Nanocarriers for targeted drug delivery

Benefits and challenges of nanotechnology for medicine

Russell Maguire

ENGI4131 Advanced Semiconductor Devices

Durham University

November 29, 2018

Nanocarrier delivery systems

Structure, types and features

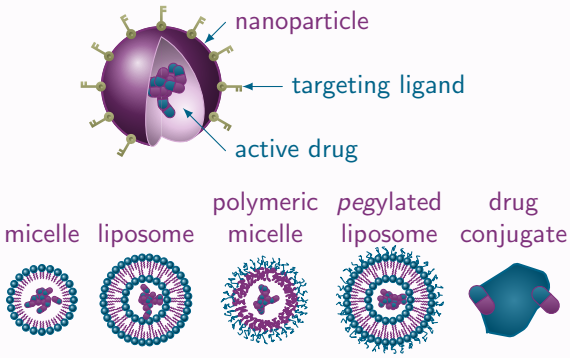

Figure 1: *Structure of common types of nanocarriers*

Definition: nanocarrier

- Biocompatible nanoparticle encapsulating a drug

Characteristics

- Nanometer scale
- Biodegradable
- Non-immunogenic
- Low toxicity
- Hydrophilic
- Soluble

Durham University

Targeted drug delivery

How is targeted drug delivery effective?

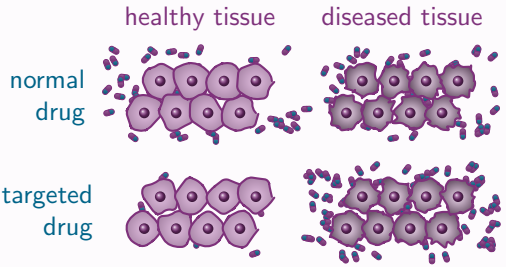

Figure 2: *Goal is to increase drug concentration ratio for diseased tissue*

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

Enhanced permeability and retention effect

Basis for **first generation** nanomedicines [1]

Illustration of the EPR effect

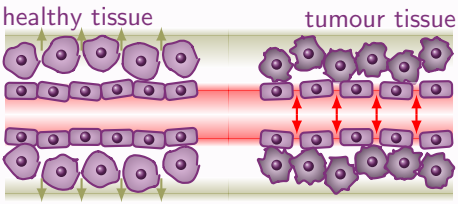

Figure 3: *Lymphatic system drainage and blood vessel permeability in solid tumours*

Definition: EPR effect

- Tendency for nanoparticles to accumulate in solid tumours [2]

Accumulation procedure

1. Molecules leak from blood into tissue due to enhanced vascular permeability
2. Blocked lymphatic system due to dense rapidly growing tumour cells [3]
3. Large particles become trapped

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

Durham University

Internal stimuli-responsive nanocarriers

Example

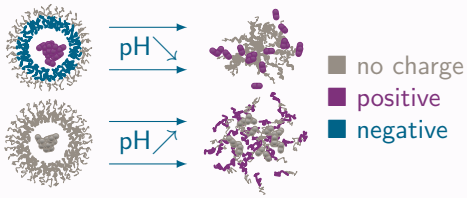

Figure 4: *Polymeric micelles with pH-responsive polymers for electrostatic release [4]*

Bioindicators used to trigger release

- pH level
- Redox potential
- Enzymes
- Temperature

Target sites for pH-responsive nanocarriers

- Tumours have been observed with lower pH than healthy tissue [5, 6]
- Individual organelles within the cell maintain their own unique pH [1]

[1] A. Wicki *et al.*, *Journal of controlled release* **200**, 138–157 (2015).
[4] T. Sun *et al.*, *Angewandte Chemie International Edition* **53**, 12320–12364 (2014).
[5] I. F. Tannock, D. Rotin, *Cancer research* **49**, 4373–4384 (1989).
[6] L. E. Gerweck, K. Seetharaman, *Cancer research* **56**, 1194–1198 (1996).

Durham University

External stimuli-responsive nanocarriers

Example

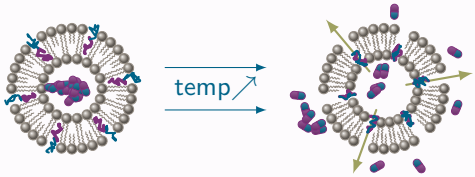

Figure 5: *Liposomes modified with thermosensitive polymers for controlled release [7, 8]*

Mechanisms used to externally trigger release

- Electromagnetic fields
- Heat
- Ultrasound
- Light

Induced local hyperthermia

- Target temperature is 40–45 °C [9, 10]
- Direct heat can be applied to target
- Magnetic fields can be used to heat iron oxide nanoparticles at target [11]

[7] T. Ta, T. M. Porter, *Journal of controlled release* **169**, 112–125 (2013).
[8] K. Kono, *Advanced drug delivery reviews* **53**, 307–319 (2001).
[9] A. Jhaveri *et al.*, *Journal of controlled release* **190**, 352–370 (2014).
[10] S. Ganta *et al.*, *Journal of controlled release* **126**, 187–204 (2008).
[11] F. Scherer *et al.*, *Gene therapy* **9**, 102 (2002).

Durham University

Surface ligands

Definition: active targeting

-

Drugs on the market and in clinical trials

Thank you, any questions?

References

1. A. Wicki *et al.*, *Journal of controlled release* **200**, 138–157 (2015).
2. H. Maeda *et al.*, *Journal of controlled release* **65**, 271–284 (2000).
3. T. P. Padera *et al.*, *Nature* **427**, 695 (2004).
4. T. Sun *et al.*, *Angewandte Chemie International Edition* **53**, 12320–12364 (2014).
5. I. F. Tannock, D. Rotin, *Cancer research* **49**, 4373–4384 (1989).
6. L. E. Gerweck, K. Seetharaman, *Cancer research* **56**, 1194–1198 (1996).
7. T. Ta, T. M. Porter, *Journal of controlled release* **169**, 112–125 (2013).
8. K. Kono, *Advanced drug delivery reviews* **53**, 307–319 (2001).
9. A. Jhaveri *et al.*, *Journal of controlled release* **190**, 352–370 (2014).
10. S. Ganta *et al.*, *Journal of controlled release* **126**, 187–204 (2008).
11. F. Scherer *et al.*, *Gene therapy* **9**, 102 (2002).

Durham University