CRITICAL CARE

LETTER

# Direct antimicrobial activity of antithrombin?

Christian J Wiedermann*[1] and Angela Djanani[2]

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 antimicrobicidals 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-X-B-X- (B: probability of a basic residue; X: hydropathic 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the direct effects of antithrombin on bacterial growth, and growth inhibition was found (C.J. Wiedermann, A. Djanani, unpublished data).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.

**Author details**

[1]Department of Internal Medicine, Teaching Hospital of Bolzano, L. Böhler Street 5, 39100 Bolzano (BZ), Italy. [2]Department of Internal Medicine, Medical University of Innsbruck, Anichstrasse 35, 6020 Innsbruck (Tyrol), Austria.

Published: 7 September 2010

**References**

1. Hofstra JJ, Cornet AD, de Rooy BF, Vlaar AP, van der Poll T, Levi M, Zaat SA, Schultz MJ: **Nebulized antithrombin limits bacterial outgrowth and lung injury in Streptococcus pneumoniae pneumonia in rats.** *Crit Care* 2009, **13:**R145.
2. Djanani A, Mosheimer B, Kaneider NC, Ross CR, Ricevuti G, Patsch JR, Wiedermann CJ: **Heparan sulfate proteoglycan-dependent neutrophil chemotaxis toward PR-39 cathelicidin.** *J Inflamm (Lond)* 2006, **3:**14.
3. Andersson E, Rydengård V, Sonesson A, Mörgelin M, Björck L, Schmidtchen A: **Antimicrobial activities of heparin-binding peptides.** *Eur J Biochem* 2004, **271:**1219-1226.
4. Cardin AD, Weintraub HJ: **Molecular modeling of protein-glycosaminoglycan interactions.** *Arteriosclerosis* 1989, **9:**21-32.
5. Smith JW, Knauer DJ: **A heparin binding site in antithrombin III. Identification, purification, and amino acid sequence.** *J Biol Chem* 1987, **262:**11964-11972.

doi:10.1186/cc9243
**Cite this article as**: Wiedermann CJ, Djanani A: **Direct antimicrobial activity of antithrombin?** *Critical Care* 2010, **14:**440.

*Correspondence: christian.wiedermann@asbz.it
[1]Department of Internal Medicine, Teaching Hospital of Bolzano, L. Böhler Street 5, 39100 Bolzano (BZ), Italy
Full list of author information is available at the end of the article