Nanocarriers for targeted drug delivery

Benefits and challenges of nanotechnology for medicine

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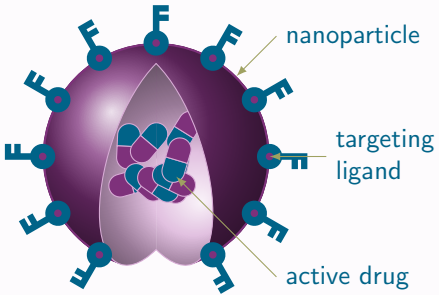
Nanocarrier delivery systems

Nanocarrier structure



Definition: nanocarrier

- Biocompatible nanoparticle encapsulating a drug

Characteristics

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

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Targeted drug delivery

How is targeted drug delivery effective?

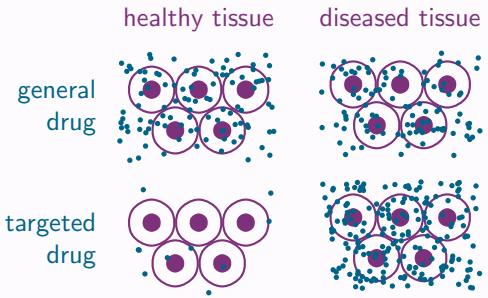

Figure 1: *Goal is to increase drug concentration ratio for diseased tissue.*

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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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).

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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

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).
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