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NEWS AND OPINIONS

Camouflaged nanoparticles circulate longer

Cordelia Sealy

Researchers at the University of California, San Diego have devised a means of camouflaging nanoparticles so that they are retained longer in the body [C.-M. Hu, Proc. Natl. Acad. Sci. USA (2011), doi:10.1073/pnas.1106634108].

Many methods, which have mainly relied upon modifying the surface of nanoparticles, have been tried to increase the amount of time that nanoparticles are retained in the body. The current 'gold standard' in 'stealth' coating is PEG, but anti-PEG immunological response has recently been observed, so researchers are on the lookout for a new approach.

The innovative approach taken by Liangfang Zhang and his team is to disguise biodegradable polymer nanoparticles as red blood cells (RBCs) by cloaking them with natural RBC membranes. The top-down approach first extracts RBCs and removes their contents to leave only the membranes, which are then fused with pre-formed 70 nm diameter PLGA nanoparticles. The resulting nanoparticles have a polymer core and a 7—8 nm outer lipid shell (Fig. 1).

''This is the first work that combines the natural cell membrane with a synthetic nanoparticle for drug delivery applications,'' says Zhang. ''This top-down fabrication technique enables the replication of complex cellular membrane composition on particle surfaces without chemical modifications.''

The researchers compared the longevity of the camouflaged nanoparticles with bare polymer nanoparticles and state-of-the-art PEG-functionalized lipid-polymer hybrid nanoparticles. Both *in vitro* and *in vivo* the RBC membrane-coated nanoparticles show similar stability to PEG-functionalized ones, but exhibit a longer retention time. In mice, the camouflaged nanoparticles appear to continue to circulate in the blood for significant times.

''RBC-membrane coated nanoparticles could rival state-of-the-art stealth nanoparticles,'' says Zhang. ''And are a promising alternative for long circulating drug delivery systems with little risk of immunogenicity.''

Because the nanoparticles are cloaked with RBC membranes, they have the potential to elicit a negligible immune response but only where the RBC membranes match the blood type of the recipient. This paradigm is both potentially limiting and also immensely powerful. While the researchers suggest that the RBC membrane could be depleted in antigens to render it useful in broad populations of patients, it could conversely provide an elegant means of personalized medicine — using a patient's own RBC membranes to disguise nanoparticles for drug delivery.

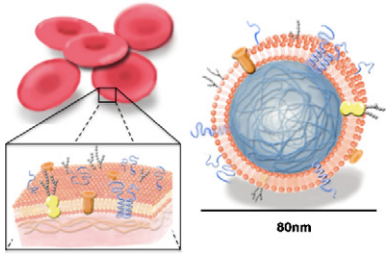

Figure 1 Schematic illustration of a polymeric nanoparticle coated with RBC membranes to evade immunological response for long particle circulation.

Omid Farokhzad of Brigham and Women's Hospital, Harvard Medical School believes that the approach could be potentially revolutionary.

''This is a creative engineering solution to a biological problem,'' he says. ''What Zhang and his team have done is unique... one of the first examples of a very effective way of mimicking of nature.''

The researchers now plan to use their technology for loading drugs into the polymeric nanoparticles to explore their potential as a delivery vessel, as well as trying to add targeting molecules to the cloaking membranes. Zhang says he also want to explore the large-scale manufacturing of the nanoparticles for clinical use.

E-mail address: cordelia.sealy@googlemail.com

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