

**LETTER**

# Direct antimicrobial activity of antithrombin?

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See related research by Hofstra *et al.*, <http://ccforum.com/content/13/5/R145>

In a study by Hofstra and colleagues [1] in a recent issue of *Critical Care*, nebulization of drotrecogin-alfa (activated), antithrombin, heparin, or danaparoid attenuated pulmonary coagulopathy during *Streptococcus pneumoniae* pneumonia in rats; only antithrombin additionally exerted lung-protective effects and reduced bacterial outgrowth. Adding antithrombin to culture medium had no effect on the outgrowth of *S. pneumoniae in vitro*; thus, less neutralizing of endogenous antimicrobials by reduced bronchoalveolar fluid levels of inflammatory proteins could have permitted better endogenous microbicidal effects in the antithrombin group [1].

Direct microbicidal effects of antithrombin would not have been surprising since antimicrobial peptides are known to bind to glycosaminoglycans similar to antithrombin [2]. Structural motifs associated with heparin affinity confer antimicrobial properties to a given peptide [3]. Thus, heparin-binding peptides (for example, from laminin isoforms, von Willebrand factor, vitronectin, protein C inhibitor, complement factor C3, and fibronectin) exerted antimicrobial activities against bacteria [3]. Similar results had been obtained using consensus sequences for heparin binding (Cardin and Weintraub motifs) determined as -X-B-B-X-B-X- and -X-B-B-B-X-B-X- (B: probability of a basic residue; X: hydrophobic residue) [4]. Antithrombin contains such a consensus sequence (130L-Y-R-K-A-N-K-S) [4,5].

When investigating the ligation of glycosaminoglycans with endogenous antimicrobials [2], we also studied the direct effects of antithrombin on bacterial growth, and growth inhibition was found (C.J. Wiedermann, A. Djanani, unpublished data). It is therefore unclear why Hofstra and colleagues [1] failed to observe a direct

inhibition of bacterial growth by antithrombin. Reasons may include (a) dose and duration of antithrombin exposure of bacteria and (b) microbial species. Given the authors' interesting observation, however, to further explore the direct antimicrobial potential of nebulized antithrombin in the lung would be worthwhile.

#### Competing interests

CJW has received fees for speaking and travel reimbursements from manufacturers of plasma-derived therapies (CSL Behring, King of Prussia, PA, USA, and Kedrion S.p.A, Castelvecchio Pascoli, Italy). AD declares that she has no competing interests.

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