Nanocarriers for targeted drug delivery

Benefits and challenges of nanotechnology for medicine

Russell Maguire

ENGI4131 Advanced Semiconductor Devices

Durham University

November 28, 2018

Durham University

Nanocarrier delivery systems

Nanocarrier structure

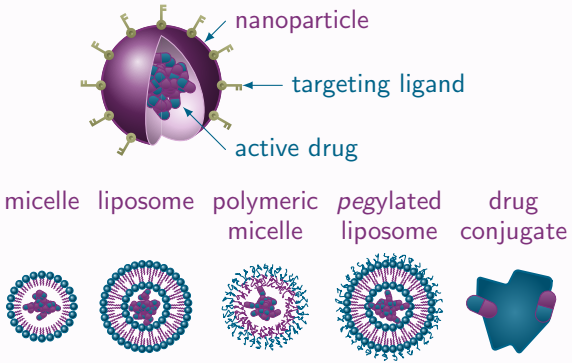

Figure 1: *Structure of common types of nanocarriers.*

Definition: nanocarrier

- Biocompatible nanoparticle encapsulating a drug

Characteristics

- Nanometer scale
- Biodegradable
- Not immunogenic
- Low toxicity
- Hydrophilic
- Soluble

Durham University

Targeted drug delivery

How is targeted drug delivery effective?

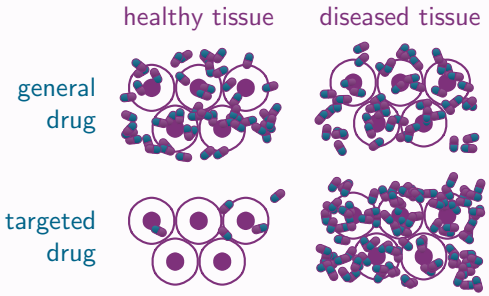

Figure 2: *Goal is to increase drug concentration ratio for diseased tissue.*

Targets diseased tissue

- Maximise therapeutic effects
- Minimise effective drug dose
- Common targets are solid tumours, inflamed and infected tissue

Avoids healthy tissue

- Minimise toxic side-effects

Durham University

Vascular permeability

Definition: vascular permeability

- Tendency for molecules to leak from blood vessels into interstitial space between cells

Contributing factors

- Permeability enhancers such as *bradykinin* and *nitric oxide*
- Dense and defective blood vessels
- Enhanced vascular permeability has been observed in solid tumours and inflamed tissue [1]

[1] H. Maeda *et al.*, *Journal of controlled release* **65**, 271–284 (2000).

Enhanced permeability and retention effect

Basis for **first generation** nanomedicines [2]

Definition: EPR effect

- Tendency for nanoparticles to accumulate in solid tumours [1]

Accumulation procedure

1. Molecules leak into interstitial space due to enhanced vascular permeability
2. Lymphatic vessels are compressed by rapidly growing solid tumour [3]
3. Large particles become trapped

[1] H. Maeda *et al.*, *Journal of controlled release* **65**, 271–284 (2000).
[2] A. Wicki *et al.*, *Journal of controlled release* **200**, 138–157 (2015).
[3] T. P. Padera *et al.*, *Nature* **427**, 695 (2004).

Internal stimuli-responsive nanocarriers

Bioindicators used to trigger release

- Tumours have been observed with lower pH than healthy tissue [4, 5]
- Individual organelles maintain their own unique pH and redox potential
- Intracellular and extracellular space maintain different redox potentials **[6]**

[4] I. F. Tannock, D. Rotin, *Cancer research* **49**, 4373–4384 (1989).
[5] L. E. Gerweck, K. Seetharaman, *Cancer research* **56**, 1194–1198 (1996).
[6] G. Saito *et al.*, *Advanced drug delivery reviews* **55**, 199–215 (2003).

External stimuli-responsive nanocarriers

Mechanisms used to externally trigger release

- Electromagnetic fields
- Heat
- Ultrasound
- Light

Surface ligands

Definition: active targeting

Surface ligands

Thank you, any questions?

References

1. H. Maeda *et al.*, *Journal of controlled release* **65**, 271–284 (2000).
2. A. Wicki *et al.*, *Journal of controlled release* **200**, 138–157 (2015).
3. T. P. Padera *et al.*, *Nature* **427**, 695 (2004).
4. I. F. Tannock, D. Rotin, *Cancer research* **49**, 4373–4384 (1989).
5. L. E. Gerweck, K. Seetharaman, *Cancer research* **56**, 1194–1198 (1996).
6. G. Saito *et al.*, *Advanced drug delivery reviews* **55**, 199–215 (2003).

Durham University