Polymeric Nano and microparticles for Drug Delivery: Does Shape Matter?

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• Polymeric nano/microparticles for drug delivery
  – Protect drugs from enzymes (proteins and peptides)
  – Sustained release (drugs with rapid elimination)
  – Targeted delivery (reduced systemic toxicity)

• Examples
  – Growth hormone and insulin
  – Many others in development

• Particle parameters impact performance
  – Polymer type (biodegradable polymers)
  – Surface chemistry (stealth properties, targeted delivery)
  – Size (few nanometers to microns)
  – Mechanical properties (rigid versus flexible particles)
  – Shape (??)
Particle Shape

• Nearly all work is done using spherical particles

• Making non-spherical polymer particles is very challenging

• Method for particle fabrication
  – Applicable over a wide range of sizes (100 nm-10 µm)
  – Controlled surface chemistry
  – Sufficient particles for testing
Making non-spherical particles

- Embed polystyrene spheres (100 nm-10 µm) in poly(vinyl alcohol) film
- Liquefy polystyrene using heat or solvent
- Stretch film, solidify particles and dissolve film to collect particles
Typical particle dimensions: 1-10 µm (scalable from 100 nm to 10 µm)
How does shape matter?

- **Phagocytosis**
  - Macrophages surround particles and remove them
  - major hurdle to particle survival in the body
Shape Dictates Internalization

Cell always internalizes particle from end

Cell spreads on particle from side, never internalizes
Membrane Coordination

- Membrane migrates uniformly from end of ellipse
- Uncoordinated membrane spreading on side of ellipse

Scale bars = 10um, 5um, 5um
Formation of Actin Structures

- Actin polymerization drives membrane movement
- Actin cup and ring form during internalization of spheres and end of ellipses
- Discontinuous actin networks form during spreading over side of ellipse

Scale bars = 10um
Phagocytosis Dependent on Shape

Particles with $\Omega$ greater than $45^\circ$ are not phagocytosed
Shape is more important than size

- Phagocytosis initiated when $\Omega < 45^\circ$ for all sizes
- If particle is larger than cell ($V^* > 1$), internalization is not completed
- Spreading occurs when $\Omega > 45^\circ$ for all sizes
Eating Manners: Humans and Macrophages

Humans (Minimal expansion of mouth)  ↔  Macrophages (minimal expansion of actin ring)

Understanding shape-bias of macrophages is important for fundamental reasons

- E. coli
- Campylobacter jejuni
- Vibrio cholera
- Bacillus anthracis
- Toxic mold spores
- Asbestos fibers
Summary

• We fabricated particles of several shapes and discovered the role of shape in phagocytosis

• Particle shape impacts several other properties. Studies in progress in collaboration with Prof. Muzykantov

• Particle shape reveals a new dimension in design of drug delivery particles