Novel Polymyxin Derivatives Effective in Treating Experimental Peritoneal E. coli Infection in Mice

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BACKGROUND
Gram-negative bacteria are progressively becoming more resistant to the clinically available antibacterial agents. This has reinstated polymyxins as the drugs of last resort to treat serious infections caused by multi drug resistant gram-negatives. In the present investigation we evaluated the in vivo efficacy of three novel polymyxin derivatives against the common opportunistic pathogen E.coli in a murine peritoneal infection model.

MATERIALS AND METHODS
Mice were inoculated intraperitoneally with 10⁶ CFU of the virulent E.coli strain IH3080 (O18:K1). At 1 and 3 hrs post infection mice (n=3-4) were treated with the polymyxin derivatives NAB737, NAB739 and NAB7061. Control mice received saline. The clinical status of the mice and bacterial load in the peritoneum were determined at the time of treatment and at 1 or 4 hrs after the last treatment.

RESULTS
- Treatment with NAB737 at 4 mg/kg resulted in a 4.9 log₁₀ bacterial kill in vivo.
- Treatment with NAB739 at 4 mg/kg resulted in a 5.3 log₁₀ protection and at 1 mg/kg a 4.8 log₁₀ bacterial kill in vivo.
- Treatment with NAB7061 at 5 mg/kg in combination with erythromycin (20mg/kg) resulted in a 2.9 log₁₀ bacterial kill in vivo.

CONCLUSION
We found that the novel polymyxin derivatives NAB737, NAB739 and NAB7061 have potent in vivo bactericidal effect against E.coli in an experimental murine peritonitis model.