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Erythro-PmBs: A Novel Polymyxin B Delivery System Using Antibody-Conjugated Hybrid Erythrocyte Liposomes

Content

As a result of the growing world-wide antibiotic resistance crisis, many currently existing antibiotics have become ineffective due to bacteria developing resistive mechanisms. There are a limited number of potent antibiotics that are successful at suppressing microbial growth, such as polymyxin B (PmB); however, these are often deemed as a last resort due to their toxicity. We present a novel PmB delivery system constructed by conjugating hybrid erythrocyte liposomes with antibacterial antibodies to combine a high loading efficiency with guided delivery. The retention of PmB is enhanced by incorporating negatively charged lipids into the red blood cells' cytoplasmic membrane (RBCcm). Anti- E. coli antibodies are attached to these hybrid erythrocyte liposomes by inclusion of DSPE-PEG malemeide linkers. We show that these Erythro-PmBs have a loading efficiency of ˜ 90%, and are effective in delivering PmB to E. coli, with values for the minimum inhibitory concentration (MIC) comparable to those of free PmB. MIC values for K. aerogenes; however, were significantly increased well beyond the resistant breakpoint, indicating that inclusion of the anti- E. coli antibodies enables the Erythro-PmBs to highly selectively deliver antibiotics to specific targets. This versatile platform can be used for different types of antibiotics and bacterial targets.

Krivic H, Himbert S, Sun R, Rheinstadter MC. Erythro-PmBs: A highly selective polymyxin B delivery system using antibody-conjugated hybrid erythrocyte liposomes. Under Review. *ACS Infectious Diseases.* 2022

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