

NANOPARTICLES AND BLOOD COAGULATION

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Mimicking the
Intrinsic
Pathway with
Silica
Nanoparticles

THE BIG PICTURE

- Trauma injury accounts for 30% of all life years lost in the U.S.
- \$406 billion a year, including both health care costs and lost productivity
- Cause of Death:
 - #1 for age group 1-44, or 47% of all deaths in this age range
 - #3 as leading cause of death overall, across all age groups

THE BIG PICTURE

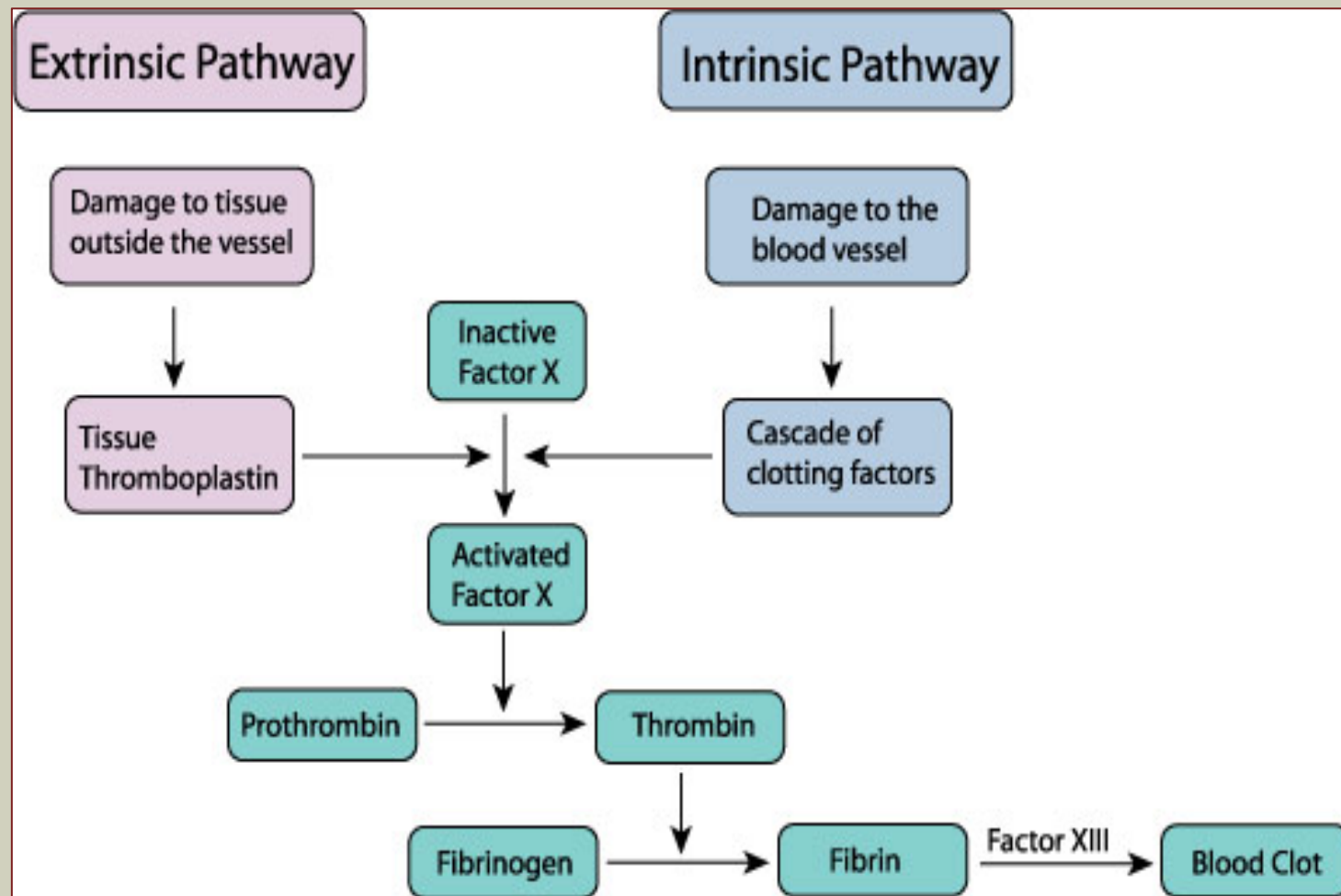


<http://www.z-medica.com/firstResponder/Home.aspx>



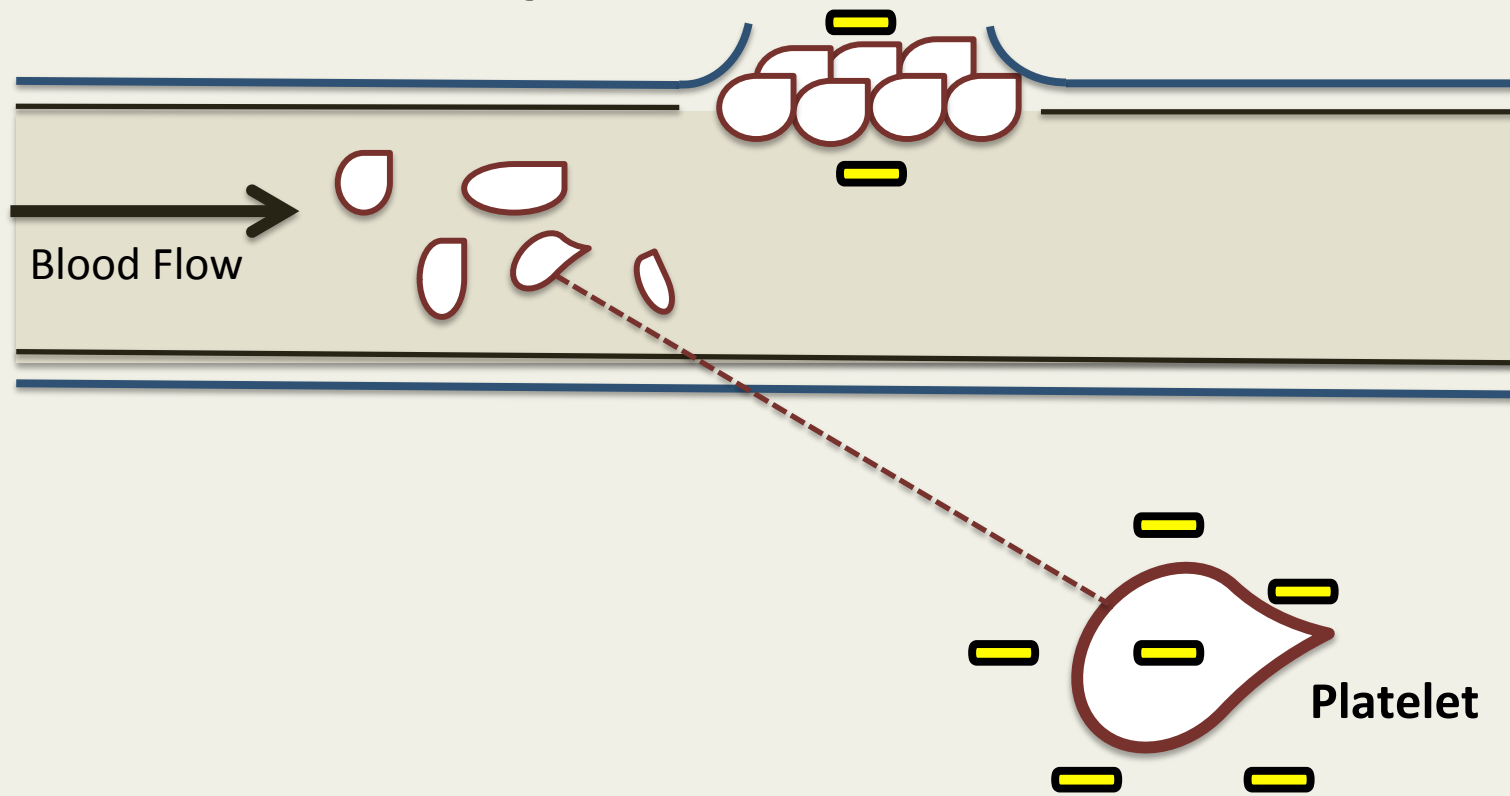
http://commons.wikimedia.org/wiki/File:Syringe_Glove_01.jpg

BLOOD COAGULATION 101

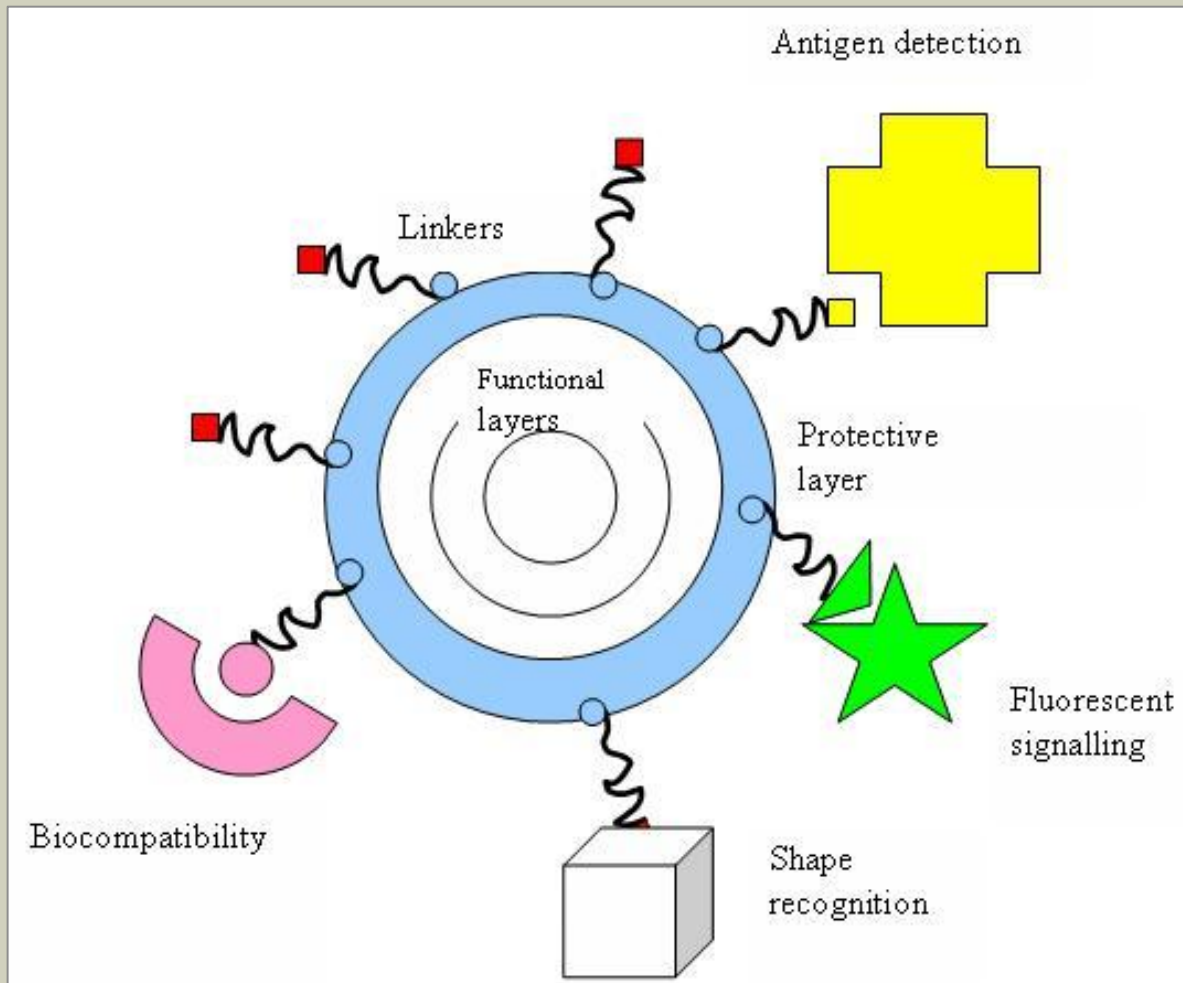


BLOOD COAGULATION 101

Intrinsic Pathway:



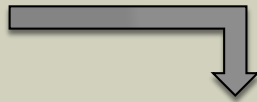
WHY NANOPARTICLES?



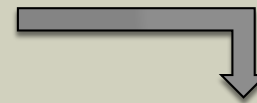
- Surface Area
- Potential for customization
- Biocompatible

HOW DO THEY WORK BEST?

1. Structure



2. Concentration



3. Mode of Delivery

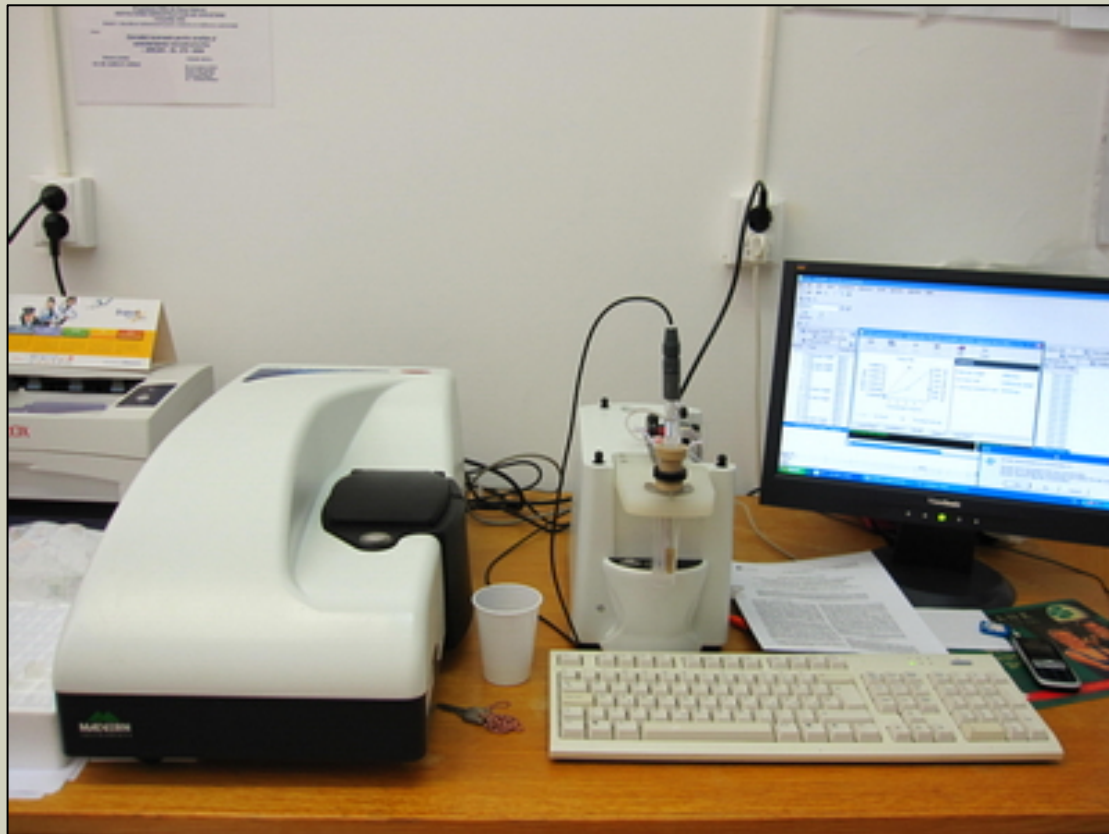


Clots Quickly, When and Where you Want it

METHODS: STRUCTURE

Size

Aggregation



The Zetasizer!!!!!!

METHODS: CONCENTRATION

Use Fluorescence to Quantify Real-Time Clotting through Thrombin

Concentration of SNP

.5 mg/mL

.25 mg/mL

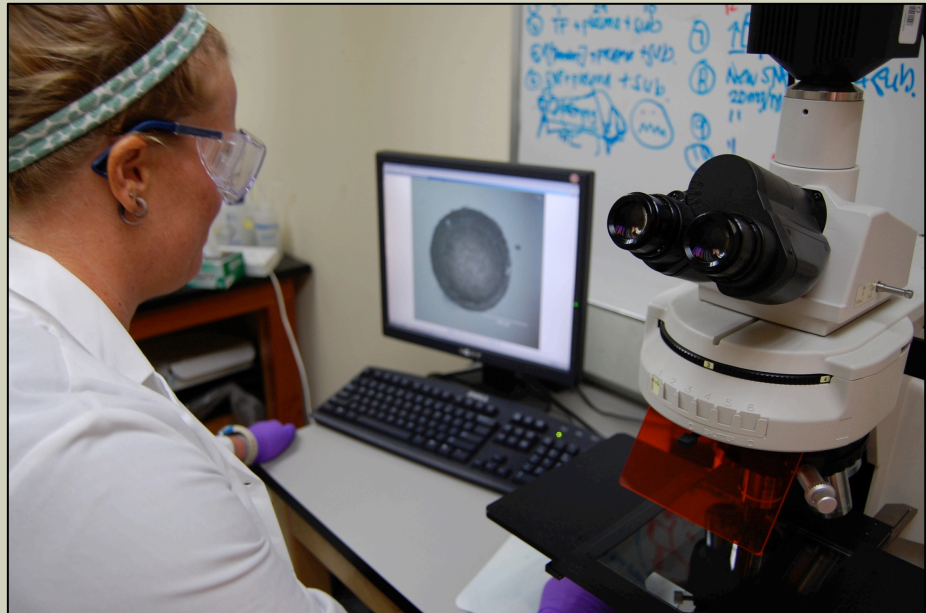
.125 mg/mL

.0625 mg/mL

.03125 mg/mL

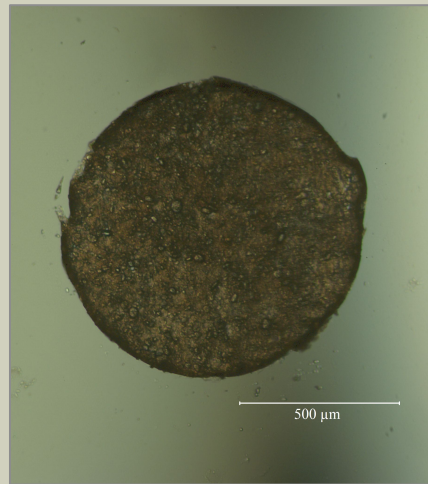
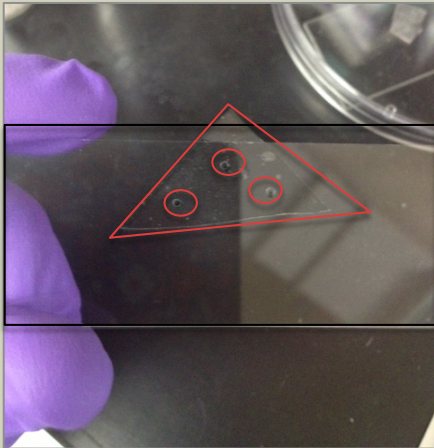
Before Clotting

After Clotting

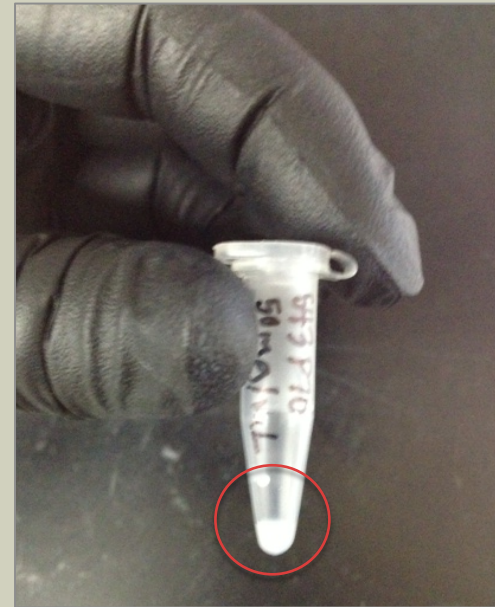


METHODS: MODE OF DELIVERY

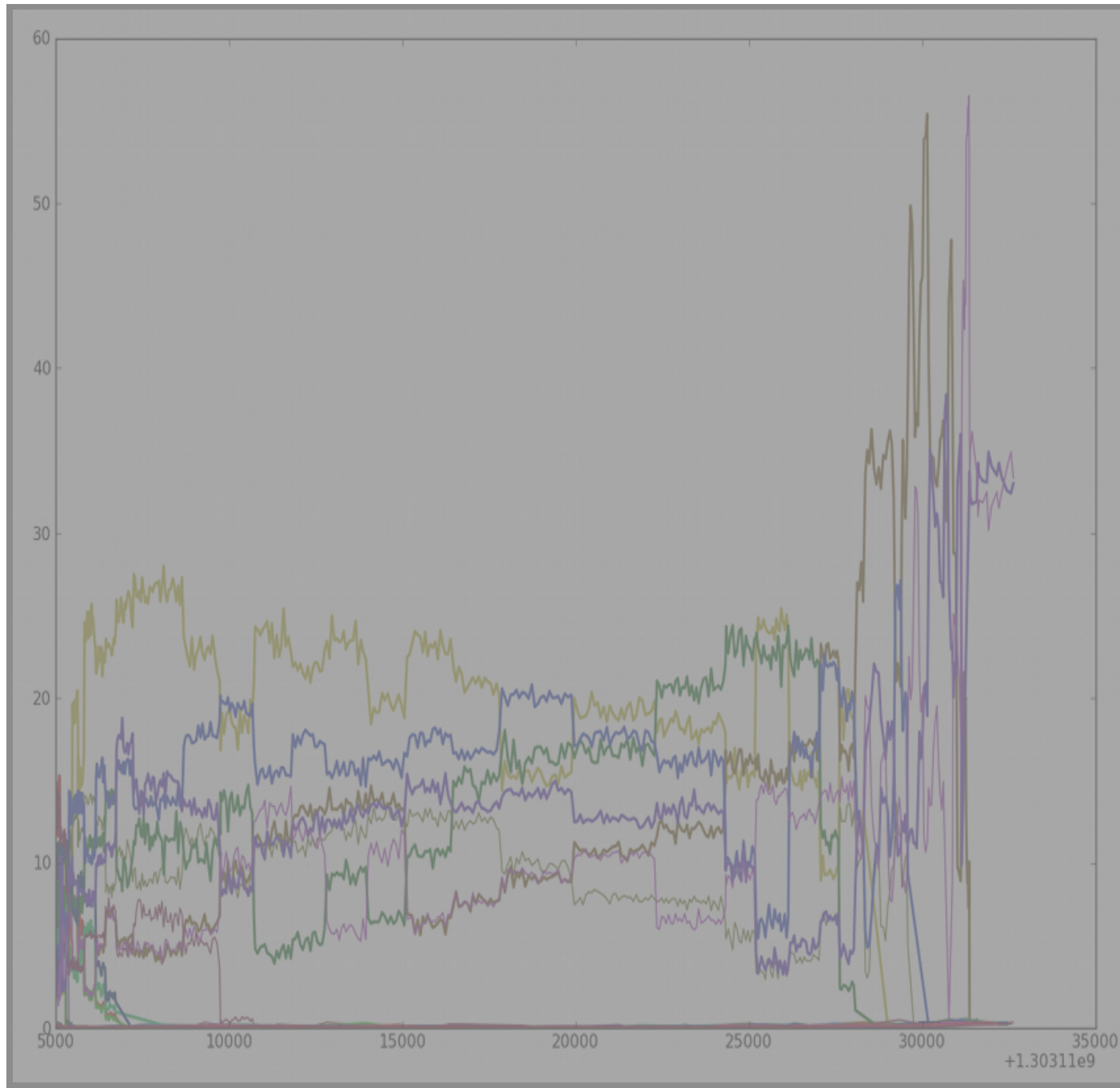
Patch



Solution



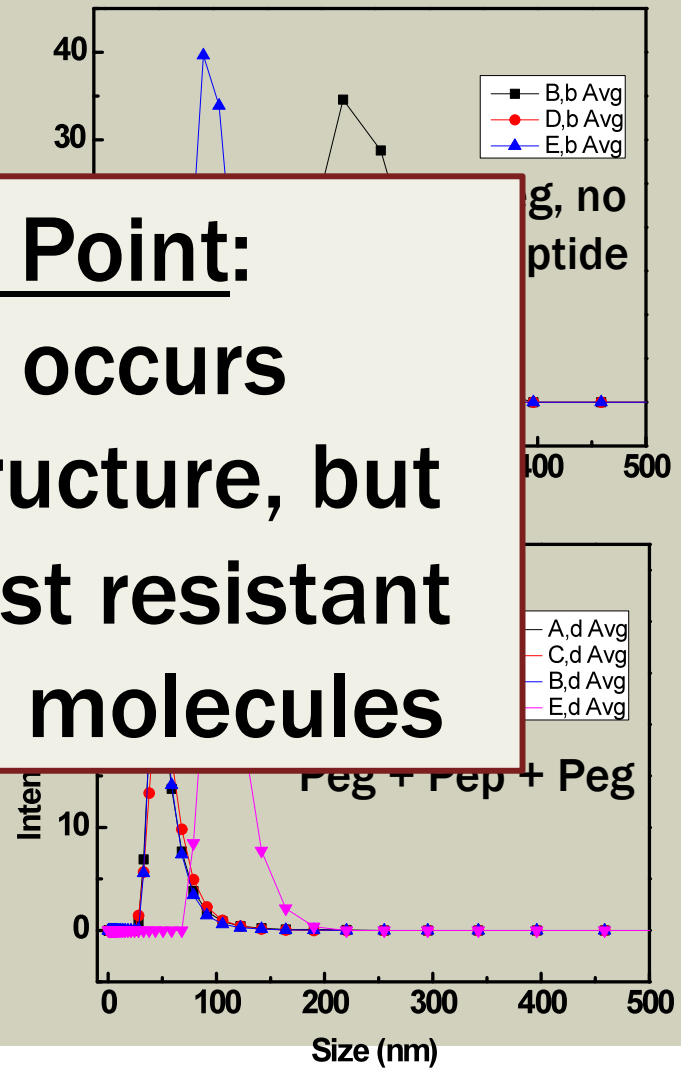
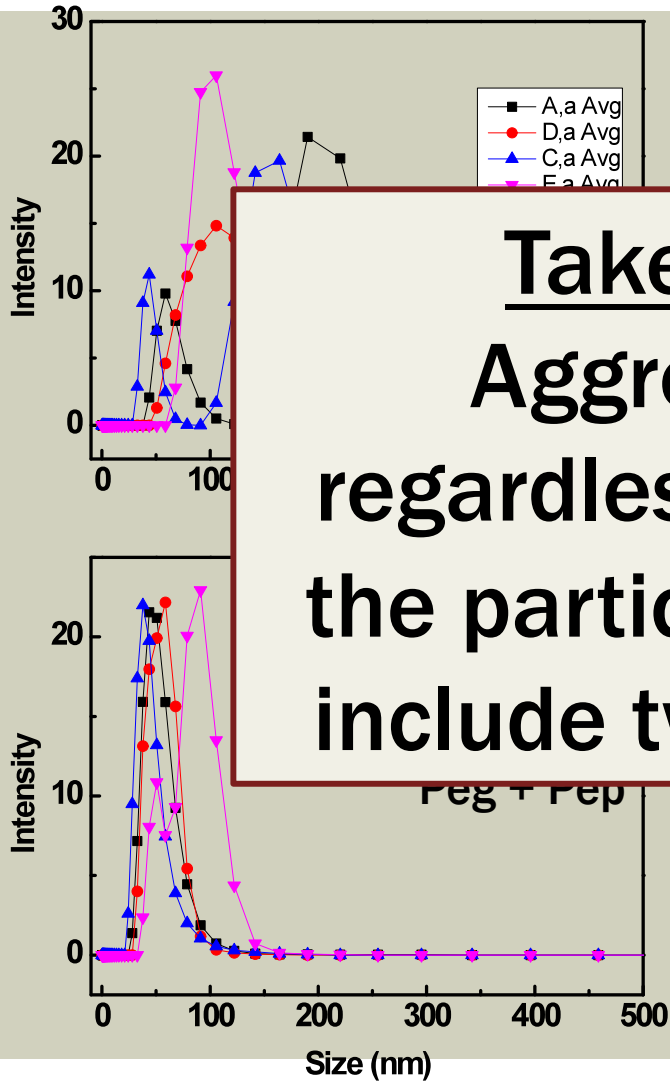
Is there a concentration threshold at which the patch clots, but the solution does not?



Results

What's the
Word?

RESULTS: STRUCTURE




Take Home Point:
Aggregation occurs
regardless of structure, but
the particles most resistant
include two PEG molecules

RESULTS: CONCENTRATION

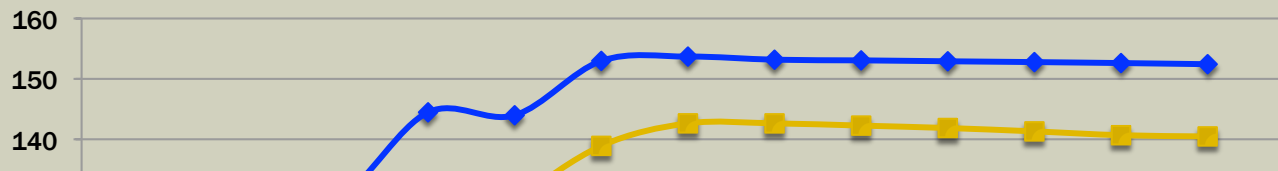
**.25 mg/mL SNP
Solution**

500 μm

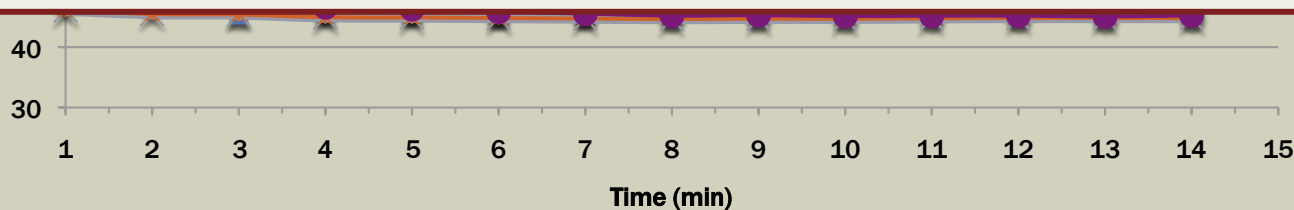


RESULTS: CONCENTRATION

Clotting Time in SNP Solution



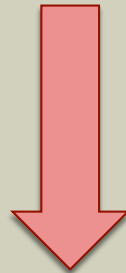
Take Home Point: The Threshold concentration of SNP in solution appears to be between .125mg/mL and .0625mg/mL



RESULTS: CONCENTRATION

.125 mg/mL solution = somewhat clotting

.0625 mg/mL solution = no clotting



Can I get a $<.125$ mg/mL patch to clot?

RESULTS: MODE OF DELIVERY

(To Patch or not to Patch)

What I see:



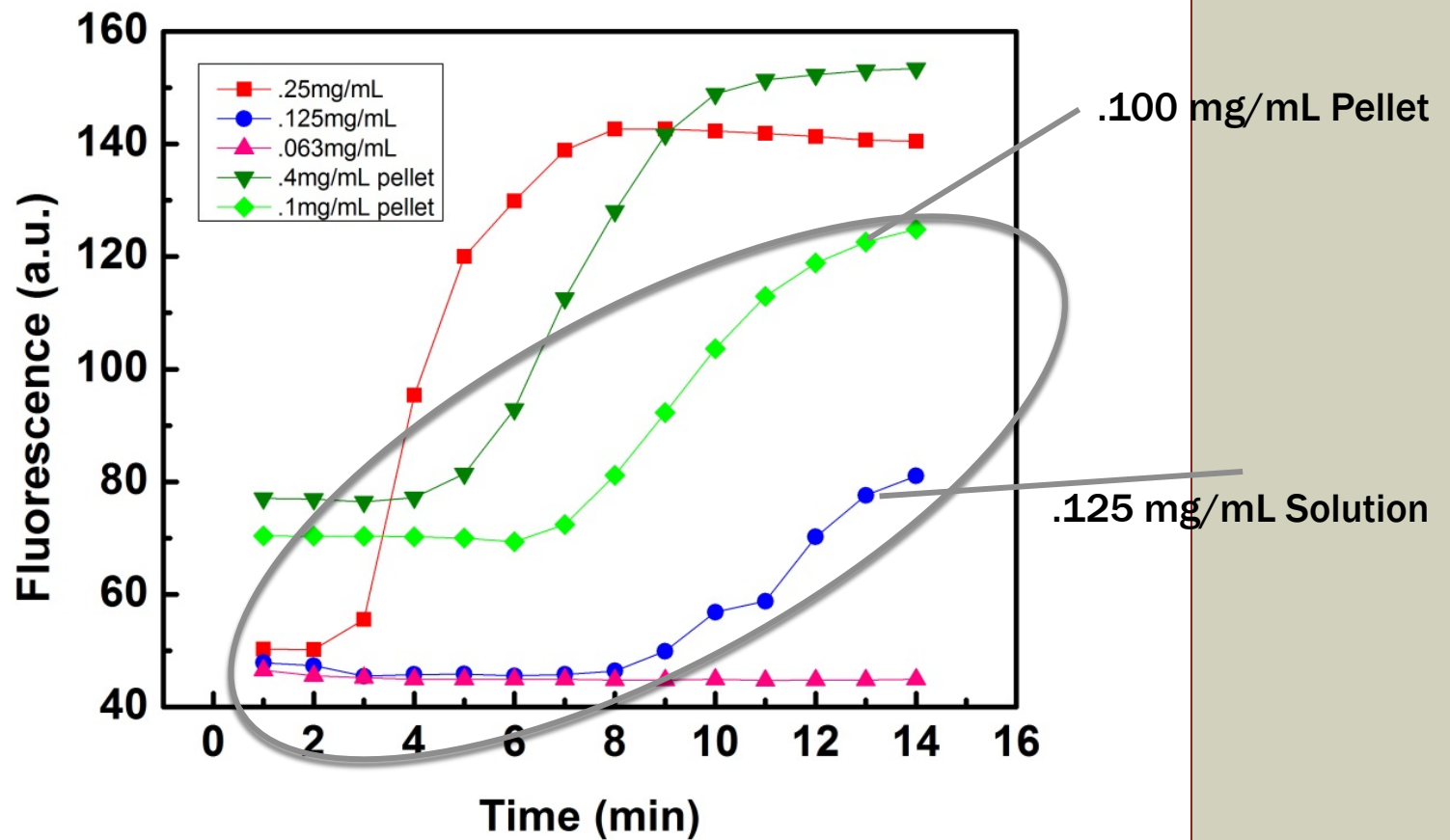
Maximum Final Concentration: 1 mg/mL
(Clotting at 10 min with .125 mg/mL solutions)

No Fluorescence seen

Possible Problems:

1. Evaporation of Plasma
2. Low Local Concentrations of SNP
3. Upper SNP threshold
4. Lower Surface Area
5. Low volumes of Factors

RESULTS: MODE OF DELIVERY



Graph by Tracy Chuong

RESULTS: MODE OF DELIVERY



Thromboelastography (TEG)

SNP in Solution: Clots around 2 min

SNP Patch: Clots around 4 min

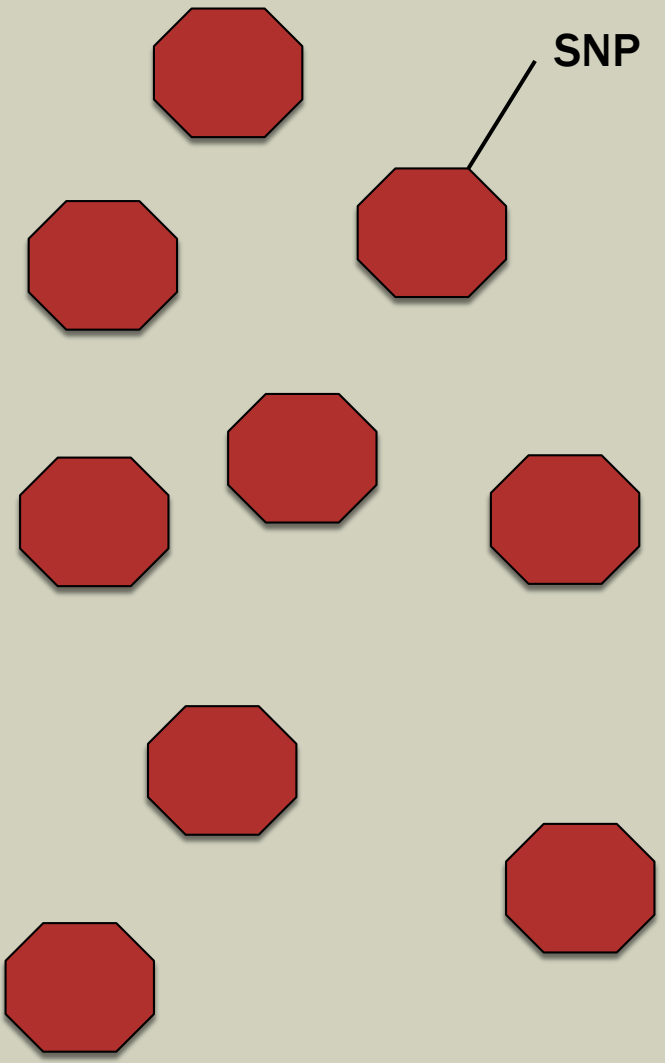


The plasma is clotting.

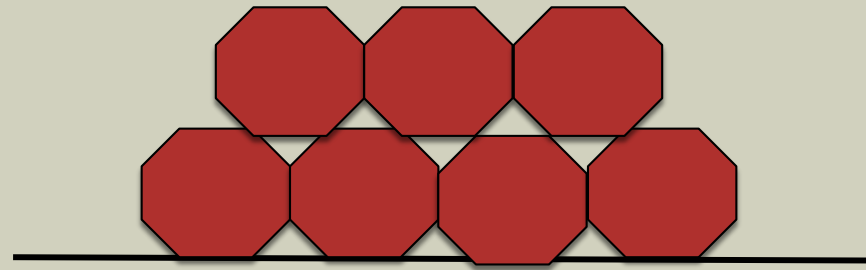
CONCLUSIONS:

1. Perhaps there is an upper threshold above .5mg/mL SNP
2. Detection Method may not be sensitive enough to respond to volume of biochemical factors produced (ex. Thrombin)
3. Surface Area may be limited by “patching” method, causing it to be an ineffective model.
4. Clotting DOES occur and can be activated by SNP patch, however we have been unable to quantify.

In Solution:



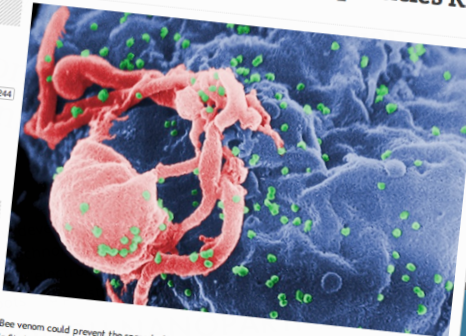
In Patch:



CLASSROOM CONNECTIONS

Bee Venom-Loaded Nanoparticles Kill HIV

MAR 9, 2013 02:05 PM ET // BY JESSE EMSPAK



Bee venom could prevent the spread of HIV. Researchers at the Washington University School of Medicine in St. Louis found that the toxin in bee venom, called melittin, puts holes in the protective protein coating that surrounds viruses and bacteria, killing them without harming healthy human cells. The finding could lead to the development of a vaginal gel that's easier for some women to use than trying to convince their partner to wear a condom. It could also help a person who is HIV positive conceive a child without spreading the virus to the fetus.

SNAP A PHOTO OF DIET DEW WITH BBQ!

UPLOAD HERE >

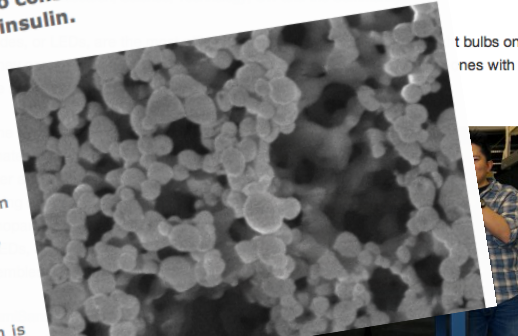
DNews: Men Vs. Women: Who Parts More?

Injectable Nanoparticles may Simplify Treatment for Type 1 Diabetes

Published on May 16, 2013 at 3:59 AM

Injectable nanoparticles developed at MIT may someday eliminate the need for patients with Type 1 diabetes to constantly monitor their blood-sugar levels and inject themselves with insulin.

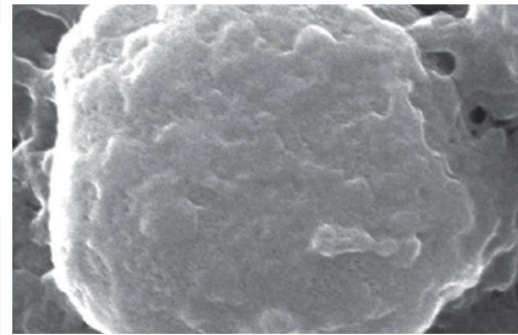
The nanoparticles were designed to sense glucose levels in the body and respond by secreting the appropriate amount of insulin, thereby replacing the function of pancreatic islet cells, which are destroyed in patients with Type 1 diabetes. Ultimately, this type of system could ensure that blood-sugar levels remain balanced and improve patients' quality of life, according to the researchers.



"Insulin really works, but the problem is people don't always get the right amount of it. With this system of extended..."

Excellent Idea of the Day: Sneaky Nanoparticles

DEC 17, 2012 03:00 AM ET // BY JESSE EMSPAK



Nanoparticles wrapped in cell membranes from white blood cells were ignored by the immune system in the experiment.

<p>Nanoparticles, bits of material smaller than cells, are a promising way to deliver drugs, but they have to get past the immune system fist.</p>

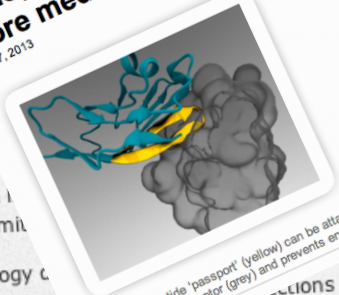
SNAP A PHOTO OF DIET DEW WITH BBQ!

UPLOAD HERE >

DNews: Men Vs. Women: Who Parts More?

Nanoparticles with protein coating help deliver more medication to tumors

Jul 17, 2013



A minimal peptide 'passport' (yellow) can be attached to therapeutic nanoparticles so that it binds to an immune cell receptor (grey) and prevents engagement. Credit: Diego Pantano

CHICAGO --- In a breakthrough for nanotechnology, researchers at Northwestern University have developed a new type of nanoparticle that could be the perfect vehicle to stealthily attack on myelin and halt a disease. Northwestern Medicine researchers have found that the new nanotechnology also could help with diabetes, food allergies and asthma.

In MS, the immune system attacks the brain and optic nerve. When the immune system attacks, it causes symptoms that range from mild numbness to paralysis. The Northwestern nanotechnology could help with the relapsing remitting form of MS, which make patients more susceptible to the disease. The nanoparticles are attached to myelin sheath, making it appear as an alien invader and halts its attack on the nerve.

"This is a highly significant breakthrough in translational immunotherapy," said Stephen Miller, a professor of immunology at Northwestern University.

A BIG THANKS TO...



Tracy Chuong

Frank Kinnaman

Damien Kudela

Galen Stucky

MRL RET Program

