Novel, modular and controllable drug delivery platform

Releasable on demand PEGylated drug-nanocarriers

Technology

Surface coating of drug-loaded nanocarriers (i.e. liposomes, micelles, etc.) with polyethylene glycol ('PEGylation') enables prolonged blood circulation and hence an effective accumulation in target organs (e.g. solid cancer tissues) but might also hold some disadvantages: hindrance of active targeting approaches, inhibition of cellular uptake and endosomal escape. 'PEG release on demand' can combine beneficial attributes: longevity (PEGylation), stimuli sensitivity (de-PEGylation on demand) and targetability (passive and active) and adds the potential of increased drug specificity, reduced drug-related side effects and reduced adverse body reactions against PEGylated particles (shortened circulation). All current switchable on demand systems, however, typically apply quiet weak triggers and/ or show other severe disadvantages, i.e. effective cleavage hindered by PEG shell (e.g. proteases), not easy to administrate in deep-tissue regions (e.g. light, temperature, ultrasound), might also dissolve carriers (e.g. temperature, ultrasound).

Innovation

- Highly modular platform
  - Various nanocarriers applicable (liposomal, dextran-beads, …)
  - Linker - Ligand system exchangeable
  - Different, optimized rates of PEGylation & PEG MW feasible
- Externally applied, strong de-PEGylation trigger
  - At any desired, most beneficial time point
  - Independent of local tissue specific factors a/o physiological triggers (better control/ monitoring)
  - Trigger strong enough while not reducing stability of carrier itself
  - Easy deep-tissue administration: in contrast to some other release triggers (light, temperature or ultrasound)
- Active targeting approaches feasible (see Fig. 1)

Main Application

- Cancer therapy
  - Solid tumors with EPR*-characteristics
  - Every other tumor type allowing passive targeting due to EPR

* EPR = enhanced permeability and retention; nanocarriers accumulate in regions of enhanced vascular permeability

Current Status

- Strong preclinical data, broadened by planed study on efficacy and safety in preclinical animal cancer models
- Sponsor for further preclinical or clinical trials wanted

Responsible Scientist

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Drug Delivery Systems

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Brief Description & Benefits

In the technology presented, nanocarriers are PEGylated via linker and ligand (see Fig. 1), allowing stable, PEGylated nanocarriers to (passively or actively) accumulate in target tissue**.** Only upon systemic administration of an excess of free ligand (remote trigger) nanocarriers are de-PEGylated and the cargo is more easily released and/ or an (targeted or passive) interaction with surrounding (target-) tissue is enabled.

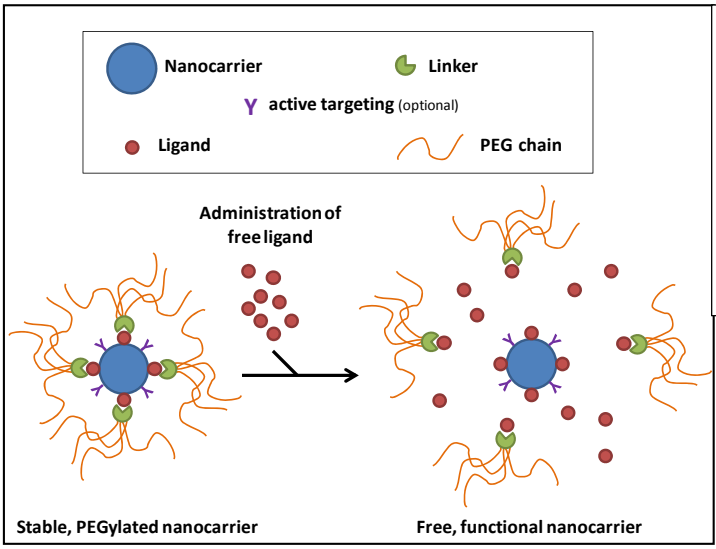

Figure 1

- Tested Linker and especially ligand are safe and approved for humans
- Interaction is highly specific and reversible
- Ligand can be effectively PEGylated

Note:

(I) Active targeting ligands also - alternatively or in addition - could be coupled to PEG-shell, recognizing e.g. overexpressed receptors in target cells.

(II) Active targeting approaches might apply one or combinations of targeting or internalization strategies or even strategies addressing drug bioavailability at the (sub-)cell level.

(III) Most of the conventional chemotherapeutic agents have poor pharmacokinetics profiles and are distributed nonspecifically in the body leading to systemic toxicity associated with serious side effects.

(IV) Preferential cargo
- small molecule anticancer drugs (individual or in combination)
- therapeutic antibody, with or without antibody drug conjugates
- siRNA or pDNA

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