L2: Nanomedicine in Drug Delivery

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Nanomedicine: Drug Delivery

- Prolong drug systemic circulation half-life
- Targeted delivery to reduce harmful side effects
- Sustained and controlled drug release
- Facilitate administration by improving drug solubility
- Improve patient compliance due to less invasive dosing
Nanotech Drugs

Historical timeline of clinical-stage nanoparticle technologies

Acc. Chem. Res. 2011, 44, 1123
What is an Ideal Drug Nanocarrier?

To become a good drug delivery nanocarrier, the system should satisfy with certain criteria.

Criteria?
The complement system is a part of the immune system that enhances (complements) the ability of antibodies and phagocytic cells to clear pathogens from an organism. The complement system consists of a number of small proteins found in the blood, and normally circulating as inactive precursors. When stimulated by one of several triggers, proteases in the system cleave specific proteins to release cytokines and initiate an amplifying cascade of further cleavages. The end result of this complement activation cascade is massive amplification of the response and activation of the cell-killing membrane attack complex.
(1) Biocompatible & Biodegradable

**Bulk erosion:** Biodegradable microparticle of 75:25 lactide:glycolide PLGA after 133 days of degradation in water.

**Surface erosion:** Biodegradable polyorthoester rods after (left) 9 and (right) 16 weeks of implantation in rabbits.
(2) High Drug Encapsulation Efficiency & Loading

- Physical encapsulation
- Chemical conjugation
- Drug self-assembly
(3) Controlled & Sustained Drug Release

Drugs in degradable polymer matrix

In body

Controlled release

Advantages:
- Reduce side effects
- Increase stability
- Increase duration of drug effect
(4) Long *In Vivo* Circulation Half-life

Immune system clears foreign nanoparticles from circulation

- Long circulation is achieved by a stealthy surface coating (i.e. PEG).
- The polymer coating creates a hydration layer that hides the particles from immune surveillance.
(5) Multivalent Targeting Ability

Classical targeting ligands:
Antibody, Peptide, Aptamer, Small molecules, etc.
(6) Easy Manufacturing

Lipid solution → Lipid film → MLV → Extrusion → LUV

Liposome extrusion
What is an Ideal Drug Nanocarrier?

Criteria:

- Biocompatible & biodegradable
- High drug encapsulation efficiency & loading
- Controlled & sustained drug release
- Long *in vivo* circulation half-life
- Multivalent targeting ability
- Simple manufacturing