

LETTER

Matrix metalloproteinases and their inhibitors as biomarkers of severity in sepsis

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See related commentary by Hoffmann *et al.*, <http://ccforum.com/content/13/6/1006>

We read with interest the commentary by Hoffmann and colleagues [1] on our manuscript recently published in *Critical Care* showing that matrix metalloproteinase (MMP)-9, MMP-10 and tissue inhibitor of matrix metalloproteinases (TIMP)-1 could be new biomarkers of severity and mortality in sepsis [2]. As they stated, the lack of serial measurements of MMPs and TIMPs over clinical evolution was as a limitation of our study. Despite this limitation, our results suggest that MMPs and TIMPs may be of pathophysiological significance in sepsis.

Some clinical studies have found higher circulating levels of MMP-9 [2-4] and TIMP-1 [2,3] in septic patients than in healthy controls, and higher levels of TIMP-1 [2,3] or MMP-9 [4] in nonsurviving than in surviving septic patients. Our study also reports, for the first time, that MMP-10 circulating levels are also elevated in septic patients [2]. According to the results of some *in vitro* studies, MMP-10 could play a role in infection, since increased MMP-10 gene transcription was observed after infective stimulation of human and mice cells.

On the other hand, we think the correlation between MMP-9, TIMP-1 and markers of coagulopathy, and the lower MMP-9/TIMP-1 ratio in nonsurviving than in surviving septic patients found in our study, may be associated with a higher prothrombotic/antifibrinolytic state, responsible for the capillary thrombosis, multiple organ dysfunction, and death.

Finally, from a therapeutic perspective, the development of modulators of MMP/TIMP activity could be used as a new class of drugs for the treatment of severe sepsis [5].

Abbreviations

MMP = matrix metalloproteinase; TIMP = tissue inhibitor of matrix metalloproteinases.

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Competing interests

The authors declare that they have no competing interests.

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References

- Hoffmann U, Brueckmann M, Borggrefe M: **Matrix metalloproteinases and their inhibitors: promising novel biomarkers in severe sepsis?** *Crit Care* 2009, **13**:1006.
- Lorente L, Martín MM, Labarta L, Díaz C, Solé-Violán J, Blanquer J, Orbe J, Rodríguez JA, Jiménez A, Borreguero-Leon JM, Belmonte F, Medina JC, Lliminana MC, Ferrer-Aguero JM, Ferreres J, Mora ML, Lubillo S, Sanchez M, Barrios Y, Sierra A, Páramo JA: **Matrix metalloproteinase-9, -10, and tissue inhibitor of matrix metalloproteinases-1 blood levels as biomarkers of severity and mortality in sepsis.** *Crit Care* 2009, **13**:R158.
- Hoffmann U, Bertsch T, Dvorsak E, Liebetrau C, Lang S, Liebe V, Huhle G, Borggrefe M, Brueckmann M: **Matrix-metalloproteinases and their inhibitors are elevated in severe sepsis: prognostic value of TIMP-1 in severe sepsis.** *Scand J Infect* 2006, **38**:867-872.
- Nakamura T, Ebihara I, Shimada N, Shoji H, Koide H: **Modulation of plasma metalloproteinase-9 concentrations and peripheral blood monocyte mRNA levels in patients with septic shock: effect of fiber-immobilized polymyxin B treatment.** *Am J Med Sci* 1998, **316**:355-360.
- Zhu S, Ashok M, Li J, Li W, Yang H, Wang P, Tracey KJ, Sama AE, Wang H: **Spermine protects mice against lethal sepsis partly by attenuating surrogate inflammatory markers.** *Mol Med* 2009, **15**:275-282.

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