Nanodiscs made of erythrocyte membranes neutralize bacterial toxins

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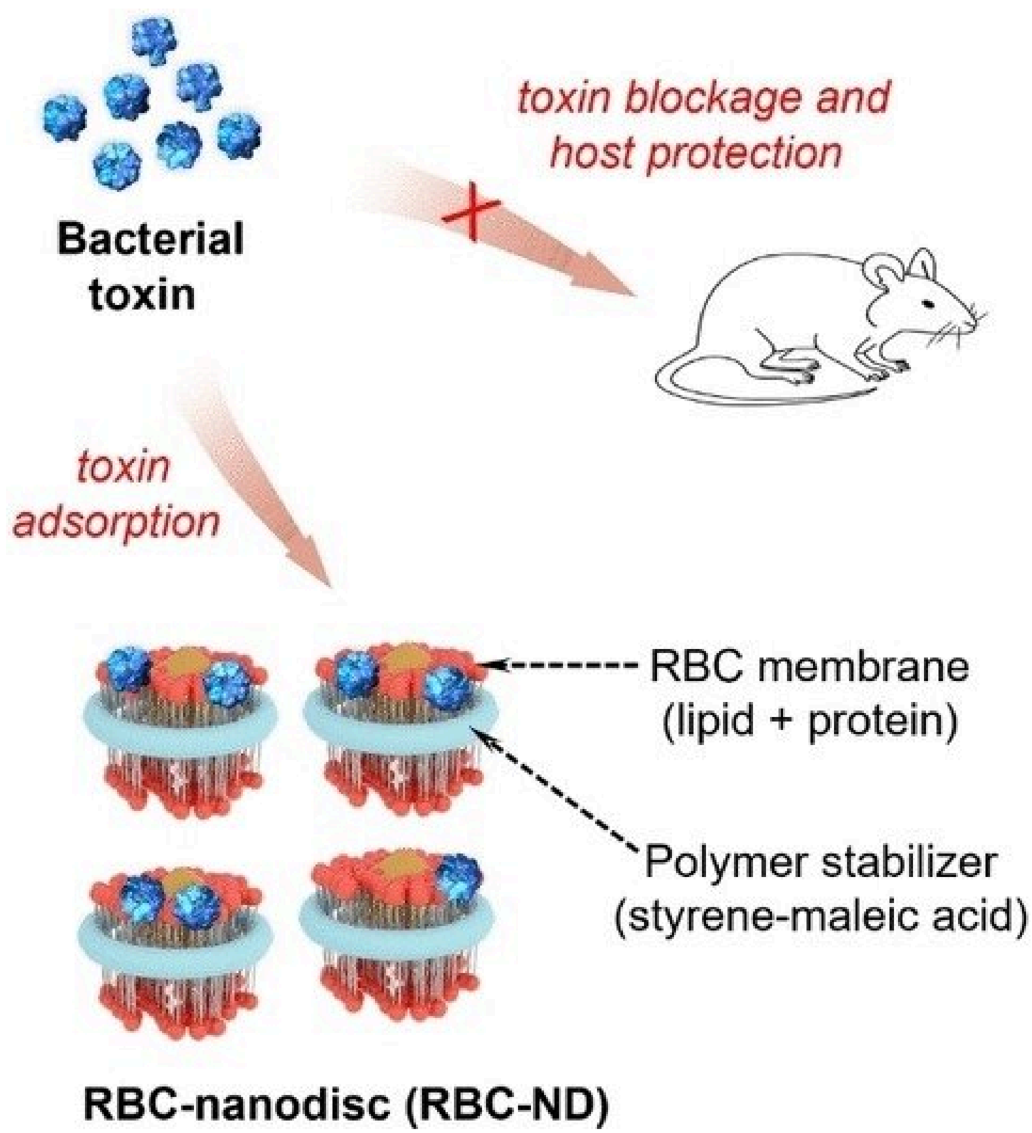

Credit: Wiley

Tiny, disc-shaped pieces of membrane called nanodiscs offer exciting possibilities for nanomedicine. Although they have previously been mostly made of synthetic lipids and proteins, a research team has now introduced nanodiscs based on the cell membranes of human red blood cells. As reported in the journal *Angewandte Chemie International Edition*, they are able to neutralize dangerous bacterial toxins.

Nanodiscs are disc-shaped lipid bilayers with diameters mostly under 20 nm. They are surrounded and stabilized by scaffolds made of proteins, peptides, or synthetic polymers. Because of their disc shape, they are significantly less likely than their spherical counterparts to be "swallowed" and destroyed by immune cells. They are thus attractive for applications like targeted drug transport. Their small size and disc shape allows nanodiscs to effectively enter lymph nodes, making them potentially useful as nanovaccines.

Previous nanodiscs have primarily been based on synthetic lipid bilayers whose lipid compositions must be carefully—and laboriously—optimized for specific applications. In addition, synthetic lipids can trigger undesirable immune reactions. A team led by Liangfang Zhang at the University of California, San Diego (La Jolla, U.S.) are using natural cell membranes as starting materials for nanodiscs. Natural membranes contain native lipids and proteins whose biological functions are maintained in the nanodiscs, which could be therapeutically useful. The team demonstrated their concept with membranes from red blood cells.

Red blood cells were made to burst, and their membranes were separated out and mixed with a copolymer of styrene and maleic acid. This resulted in the formation of nanodiscs (NDs) consisting of the natural membrane lipids and proteins from the red blood cells (RBCs) and stabilized by the copolymer. Called RBC-NDs, these tiny structures can be stored for long periods and are both biocompatible and non-toxic.

Interestingly, these RBC-NDs are capable of effectively neutralizing certain bacterial toxins, as demonstrated in tests with α-toxin from a strain of methicillin-resistant Staphylococcus aureus. S. aureus is found almost everywhere and is usually harmless. However, in immunocompromised patients, open wounds, or after operations, for example, it can spread and cause life-threatening lung infections, toxic shock, and sepsis. Strains that are resistant to antibiotics are particularly dangerous. The primary toxin from these bacteria, α-toxin, destroys blood cells (hemolysis). In vitro, RBC-NDs can bind α-toxin and neutralize its hemolysis and cytotoxicity. In vivo, injection of RBC-NDs significantly improved the chances of survival in mice that had been given α-toxin or a complex mixture of the various proteins excreted by S. aureus.

The design strategy used for the RBC-NDs could also be extended to other types of membranes for a wide range of applications.

More information: Lei Sun et al, Synthesis of Erythrocyte Nanodiscs for Bacterial Toxin Neutralization, *Angewandte Chemie International Edition* (2023). DOI: 10.1002/anie.202301566

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