Nanocarriers for targeted drug delivery

Benefits and challenges of nanotechnology for medicine

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ENGI4131 Advanced Semiconductor Devices

Durham University

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Nanocarrier delivery systems

Nanocarrier structure

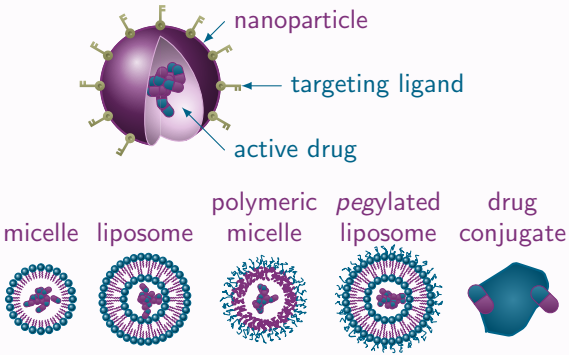

Figure 1: *Structure of common types of nanocarriers*

Definition: nanocarrier

- Biocompatible nanoparticle encapsulating a drug

Characteristics

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

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Targeted drug delivery

How is targeted drug delivery effective?

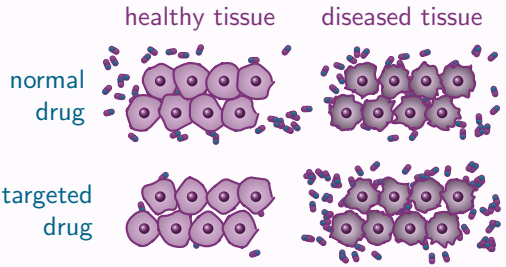

Figure 2: *Goal is to increase drug concentration ratio for diseased tissue*

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

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Enhanced permeability and retention effect

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

Illustration of the EPR effect

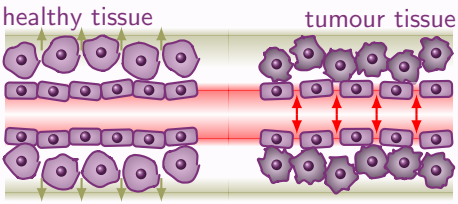

Figure 3: *Lymphatic system drainage and blood vessel permeability in solid tumours*

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).

Internal stimuli-responsive nanocarriers

Example

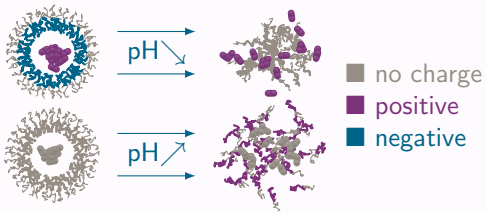

Figure 4: *Polymeric micelles with pH-responsive polymers for electrostatic release [4]*

Bioindicators used to trigger release

- pH
- 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).

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External stimuli-responsive nanocarriers

Example

Figure 5: *Liposomes with thermosensitive polymers for diffusive release [7]*

Mechanisms used to externally trigger release

- Electromagnetic fields
- Heat
- Ultrasound
- Light

[7] T. Ta, T. M. Porter, *Journal of controlled release* **169**, 112–125 (2013).

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).
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7. T. Ta, T. M. Porter, *Journal of controlled release* **169**, 112–125 (2013).

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