CORRESPONDENCE

To the Editor: We read with interest the paper by Chromek *et al.* (1) concerning matrix metalloproteinase-9 in acute pyelonephritis and renal scarring and would like to comment on some of the methodological aspects of the study.

The authors found that total MMP-9 levels in renal tissue homogenates from infected mice were significantly higher than those from uninfected mice. However, from the information provided in the Materials and Methods section, we are concerned that the Chromek *et al.* findings might be biased by technical procedures. It is stated that mouse MMP-9 activity assay, specific for total and active, was used in supernatants from renal mice tissue. The activity assays are in fact specific for endogenous active or total active – the latter involves activation of pro-MMP-9 by p-aminophenylmercuric acetate. On the other hand, the total human assay, which measures pro-MMP-9 and active levels, was used for the measurement of the MMP-9 in the urine of children with acute pyelonephritis. The Results section, however, clearly shows that total (as we understand pro-MMP-9 and active) levels were measured in mice renal tissue homogenates. So neither specificity as to the form of the enzyme nor species assignment (human versus mouse) was appropriate.

An additional concern exists as to the explanation of the hypothesis about the association between MMP-9 and scar development. The authors claim that because TIMP-1 urinary levels were higher than the corresponding MMP-9 levels, it did not reflect the “induction phase” of renal scarring but the “phase of matrix synthesis,” which is characterized by decreased gelatinolytic activity with accumulation of collagen. It does not seem plausible since measured MMP-9 levels were in fact total (pro-MMP-9 and active), and no data as to the activity of the enzyme in urine was presented in the study.

In our recent study we found that the total values of MMP-9 were significantly higher in peritoneal fluid of women with endometriosis (reproductive-age, inflammation-associated disease of women), than in healthy controls. No differences, however, in the concentrations of the active form were found between the two groups. We suggested it was due to the presence of a pro-MMP-9 form and possibly attenuation of the pro-MMP-9 activation processes in peritoneal fluid (2). The authors did not measure the active form of MMP-9 in urine, which, as shown in our study, could possibly not differ from healthy controls, and this consequently would not have resulted in decreased gelatinolytic activity with accumulation of collagen.

We are in agreement with the authors that scarring associated with decreased MMP-9/TIMP-1 ratio may favor an accumulation of collagen. Nonetheless, we are in disagreement with the conclusion that because increased MMP-9/TIMP-1 is not a factor inducing renal scarring, possible treatment attempting to inhibit MMP-9 activity may not be beneficial for the patient. We believe this conclusion could only be made if activity of

the enzyme was measured and appropriate assays used in human and animal sets.

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References

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2. Szamatowicz J, Laudanski P, Tomaszewska I 2002 Matrix metalloproteinase-9 and tissue inhibitor of matrix metalloproteinase-1: a possible role in the pathogenesis of endometriosis. *Hum Reprod* 17:284–288

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