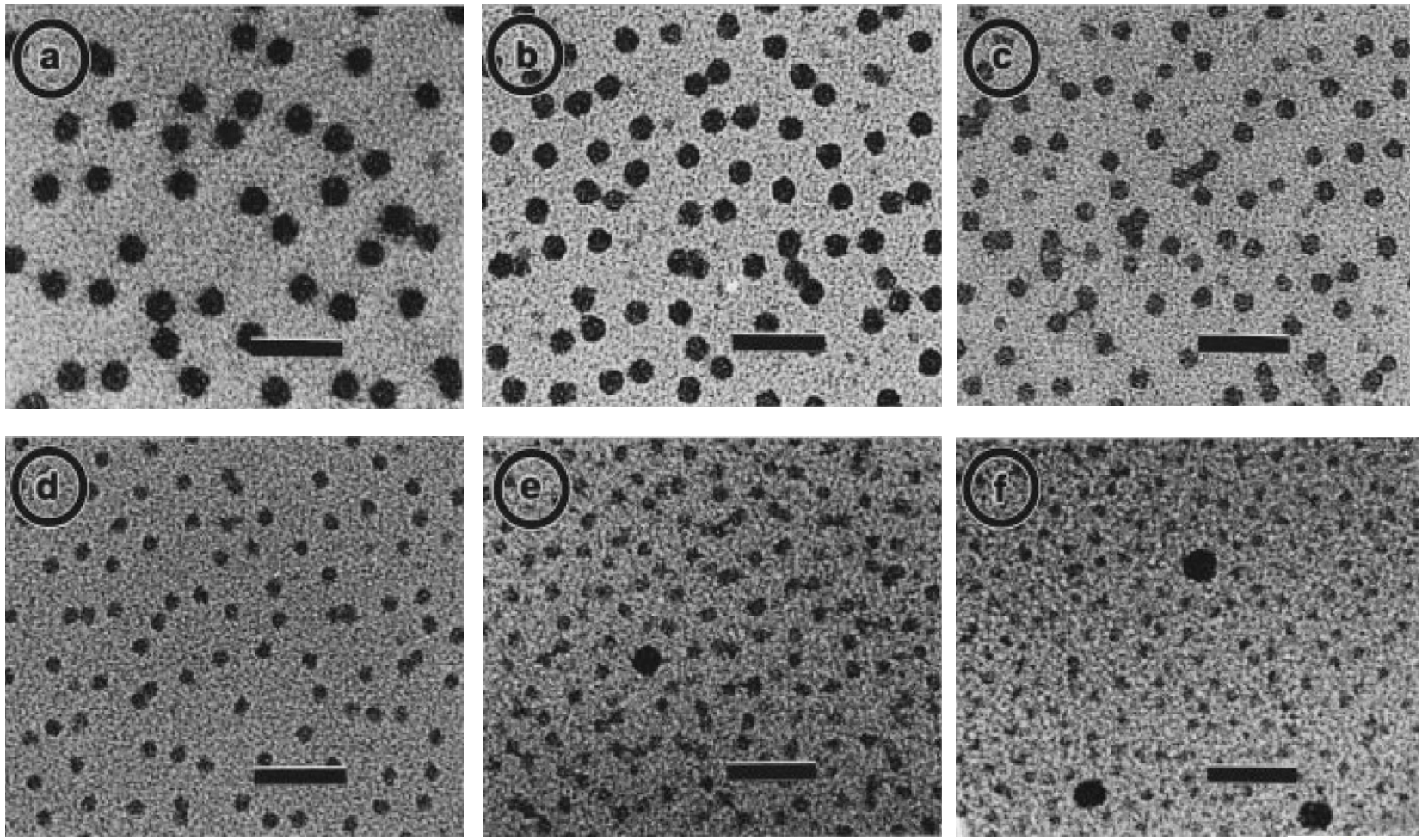
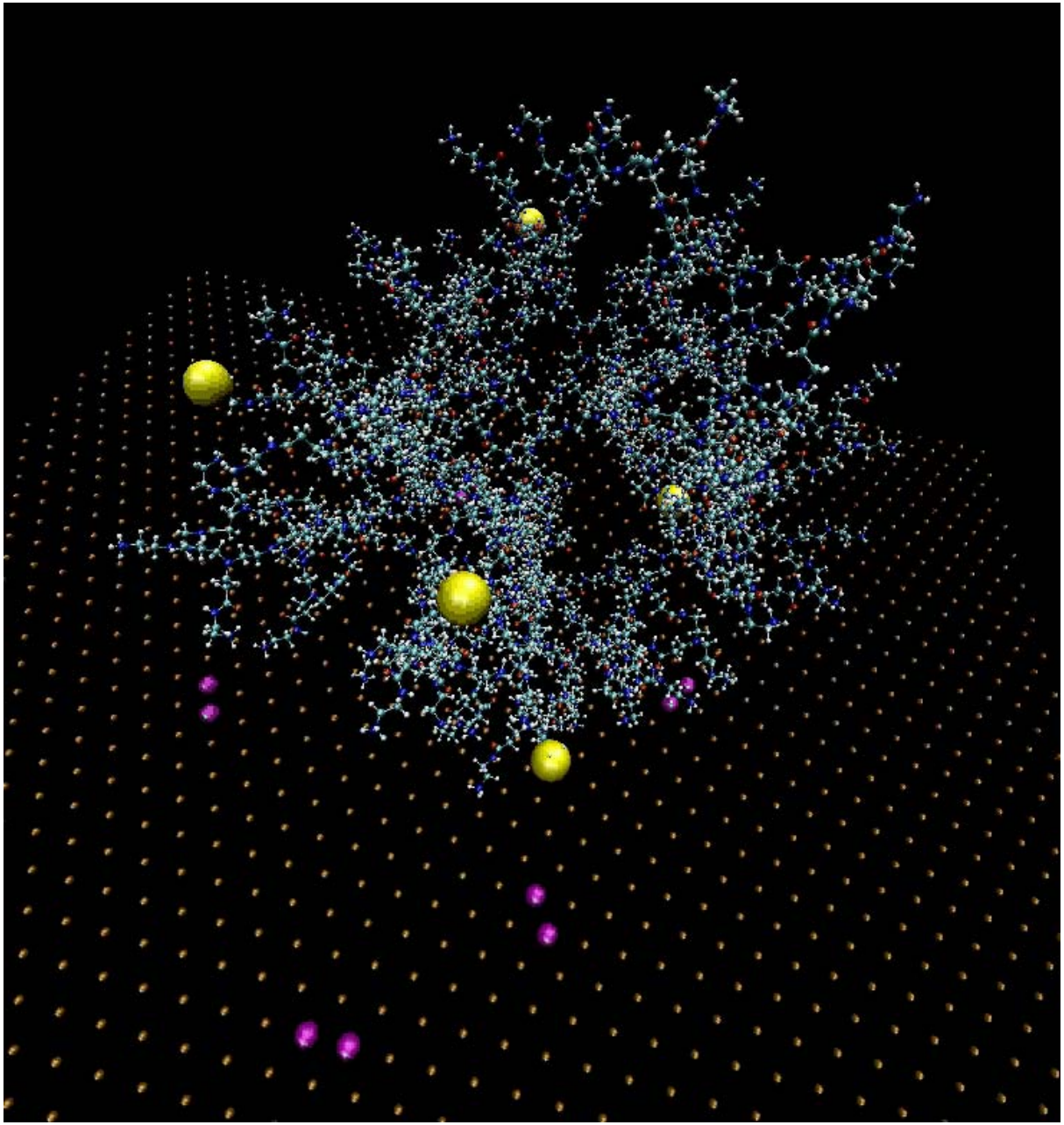
Structure and Synthesis of Dendrimers



Generation	**G0**	**G1**	**G2**	**G3**
Surface Amine Groups	**3**	**6**	**12**	**24**
Molecular Weight	**359**	**1,044**	**2,414**	**5,154**

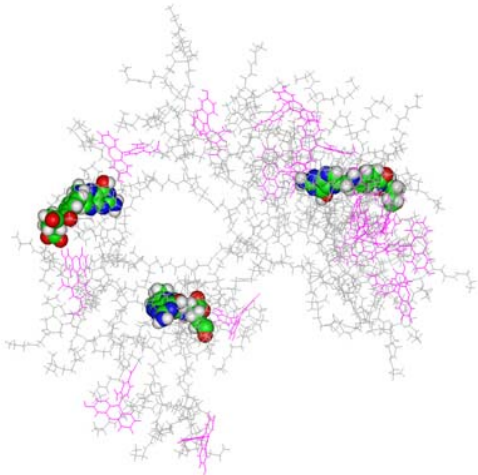
Uniformity of Dendrimers



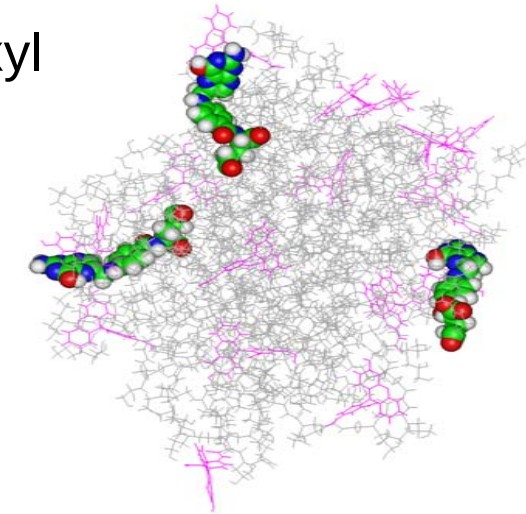


Dendrimer/Folate Surface Modeling

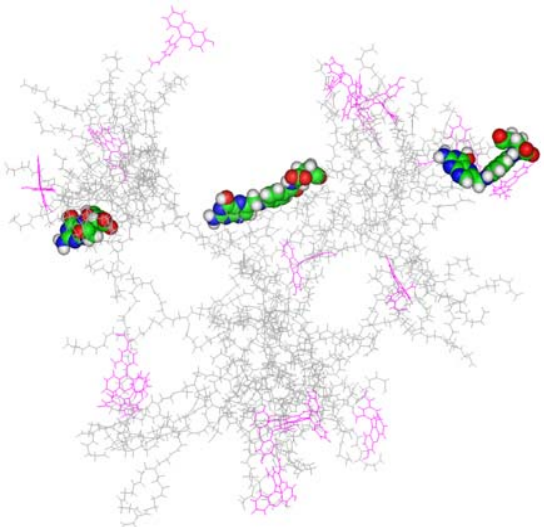
Amine



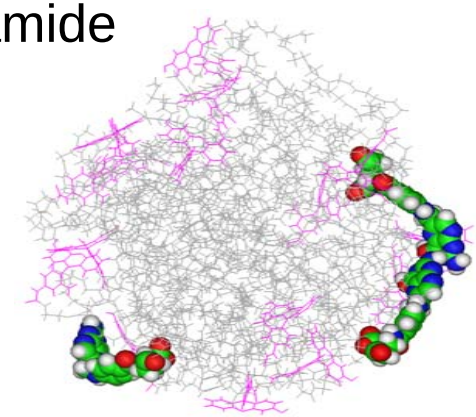
Hydroxyl



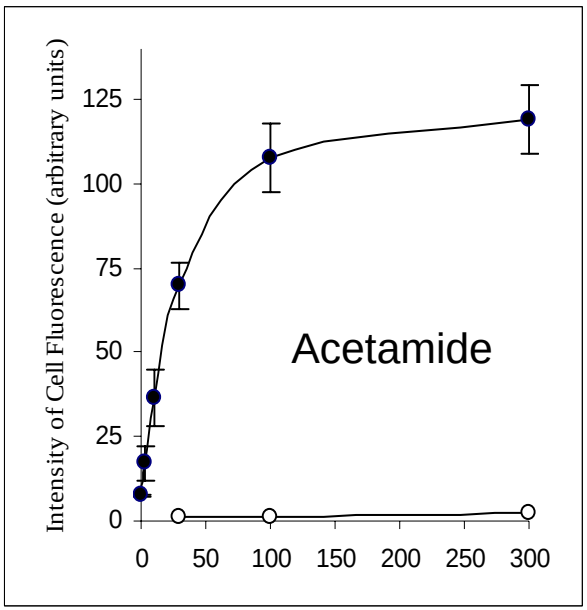
Carboxyl

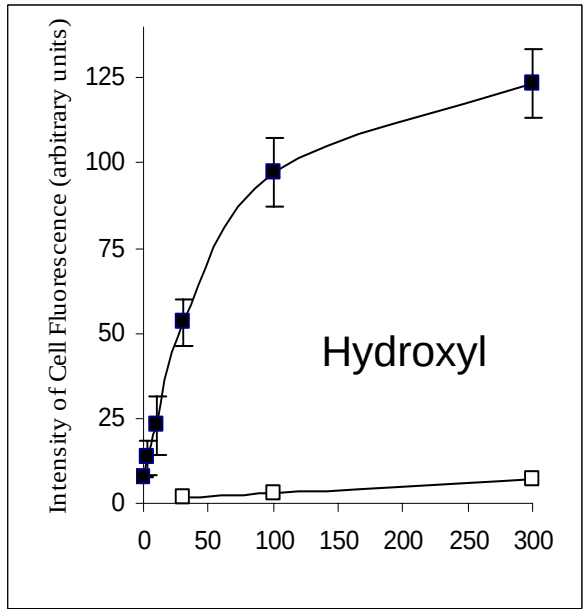


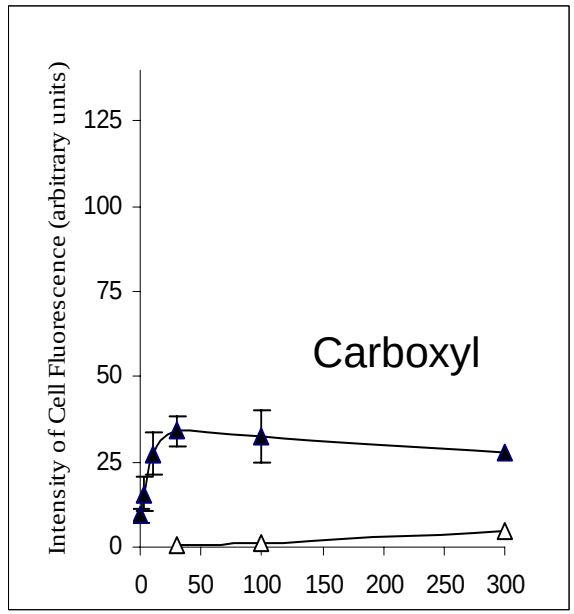
Acetamide



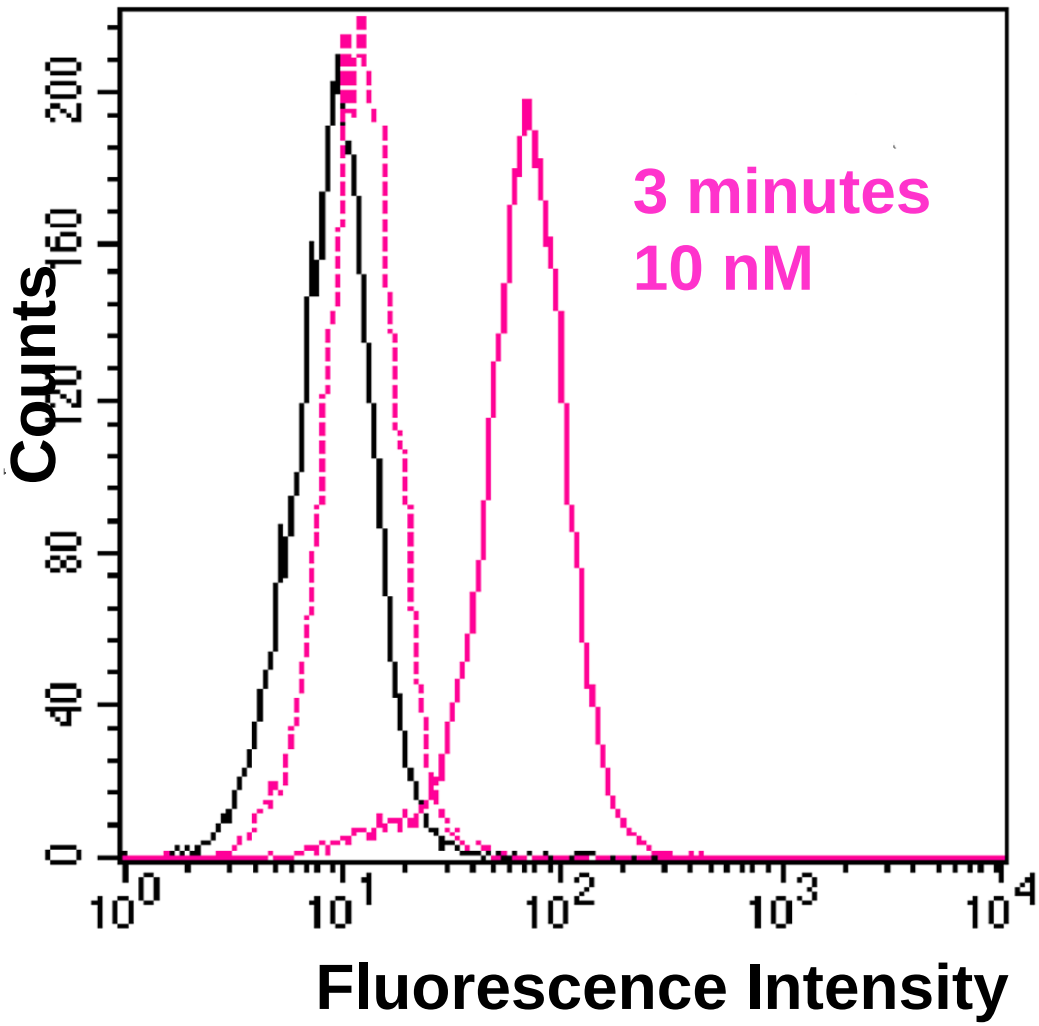
Uptake of Acetamide, Hydroxyl and Carboxyl-Surfaced Dendrimers

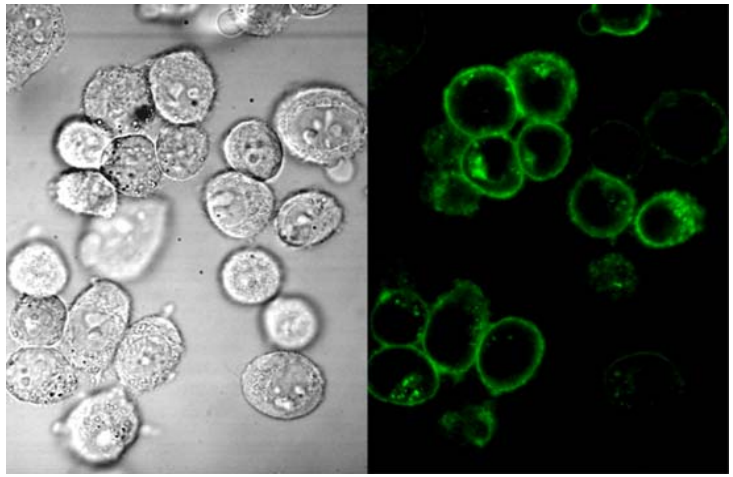




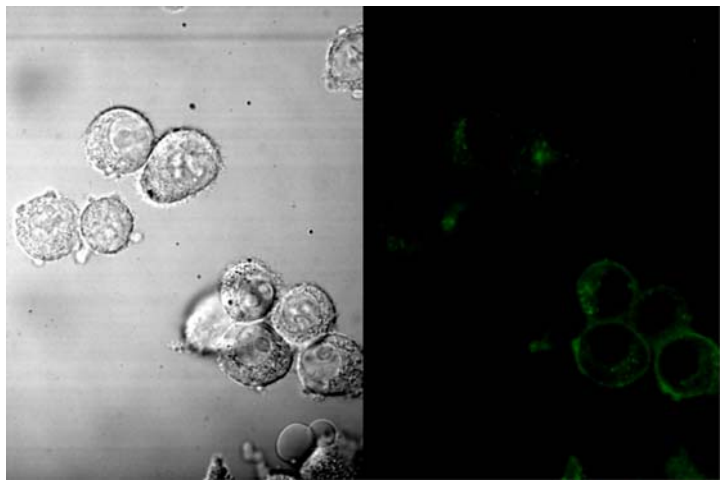


G5-FITC-Folate Acetamide Binding and Uptake in KB Cells





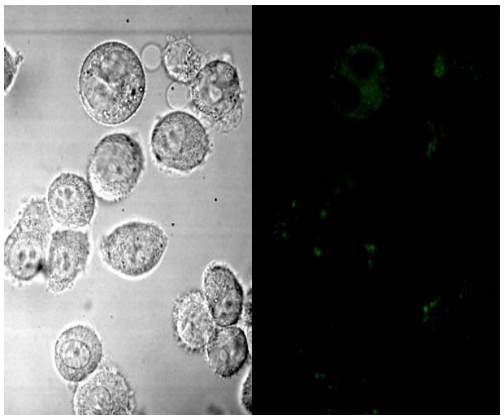
G5-FITC-Folate Acetamide (10 nM)



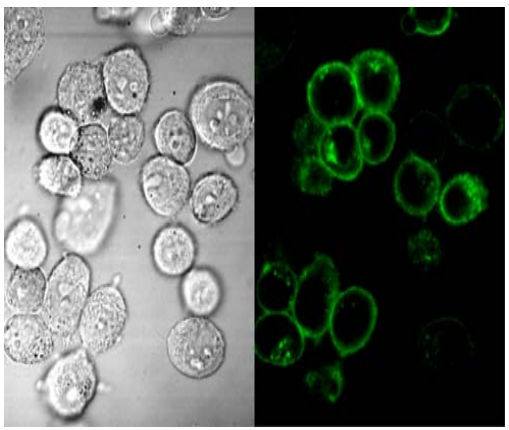
Antagonism with Free Folic Acid

Time Course of Binding and Uptake (KB Cells)

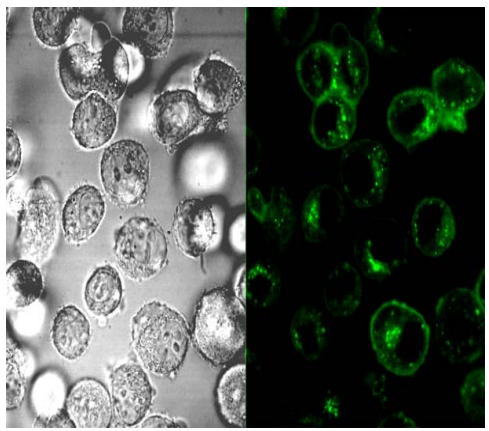
G5-FITC Acetamide (no folate)



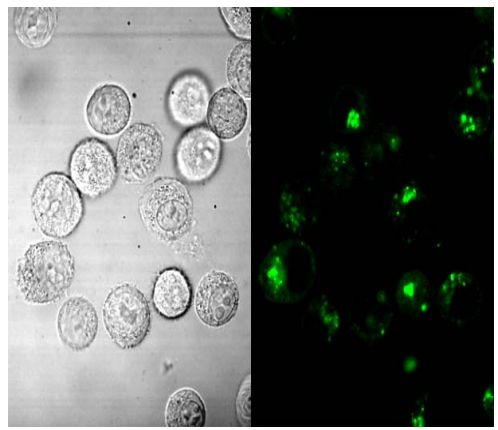
G5-FITC-Folate Acetamide



30 min

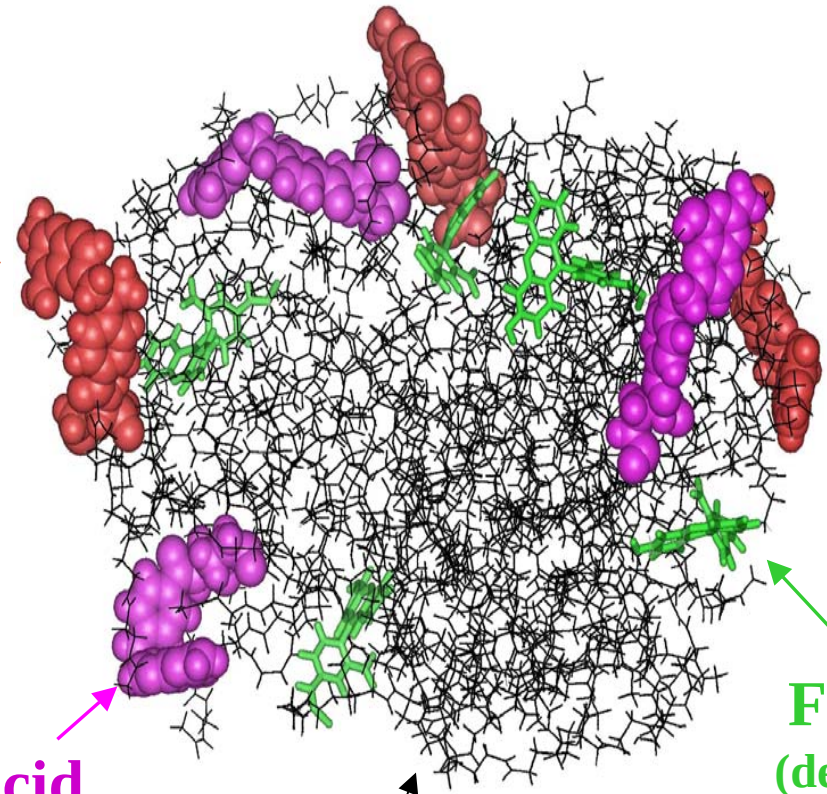


6 hr



24 hr

Computer Model of a Tri-functional Dendrimer



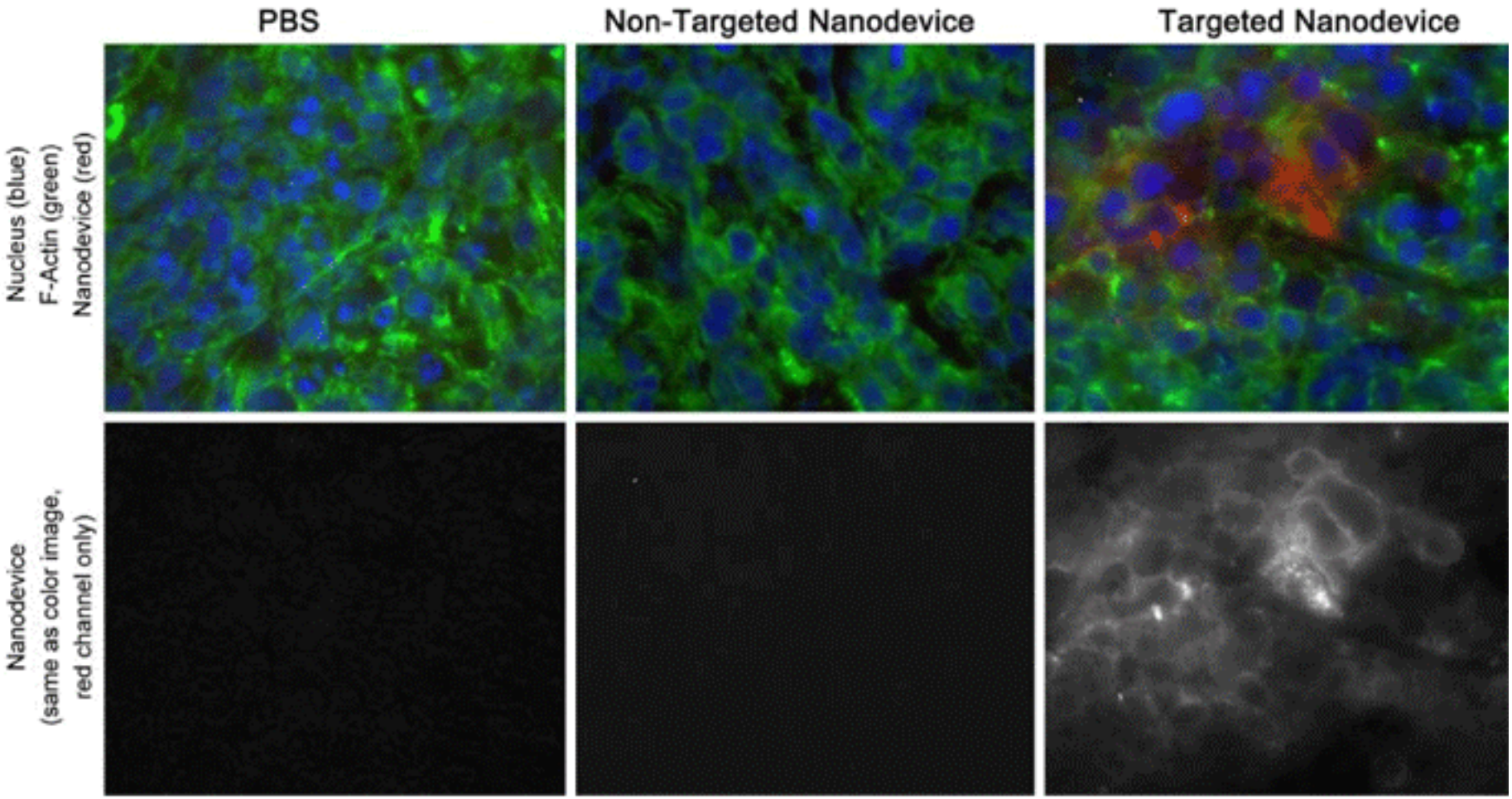
Methotrexate
(ester-linked therapeutic agent)

Folic acid
(amide-linked targeting agent)

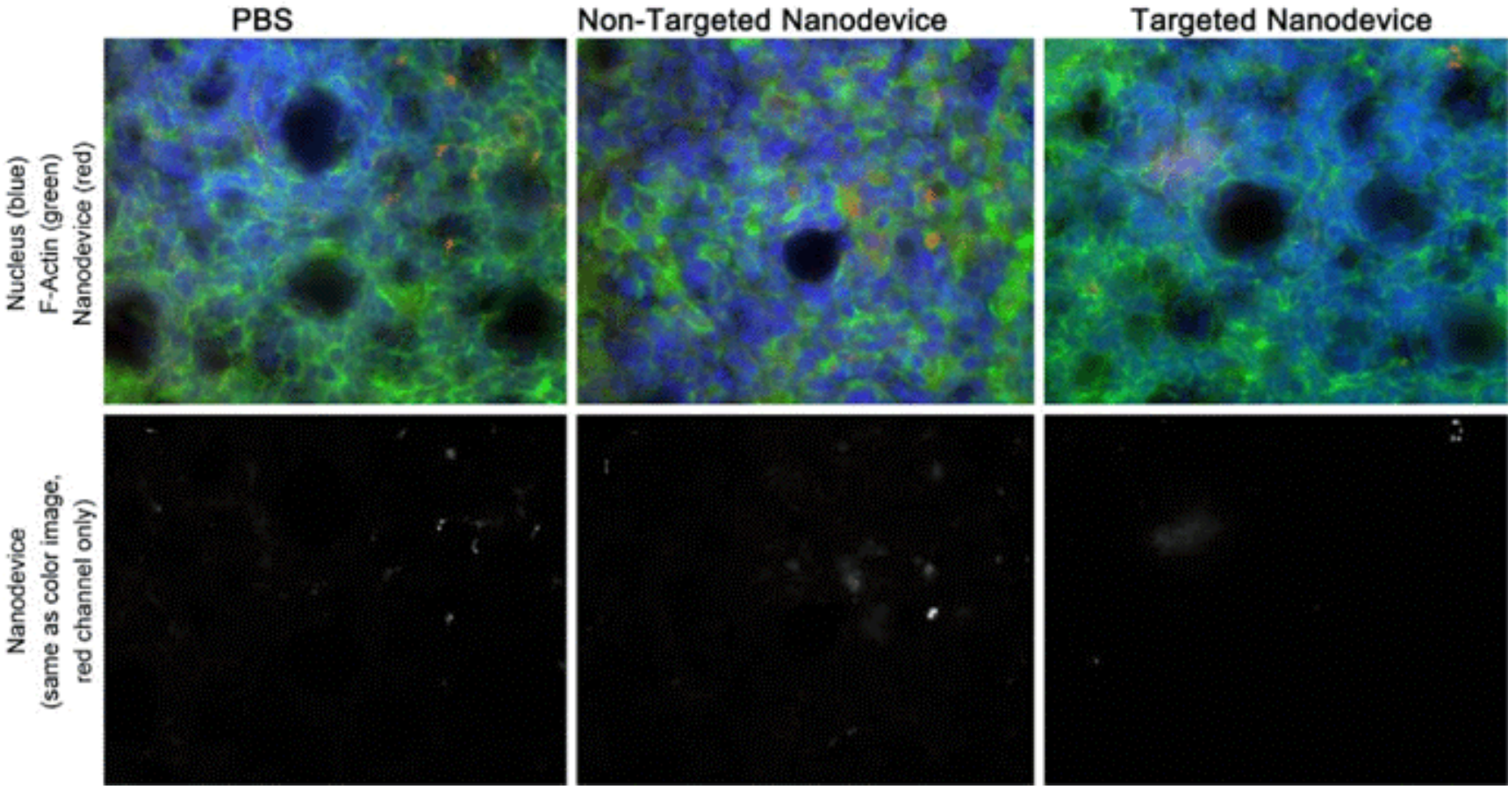
G5-polyamidoamine
(dendrimer platform)

Fluorescein
(detecting agent)

Images of Tumor Samples

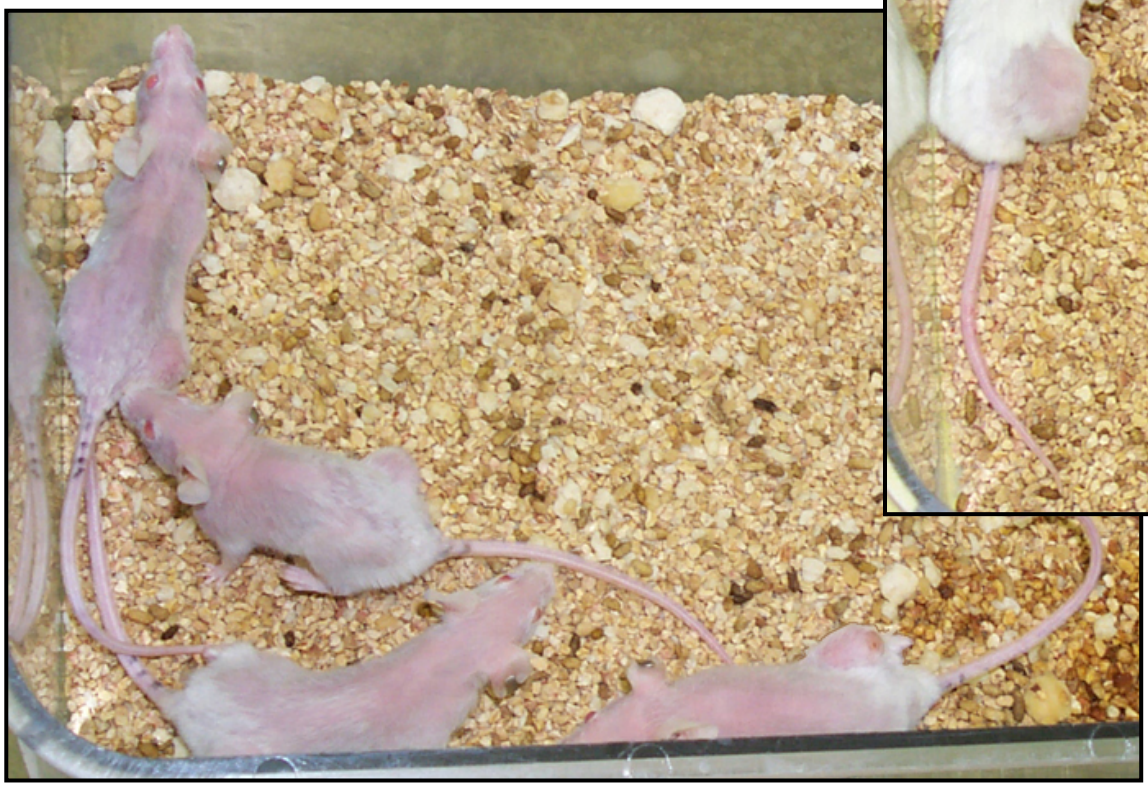


Images of Spleen Samples



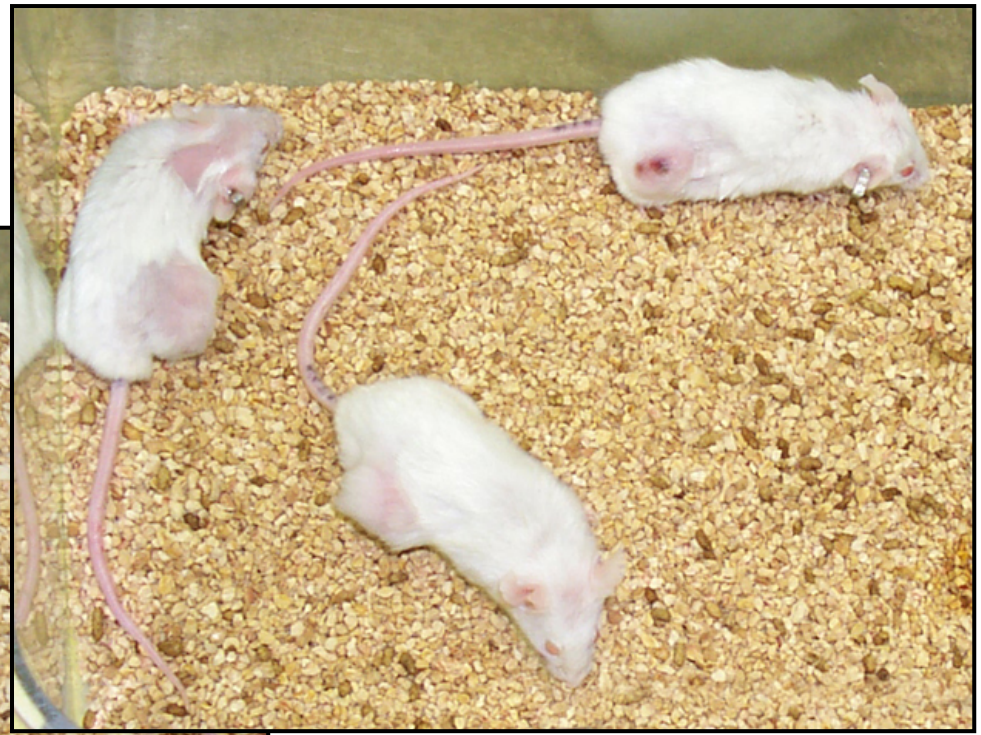
Free MTX

30 mg/kg total



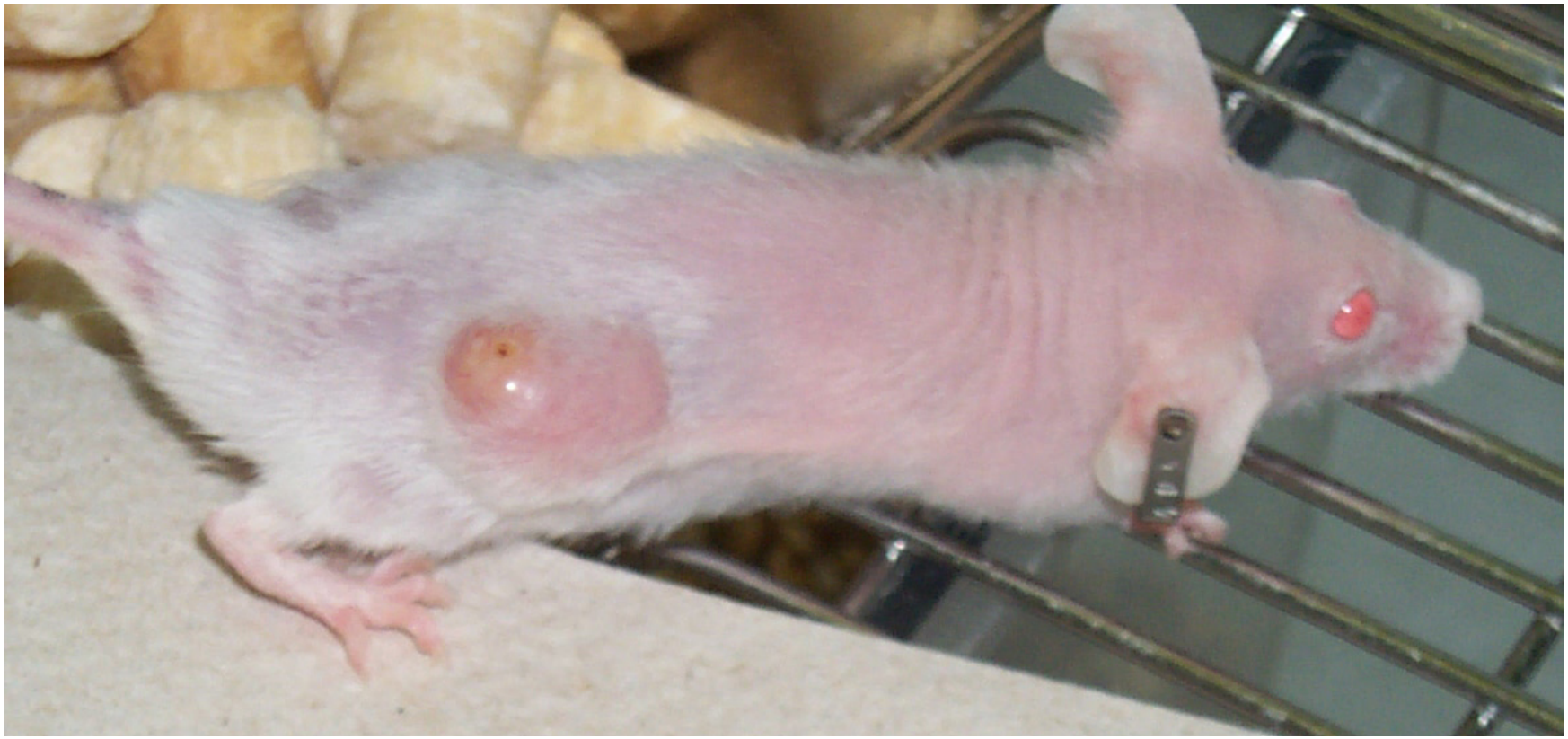
Nanodevice

3 mg/kg total MTX



Free MTX

30 mg/kg total



Note the systemic toxicity and lack of tumor necrosis

Nanodevice Causes Tumor Necrosis

also note the lack of systemic toxicity

NanoCure ™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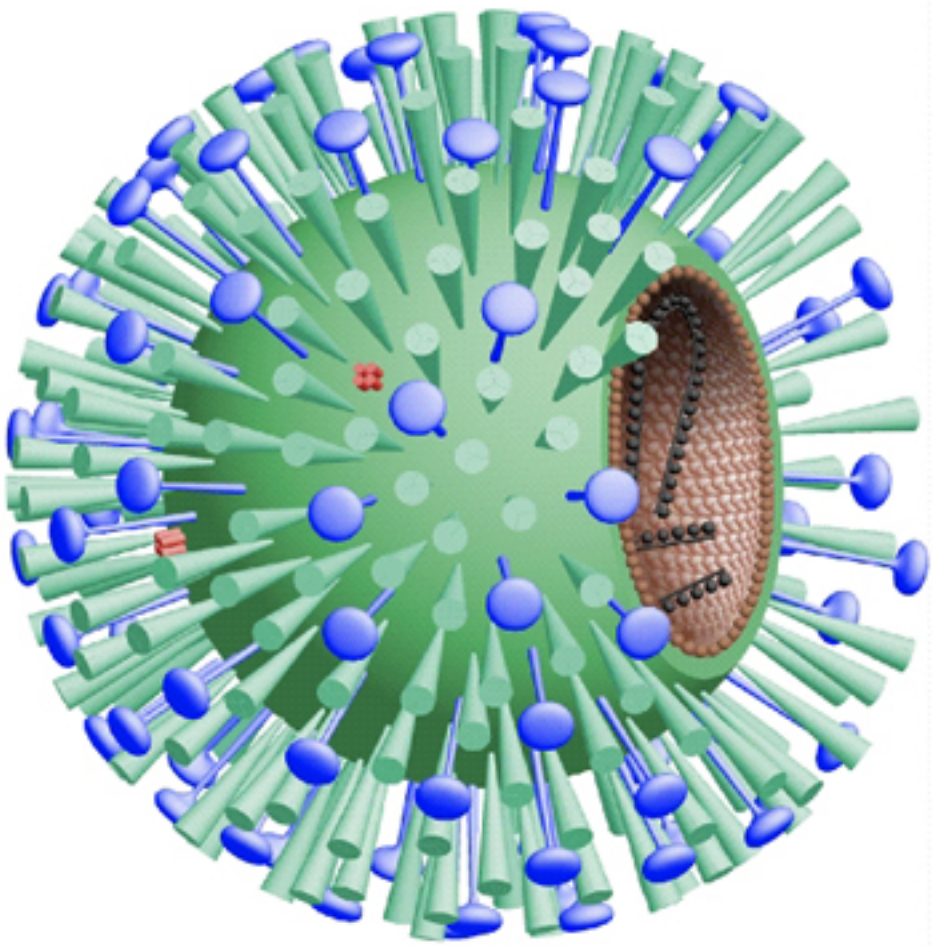
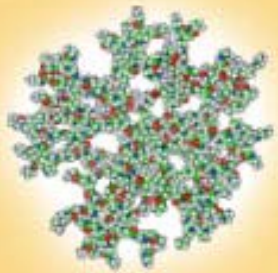


red: M2 protein
green: Haemagglutinin
blue: Neuraminidase
inside: viral RNA

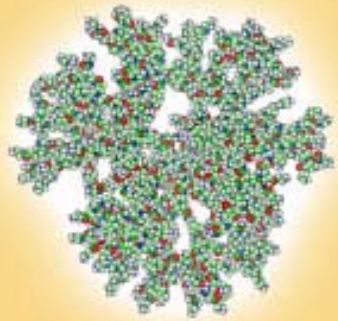
Dendrimer Size Comparison

G3 Dendrimer

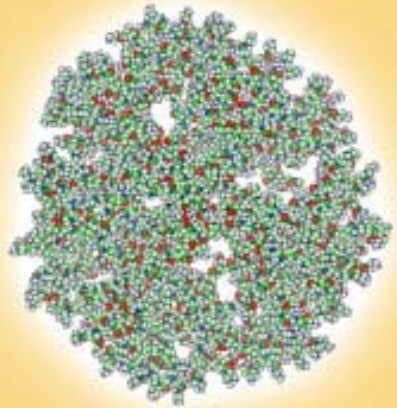
G4 Dendrimer



G5 Dendrimer



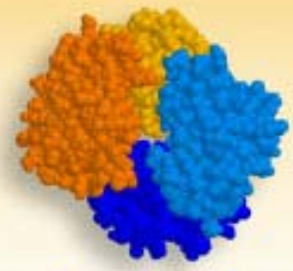
G6 Dendrimer



G7 Dendrimer

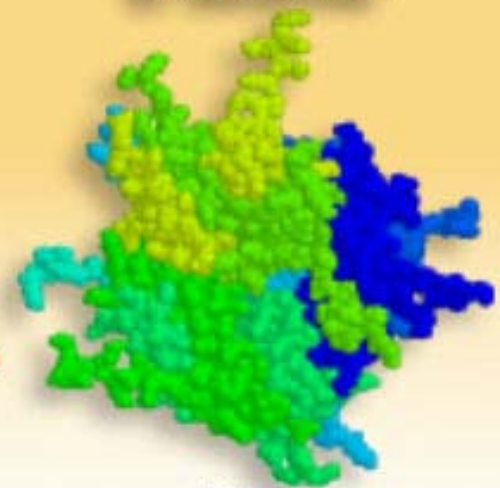
Insulin

Cytochrome C



Hemoglobin

Transthyretin



Histone

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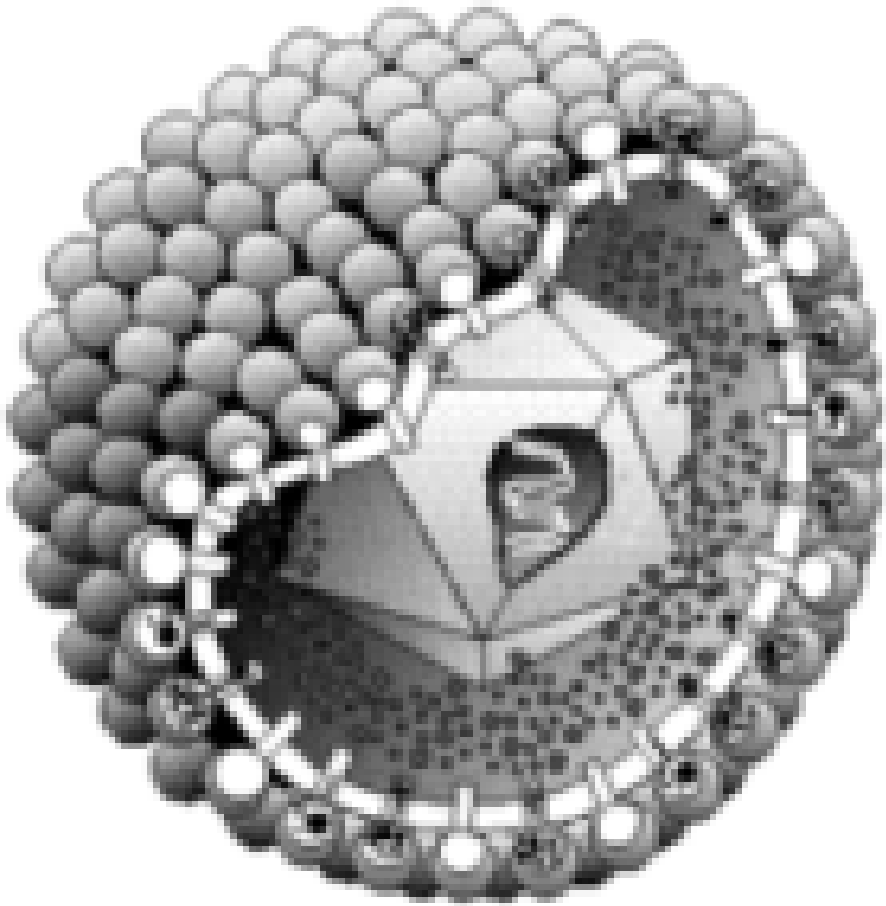
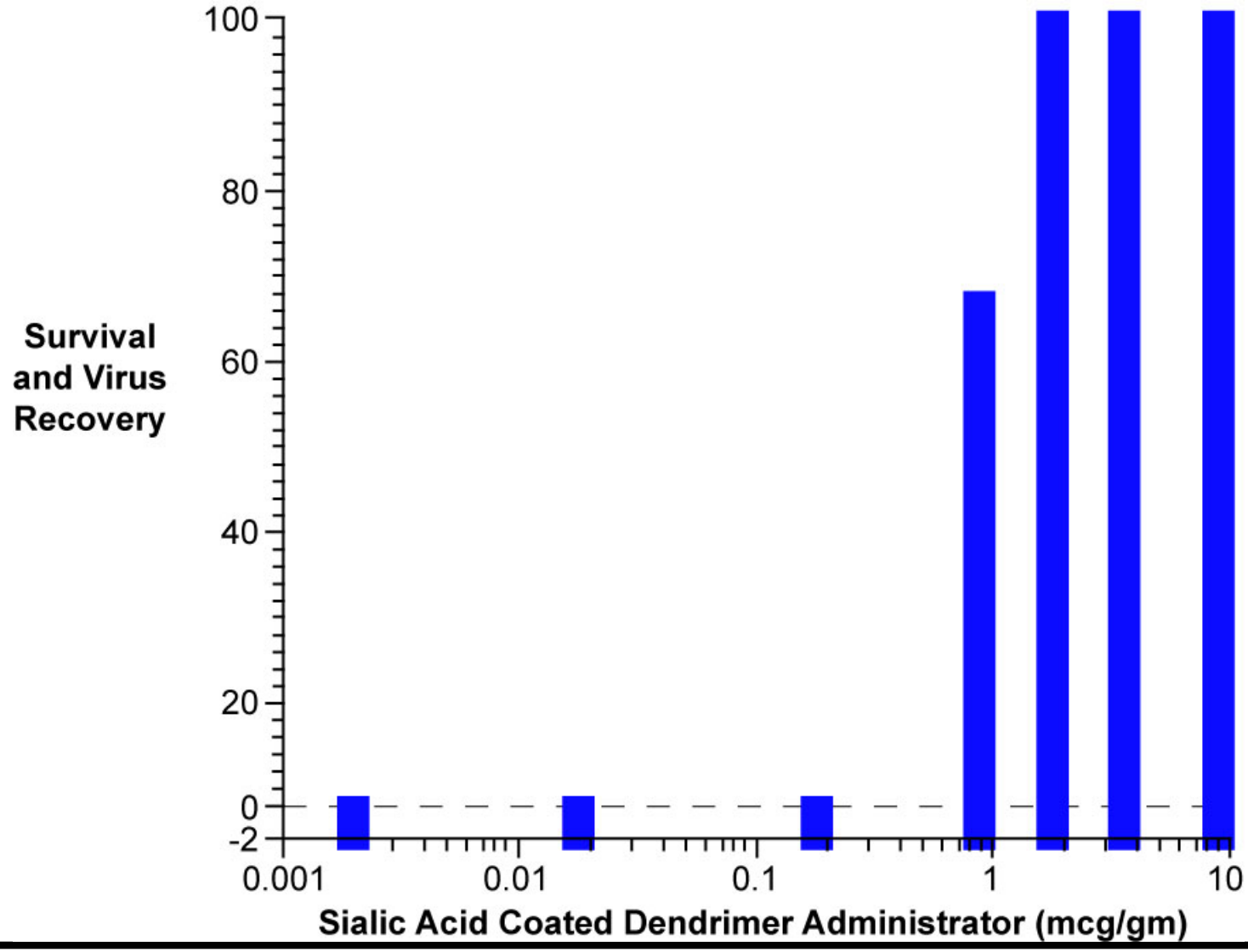
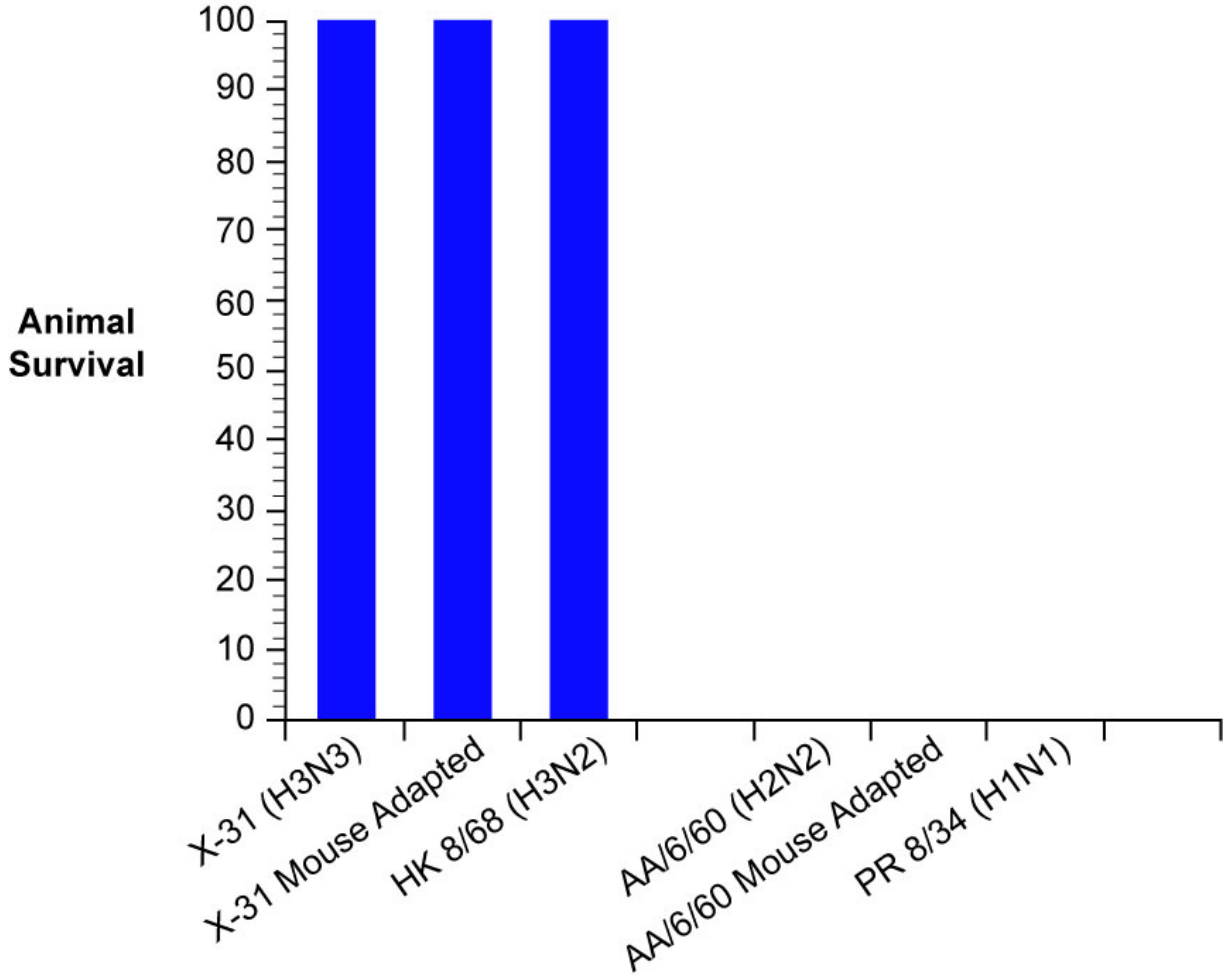
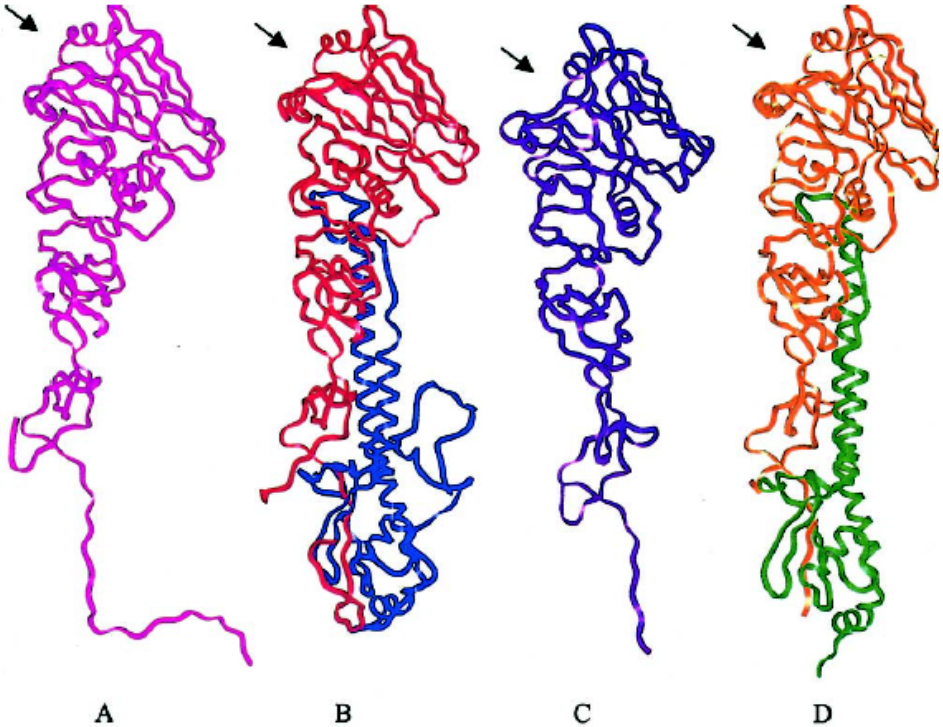


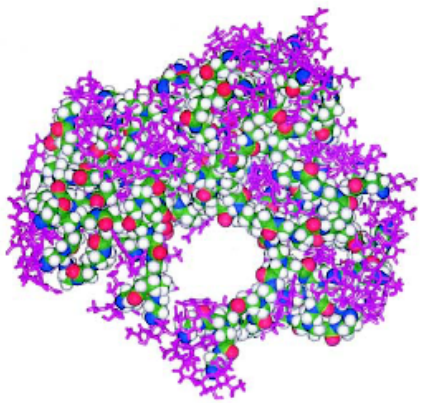
Survival of Mice Pretreated with Dendrimer/Sialic Acid Decoys

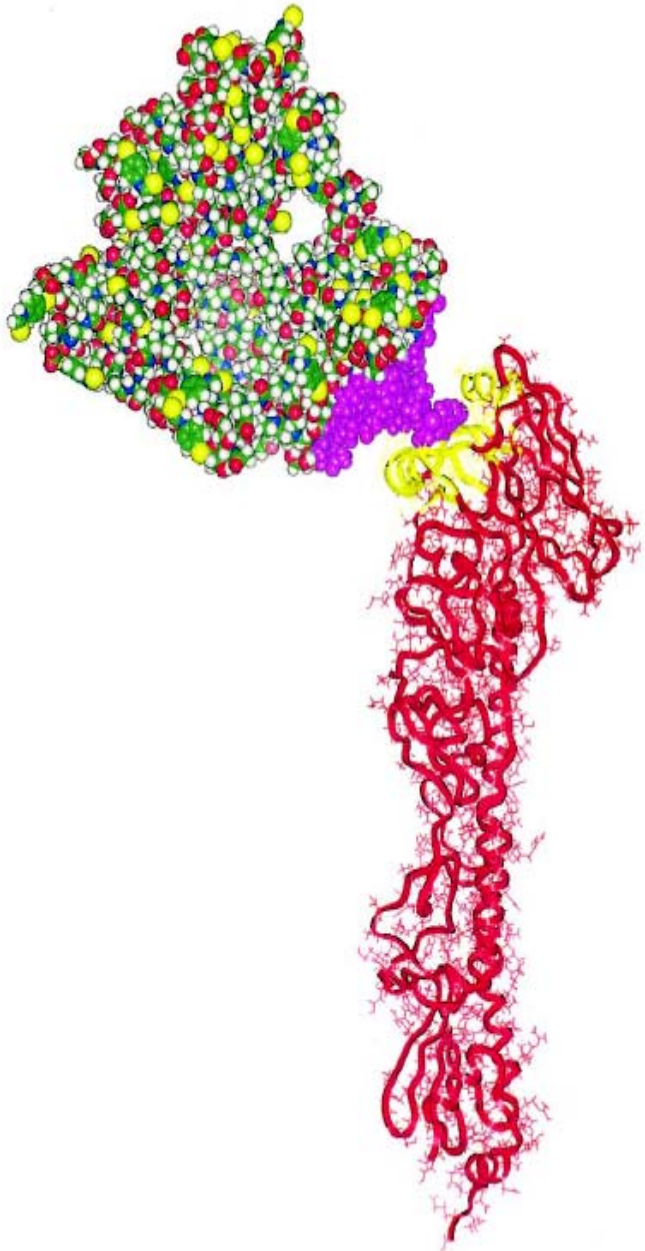


HA Inhibition Using Sialic Acid or Dendrimer/SA Decoys




A
B
C
D


E



Future Potential for NanoMedicine”

- Multifunctional “Smart” Therapeutic
  - Drug/gene delivery with regulation
  - Imaging/Sensing/Response
- Molecular Surgery
- Remote Real-time Medical Monitoring
- Functional Augmentation; Energy, Memory, etc.
- Replacement Molecules
- Brain Monitoring

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