Reviewer's report

Title: TNF-alpha blockade is ineffective in animal models of established polycystic kidney disease

Version: 3 Date: 3 September 2013

Reviewer: Vishal Patel

Reviewer's report:

The authors have submitted a manuscript entitled ‘TNF-# blockade is ineffective in animal models of established polycystic kidney disease’ for peer-review.

Summary: The aim of the study was to test whether Etanercept, a TNF-# blocker, is a feasible therapeutic agent for polycystic kidney disease. The authors studied two orthologous rodent models: the pck rat (Pkhd1 mutation, ARPKD) and PKD2 ws25/w183 mouse (Pkd2 mutation, ADPKD). They show that administration of Etanercept in these mice does not attenuate cyst growth. The authors tried several doses of Etanercept and different administration regimens. The authors also tested Mozavaptan, a vasopressin receptor antagonist, in animal models of PKD. Surprisingly, the authors report that Mozavaptan is also ineffective in retarding cyst growth in animal models.

Overall, this a nice study. The strengths include: (i) the TNF-a pathway has not been extensively studied in PKD. Therefore, this study is of general interest. (ii) The use of two orthologous rodent models and testing various doses of the drug. (iii) The study was statistically powered to reduce the chances of obtaining a false-positive of false-negative results.

Minor essential points:
(i) Please provide the number of mice that were analyzed for Figure 1.
(ii) Please provide the breakdown of # of male and female animals analyzed in the study.
(iii) Is NF-kB, ERK2 or p38 expression reduced in cyst epithelial cells in figure 1?
(iv) The authors should show representative histological sections for mice analyzed in table 1 and 2.
(v) Are NF-kB, ERK2 or p38 levels also decreased in the PKD2 ws25/w183 mice-treated with Etanercept?
(vi) Is cAMP level reduced in kidneys of mice treated with Mozavaptan?

Level of interest: An article of importance in its field

Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests