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Dendritic Nanocarriers for Drug Delivery

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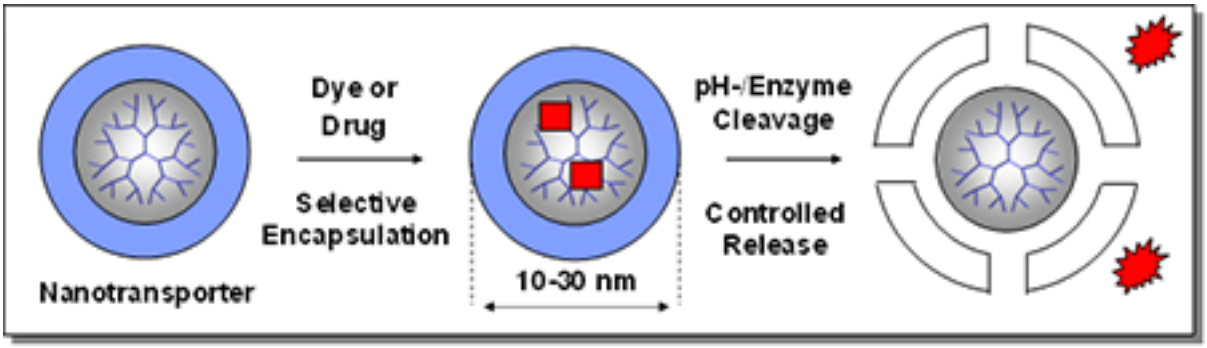
Polymeric nanocarriers can act as “molecular parcels” with an interior to transport guest molecules and an address label to tell the body, where to deliver it. In this respect polymeric nanoparticles can be designed as suitable carriers, because they offer the possibility to (1) solubilize poorly soluble drugs, (2) to transport several drugs at the same time (optimal for a combinatorial therapy) and to (3) shield sensible drugs from either degradation in the body (e.g. RNA from nucleases) or adverse side effects in –of target tissue- before they reach the target. To act as such a nanocarrier they need an interior, into which the drug can be placed first. Thus, hard and solid nanoparticles are not attractive as carriers.

In addition, it must be possible to target a tissue/ cells. For nanoparticles> 5 nm the leaky vasculature of the tumor tissue leads to an enhanced permeation and retention(EPR), which isa simple size effect and does not require any targeting ligands. Hence, it is intrinsic to all types of nanoparticles. It should, however, be noted that the magnitude of the EPR-effect depends strongly on the type of tumor and it is not effective to target small secondary tumor sites (metastases). Thus an additional active targeting with a “homing device” (e.g. an antibody) is also very important to address metastases. Multifunctional nanocarriers offer the possibility to add several antibodies to their surface to increase selectivity. There are, so far, however only few attempts in this direction.

Self-organization looks –at first- like a more simple approach. It needs, however, a lot of planning and synthesis to assess partial structures, which self-assemble into the desired, well-defined core-shell structures. In so far chemical design and self-assembly are closely linked to each other. Self-organization happens, in addition, often quiet unexpectedly, e.g. if polar and less polar subunits are linked. The results are then simple (sometimes more complex) micellar structures, which modify size, cellular recognition or the body distribution of the nanoparticular carriers.

Therefore several groups have focused on stimuli-responsive structures that allow for a controlled release from the nanocarrier by an external stimulus, such as the reduced pH-value in the tumor tissue.[1] In this respect the use of external stimuli and controlled release has been achieved,[2] however, many open questions, such as stability and long-term toxicity remain open. This demonstrates the complexity of the problem: A safe and stable nanocarrieris needed during most of its journey in the body, but at the final target site, it should decompose to set the cargo free. It may be that a clever combination of self-assembly and chemical design is capable to solve this problem.[3]



References

[1] E. Fleige, R. Haag, et al. Advanced Drug Delivery Reviews64, 866 (2012)
[2] M. Calderón, R. Haag, F. Kratz, J. Controlled Release 151, 295 (2011)
[3] M. C. Lukowiak, B. N. S. Thota and R. Haag, Biotechnol. Adv., 2015, accepted