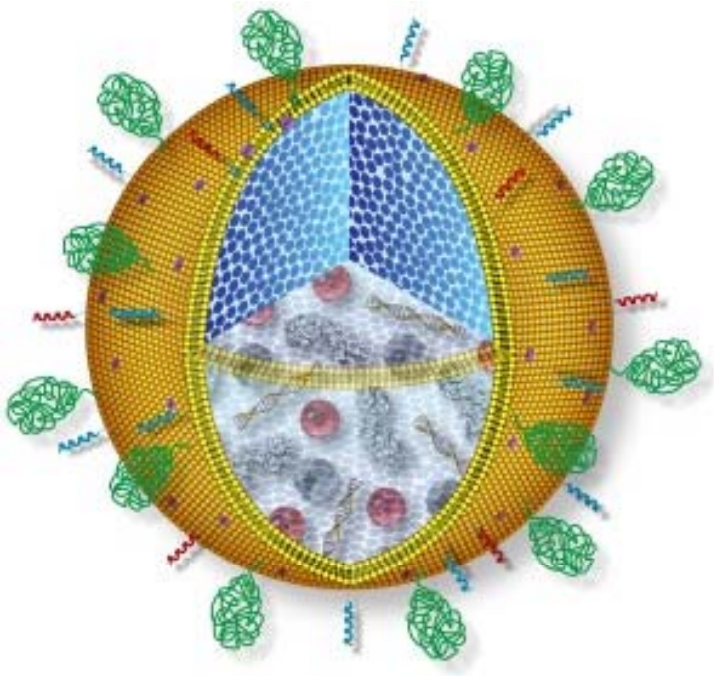
Nanoparticles as Drug-Delivery Systems

Melissa Herman
Infectious Minds
Jan 19th 2012

Advantages in drug delivery

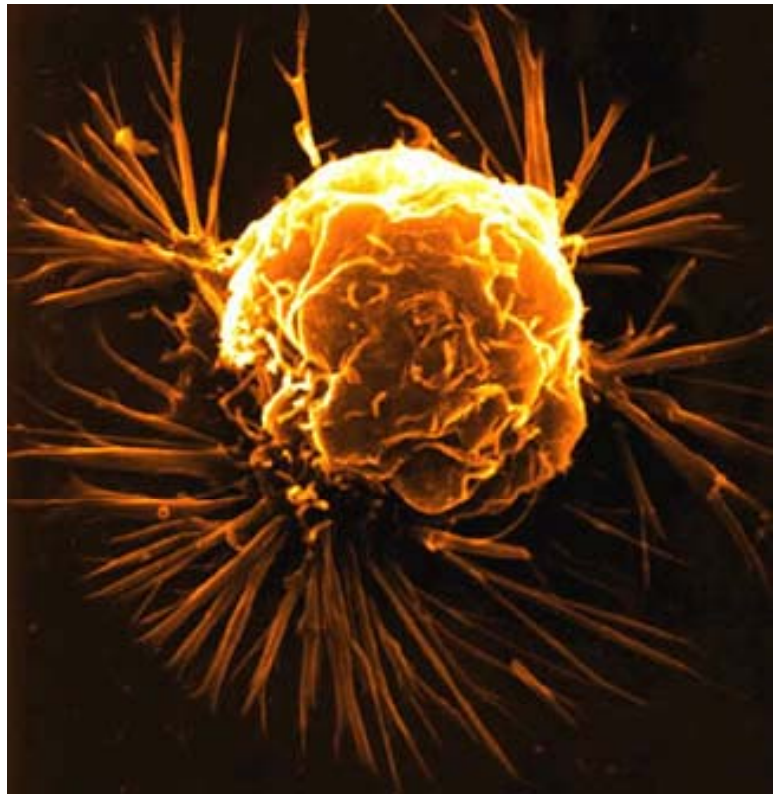
- Small: allows uptake into cells and areas that are not easily accessible by larger particles
- Can be manufactured to avoid detection by the immune system
  - Prolongs time in the body, allowing a decrease in dosage
- Better precision: can specifically target cell types
  - Improves treatment outcome, decreases toxic side effects
- Encapsulation of drugs provides better protection



http://www.polymersolutions.com/blog/wp-content/uploads/2011/04/041911_nanoparticle1-300x281.jpg

Cancer

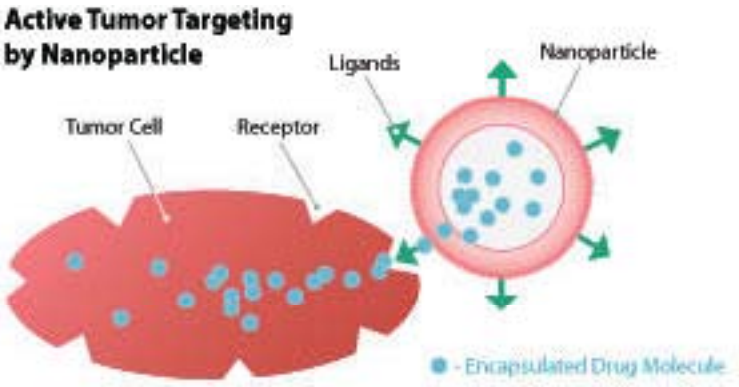
- Many current issues with cancer therapies:
  - Tumors present in vital organs or inaccessible areas
  - Low target specificity, leaving possibility for major side effects and toxicity
- Nanoparticles can target tumor cells specifically
  - Allows access into otherwise difficult to operate areas
  - Lower side effects or toxicity to surrounding tissue



http://www.topnews.in/health/scientists-reveal-cancers-hiding-spots-28978

Target Specificity: Cancer

- Nanoparticles are coated with ligands specific to tumor cells
- Contact with tumor cells with proper receptors leads to binding, activation, and release of the drug
- This method much more efficient- more drug reaches the tumor, and less surrounding tissue is negatively affected
- Example: Folate receptors overexpressed on many carcinomas



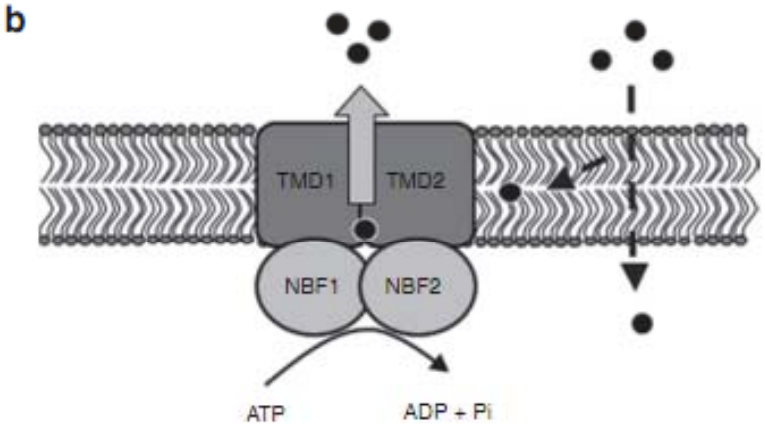
Irvine et al Nature Materials 10 342-243, 2011

Cancer: Drug resistance

- Enduring several rounds of chemo can result in MDR
  - Many MDR mechanisms; efflux pumps are one
  - Use "ABC" transporters (ATP binding cassette), using ATP as an energy source to transport drugs out of the cancer cells

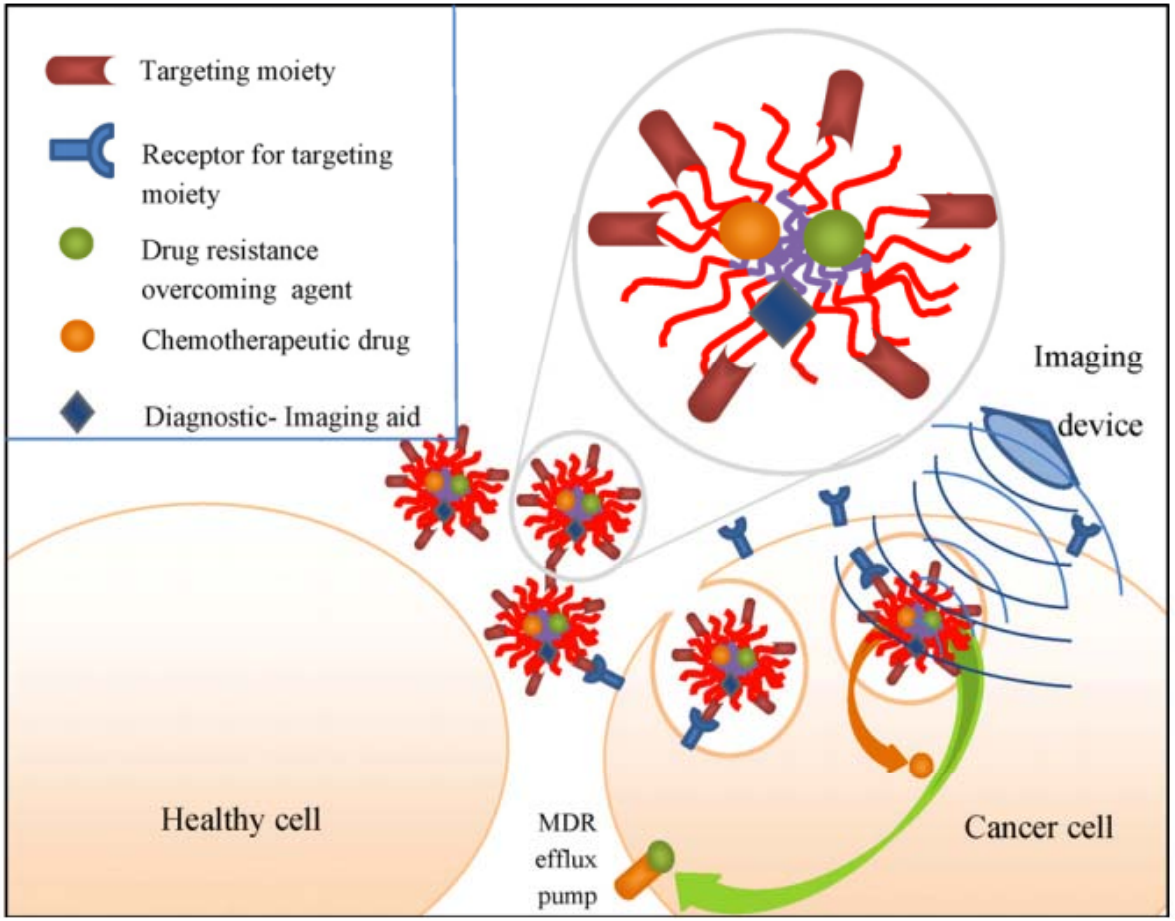
- Nanoparticles can package chemosensitizers which can block the efflux pumps

- Greatly reduces the chances of MDR



Moitra et al, Clin. Pharm. Ther. 2011. 89(4) 491-502

New Theory: Ultimate Nanoparticle



Treating the Brain!

- Treating neurological diseases is often complicated due to difficulties of drugs crossing the BBB
  - BBB: composed of endothelial cells with tight junctions, nearly impermeable when in tact
  - Many drugs and proteins too large to cross it
- Specificity also tricky- lots to damage!

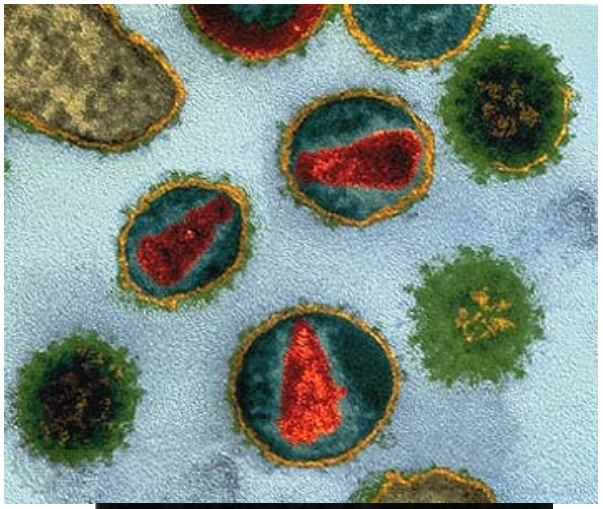
Nanoparticles and drug delivery to the brain

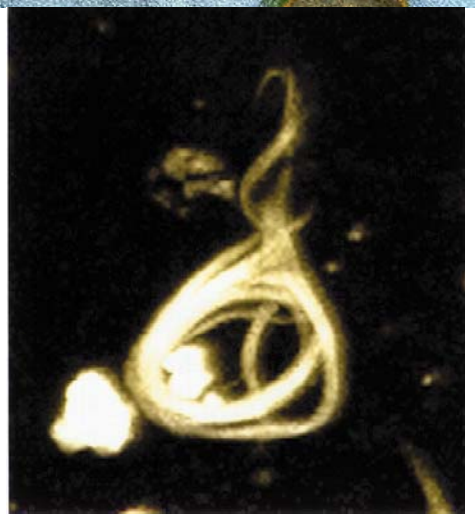
- Nanoparticles can be manufactured to interact well with the BBB endothelial cells
  - Can be made to bind to transporters or receptors at the BBB
  - Allows better transport across the BBB, and better delivery of drugs for neurological issues
- Applications in several CNS related disorders: Alzheimers, Parkinsons, strokes, brain tumors, HIV

http://www.materialsviews.com/details/news/1442719/Stain_Your_Brain_Nanoparticles_Enable_Brain_Surgery.html

Neurological disorders

- **HIV encephalitis:** Nanoparticles complexed to ARTs can increase the concentration of drugs in the brain 10 fold +
- **Alzheimers:** Nanoparticles complexed to copper/zinc chelators used to cross BBB and break down amyloid plaques
- **Parkinsons:** Nanoparticles containing condensed DNA may help repair damaged neurons and restore production of dopamine
- **Ischemic stroke:** Nanoparticles can target blood clots and deliver plasminogen to break them down and improve blood flow

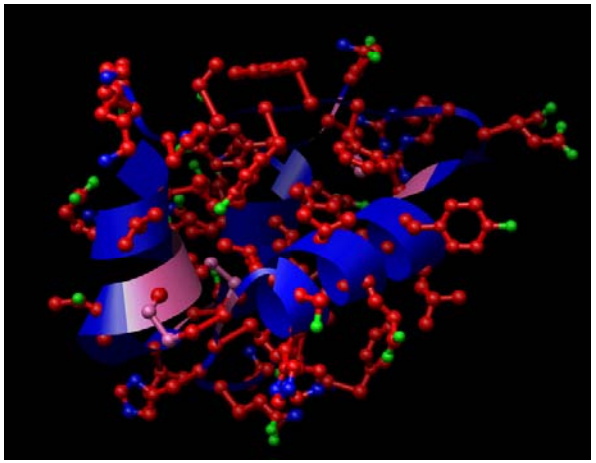




http://techfreep.com/aids-strain-fights-aids.htm

Insulin Delivery in Diabetes

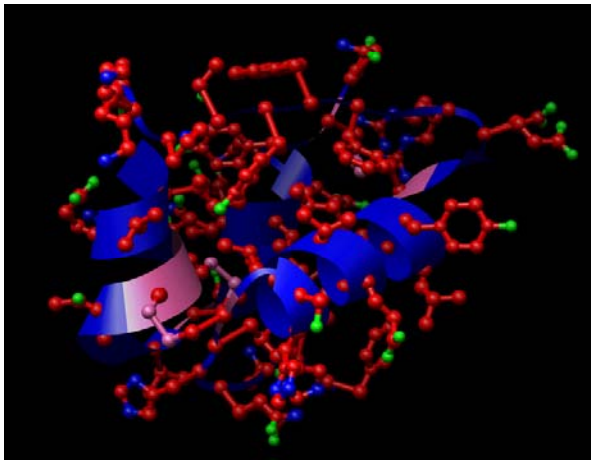
- Diabetes: not enough insulin produced, or it is not properly utilized
- Insulin injection primary treatment
  - Fraught with complications- low compliance, edema, hypoglycemia
- Research into a potential oral insulin delivery system thought to be very useful



http://upload.wikimedia.org/wikipedia/commons/d/d9/Insulin.jpg

Insulin Delivery in Diabetes

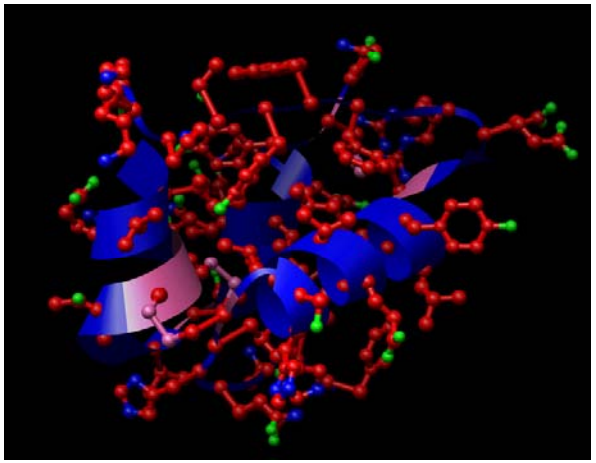
- Oral insulin delivery difficult due to several barriers
  - Physical: mucosal/fluid lining of the intestines
  - Enzymatic: enzymes in the stomach that break down proteins including insulin
  - Instability: insulin generally unstable in the GI tract due to variations in pH and enzymes
- Overall: little absorption, rendering oral insulin mostly useless



http://upload.wikimedia.org/wikipedia/commons/d/d9/Insulin.jpg

Nanoparticles: Oral insulin

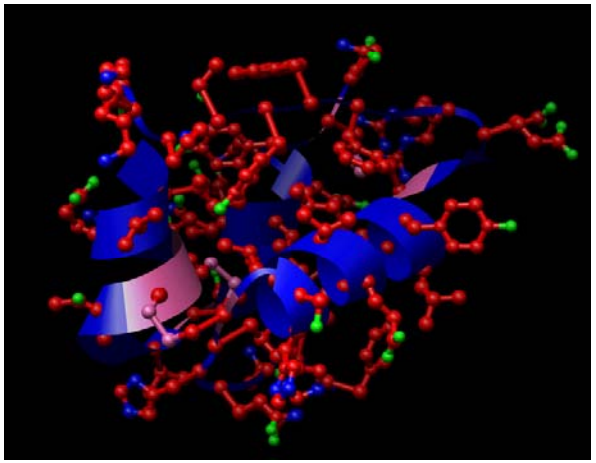
- Insulin can be encapsulated in nanoparticles for protection from gastric enzymes
- Use of the natural polymer chitosan very common for delivery of peptides, vaccines, and genes through several routes
- Several benefits: mucoadhesive, low toxicity, and able to time-release contents
- Chitosan and chitosan derivatives thought to have strong potential in delivery of oral insulin



http://upload.wikimedia.org/wikipedia/commons/d/d9/Insulin.jpg

Nanoparticles: Oral insulin

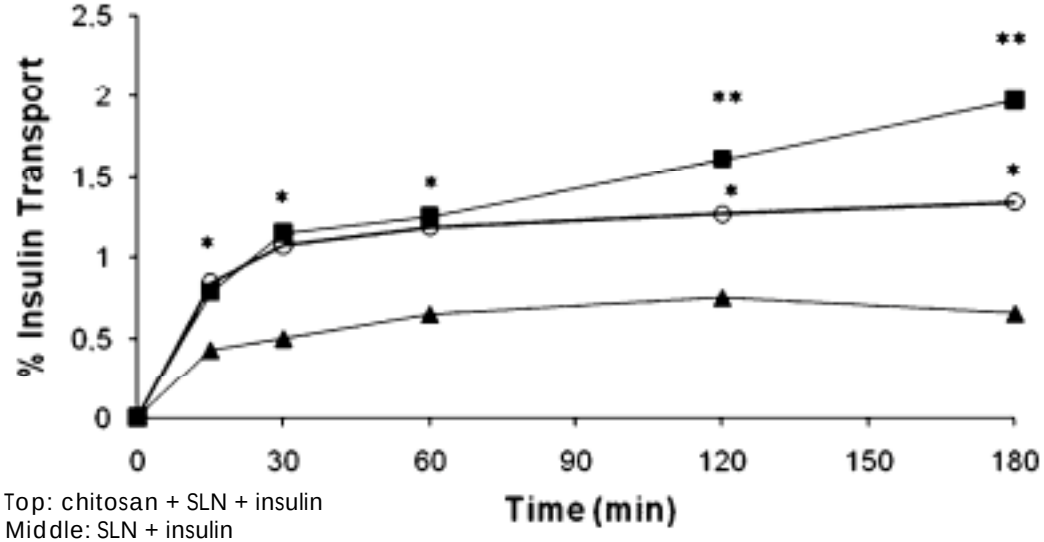
- Insulin packaged with chitosan or its derivatives:
  - Secures the packaged insulin to the intestinal walls, increasing absorption
  - Drug release can be time controlled or pH dependent
  - Bioavailability is good



http://upload.wikimedia.org/wikipedia/commons/d/d9/Insulin.jpg

Nanoparticles: Oral insulin

- Insulin packaged in solid lipid nanoparticles, with chitosan coating
- Better insulin transport in cell model
- In rats, SLN + chitosan + insulin resulted in lower glucose levels
- Without chitosan, the effect was less pronounced; insulin alone had little effect
- SLN thought to help protect insulin, chitosan helps with attachment



Top: chitosan + SLN + insulin
Middle: SLN + insulin
Bottom: insulin

http://upload.wikimedia.org/wikipedia/commons/d/d9/Insulin.jpg

Conclusions

- Nanoparticles have several applications for drug delivery
- Greatly increases specific targeting of cells
- Major advances in cancer therapy
- Good potential in neurological disorders and diabetes

References

H.L. Wong, et al., Adv. Drug Deliv. Rev. (2011)

J. Card et al. Am J Physiol Gastrointest Liver Physiol 301: G956 –G967, 2011.

A. Shapira et al. / Drug Resistance Updates 14 (2011) 150–163

Methods Mol Biol. 2010 ; 596: 467–488. doi:10.1007/978-1-60761-416-6_21

Shapira et al, Drug Resistance Updates 14 (2011) 150–163

Kahlil N et al, Expert opin drug deliv. (2011) 8(1) : 95-112

Mallipeddi et al 2010, Int. J. Nanomed. 5 553-557

Moitra et al, Clin. Pharm. Ther. 2011. 89(4) 491-502

P Fonte, Drug Deliv. and Transl. Res. (2011) 1:299–308