Nano-mupirocin for Systemic Treatment of Invasive *Staphylococcus aureus* Infections

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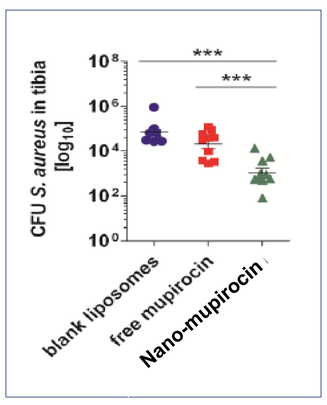
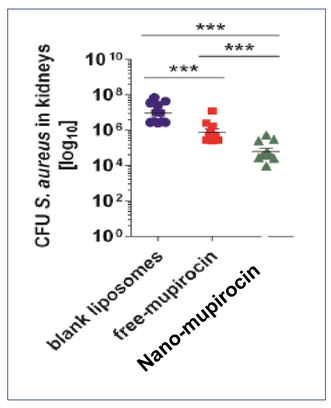
Background

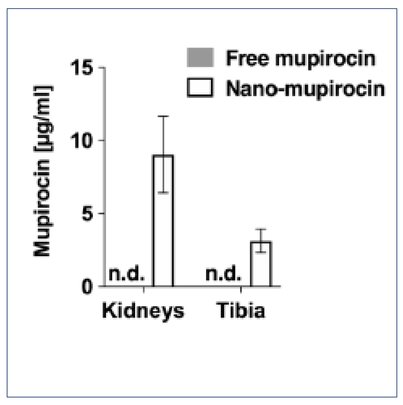
Mupirocin is an antibiotic with a unique mode of action used for the treatment of staphylococci skin infections. It has high protein binding and is rapidly eliminated from the circulation, limiting its use to topical settings. Loading mupirocin into PEGylated nano-liposomes to form Nano-mupirocin protects the drug and potentially allows parenteral use against a wider range of infections. Here we present the in vivo activity of Nano-mupirocin in mice models of bloodstream infection and pneumonia models caused by *S. aureus*.

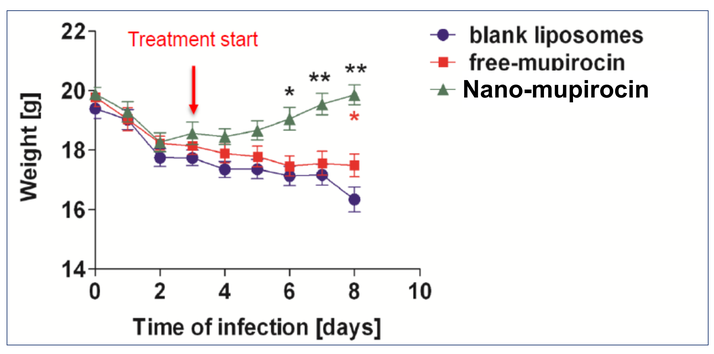
A murine model of *S. aureus* bloodstream infection

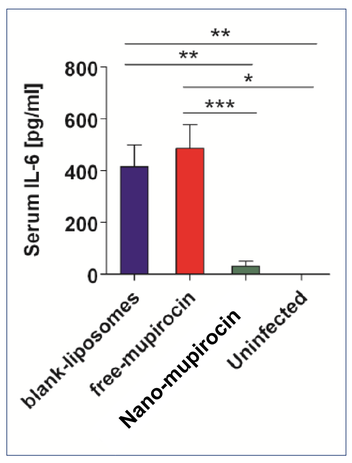
C57BL/6 mice were infected intravenously with 10^6 CFU of S. aureus strain 6850 and treated with either free mupirocin, Nano-mupirocin (both at 50 mg/kg), or empty nanoliposomes (blank liposomes) intravenously on day 3 and intraperitoneally on days 4, 5, 6 and 7 of infection. Mice were sacrificed at day 8 of infection and mupirocin concentration and bacterial loads were determined in kidneys and tibia.











Mupirocin was only detectable by HPLC in the infected organs when the antibiotic was administered with the nanoliposome formulation but not when administered as free drug. Accordingly, treatment with Nano-mupirocin was significantly more effective at reducing the bacterial loads in kidneys and tibia than free mupirocin. Furthermore, signs of morbidity like body weight loss and systemic inflammation shown by the serum levels of IL-6 were also significantly lower in mice treated with Nano-mupirocin than in those treated with blank liposomes or free mupirocin.

Thus, treatment with Nano-mupirocin resulted in a more effective delivery of active mupirocin to the sites of infections and superior bacterial killing than treatment with the free antibiotic.

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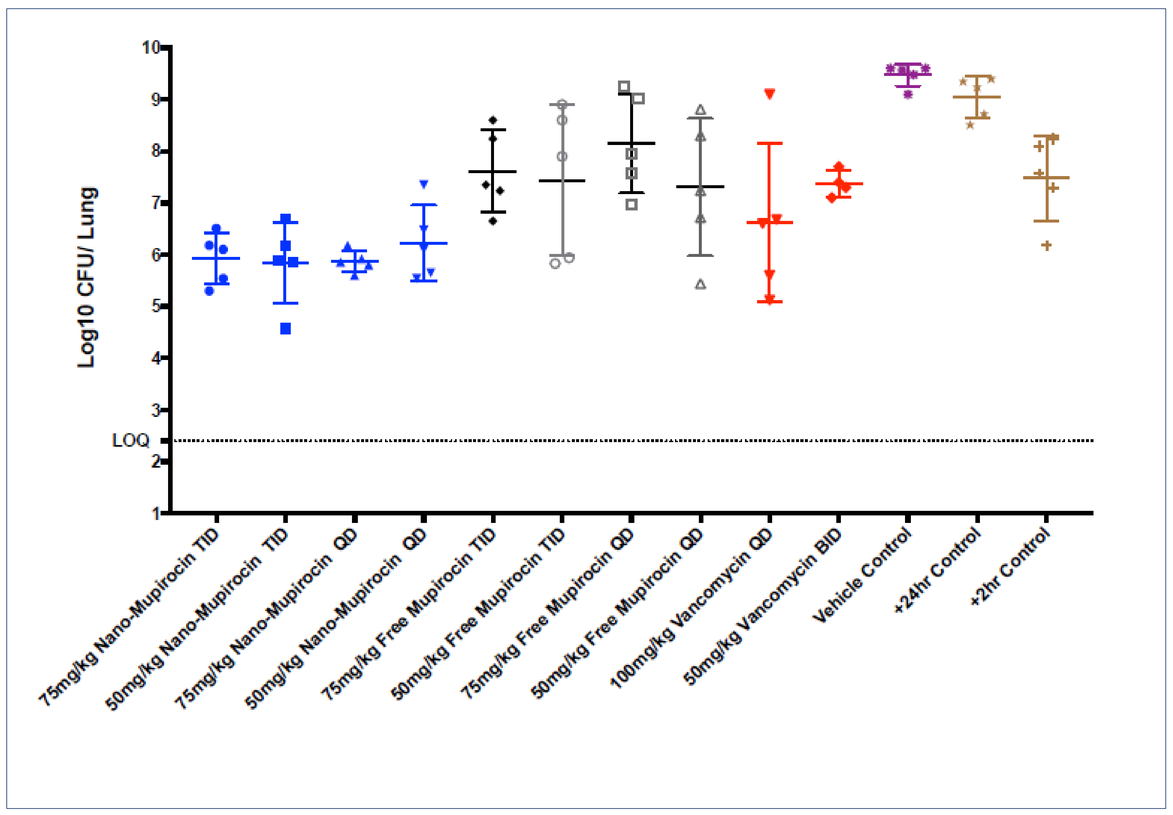
A neutropenic mouse lung infection model

Mice were rendered neutropenic by intraperitoneal injections of cyclophosphamide, intranasally inoculated with MRSA (UNT141-3) and treated with either 50 mg/kg or 75 mg/kg of Nano-mupirocin or free mupirocin. Control mice received blank nanoliposomes. Positive control mice received vancomycin 50 or 100 mg/kg SC.



Nano-mupirocin treated mice exhibited significantly lower numbers of MRSA in the lungs compared to vehicle control and 24 h control mice.

Reference

O. Goldmann, A. Cern, M. Müsken, M. Rohde, W. Weiss, Y. Barenholz, E. Medina, Liposomal mupirocin holds promise for systemic treatment of invasive Staphylococcus aureus infections. Submitted for publication

Conclusions

Nano-mupirocin efficacy in *S. aureus* models was demonstrated in bloodstream infection model and in a neutropenic mouse lung infection model.

Nano-mupirocin administered parenterally suggest a potential treatment for *S. aureus* infections.