Reviewer's report

Title: The expression of type 1 plasminogen activator inhibitor (PAI-1) in clear cell renal cell carcinoma (CCRCC) and its impact on angiogenesis, progression and patient survival after radical nephrectomy

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Reviewer: Ted Skolarus

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BMC Urology

Title: The expression of type 1 plasminogen activator inhibitor (PAI-1) in clear cell renal cell carcinoma (CCRCC) and its impact on angiogenesis, progression and patient survival after radical nephrectomy

Decision: Minor revisions

Summary: This study sought to characterize the expression of PAI-1 in clear cell renal cell carcinoma specimens over a ten year period at a single institution. Using immunohistochemistry, they classify tumors as no, low, medium or high expression of PAI-1 and examine relationships between PAI-1 and nuclear grade, stage, and cancer-specific survival. They find that PAI-1 is expressed in 9% of tumors, it is correlated with tumor stage and nuclear grade, and that it is independently associated with worsened cancer-specific survival on multivariate Cox regression. This is a well written manuscript however a few concerns are noted below.

Major Concerns:

• The high correlation with tumor stage, tumor size, nuclear grade, sarcomatoid differentiation and other markers of tumor aggressiveness (e.g., MVD) may limit the added utility of this marker in RCC. This should be mentioned in a limitations section added to the discussion prior to the last paragraph.

• In this limitations section, the authors may want to discuss how their study population differs from more recent clinical series as over half of their patients had T3/T4 disease and how this may impact their findings. Very few PAI-1 positive tumors were present in low risk patients (3 in T1/T2) making its prognostic utility for the majority of current patients with RCC limited. Did these 3 patients die of disease?

• I would caution the authors from overstating their conclusions in the last paragraph as only 9% of tumors had PAI-1 positivity. This low prevalence may not deserve a tremendous investment in terms of targeted therapeutics toward PAI-1.

Concerns:

• The authors do not discuss the current targeted agents for RCC, is there any
way these could impact the PAI-1 pathway?

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.