Dietary protein loading modulates disease progression in an orthologous mouse model of ADPKD

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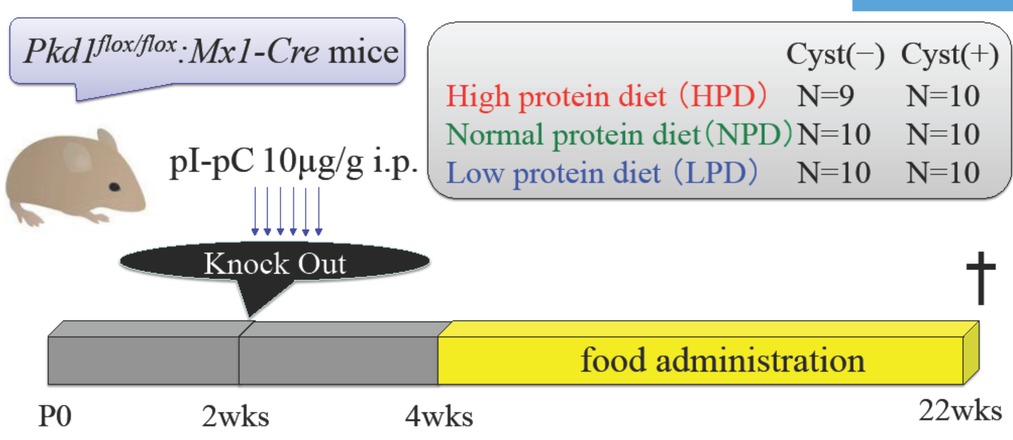
Introduction and Aims

Autosomal dominant polycystic kindney disease (ADPKD) is a progressive hereditary disorder, leading to end-stage kidney disease. Dieatery protein restriction is a useful treatement for chronic kidney disease, but the effects of dieatery protein restriction in ADPKD remain controversial. The purpose of this study is to investigate the influence of dieatery protein modification on ADPKD model mice.

Methods



	Cyst(−)	Cyst(+)
High protein diet (HPD)	N=9	N=10
Normal protein diet (NPD)	N=10	N=10
Low protein diet (LPD)	N=10	N=10

- *Pkd1*$^{flox/flox}$:*Mx1-Cre* mice were injected with polyinosinic-polycytidylic acid (pI-pC) to inactivate *Pkd1*.
- Mice were fed 40% protein diet (high protein diet: HPD), 20% (normal protein diet: NPD) and 6% (low protein diet: LPD) from 4 weeks to 22weeks.
- All diets were isocaloric (3.5kcal/g) and protein resource was casein. The difference in caloric content was made up by cornstarch.
- Diacron-reactive oxygen metabolites (d-ROM), as a reliable biomarker of oxidative stress were measured by Free carpe diem (Wismerll, Tokyo, Japan).

Results

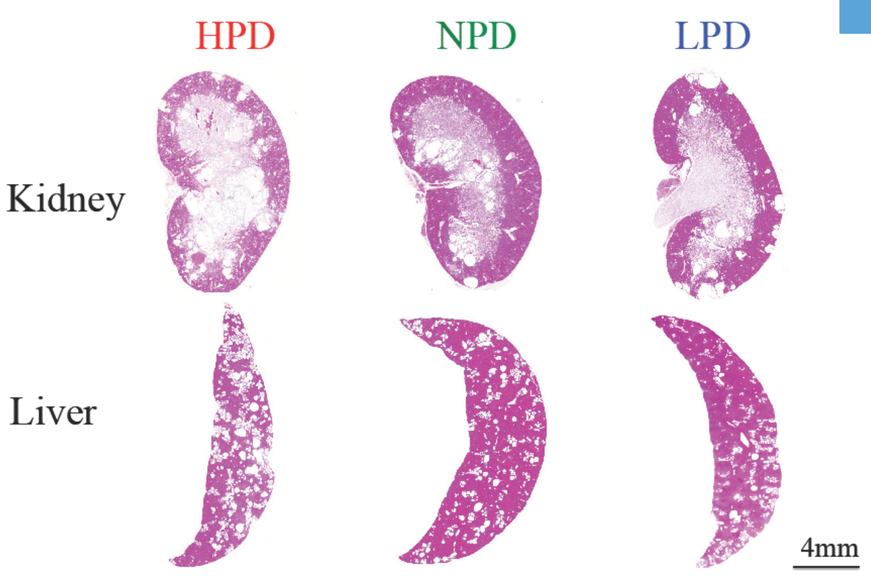
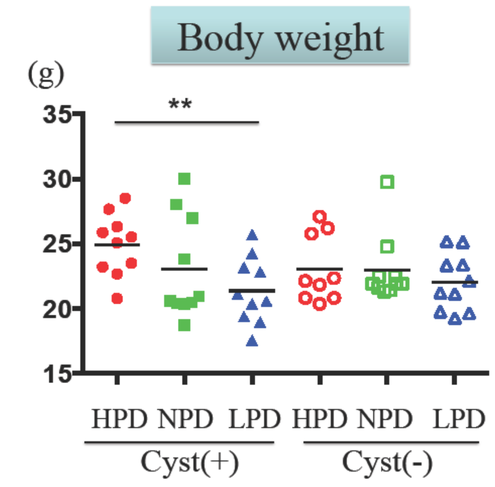


Fig 1. Kidney and liver in HPD showed more severe cysts.



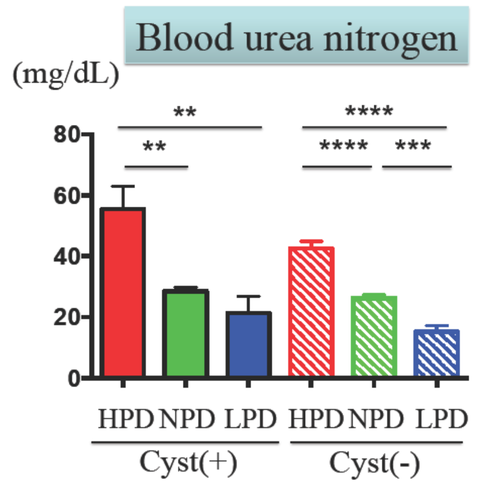


Fig 2.
✓ Body weight was significantly greater in HPD than LPD.

✓ Blood urea nitrogen levels elevated in HPD.

✓ There was no difference in serum albumin levels.

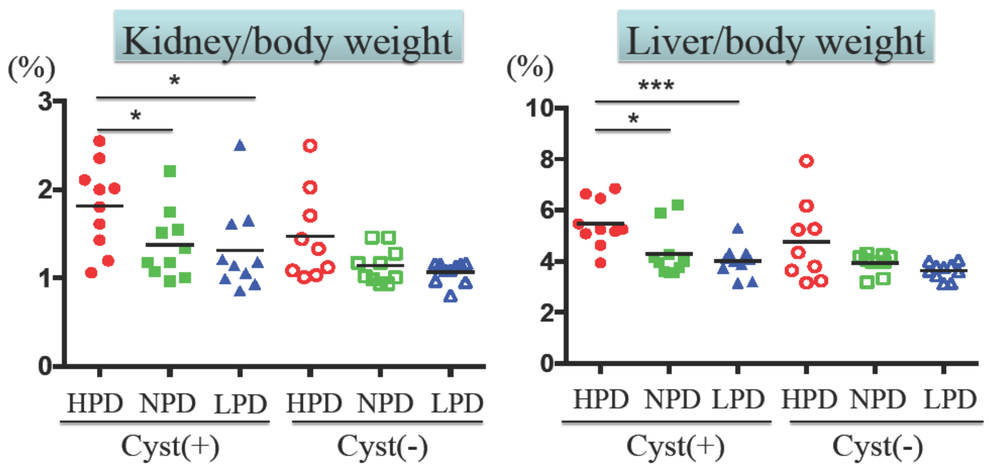


Fig 3. Kidney/body weight ratio and liver/body weight ratio in HPD were significantly greater than NPD and LPD.

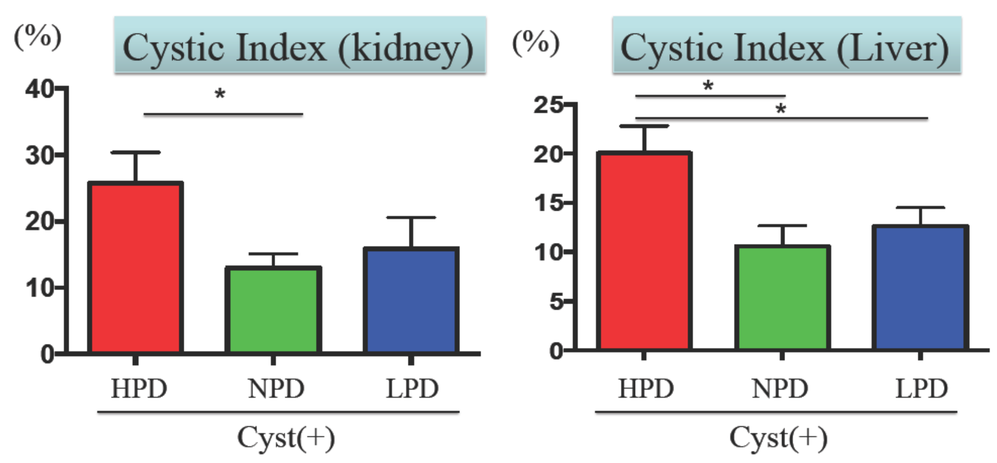


Fig 4. CI in kidney was significantly higher in HPD than NPD. CI in liver was significantly higher in HPD than NPD and LPD.

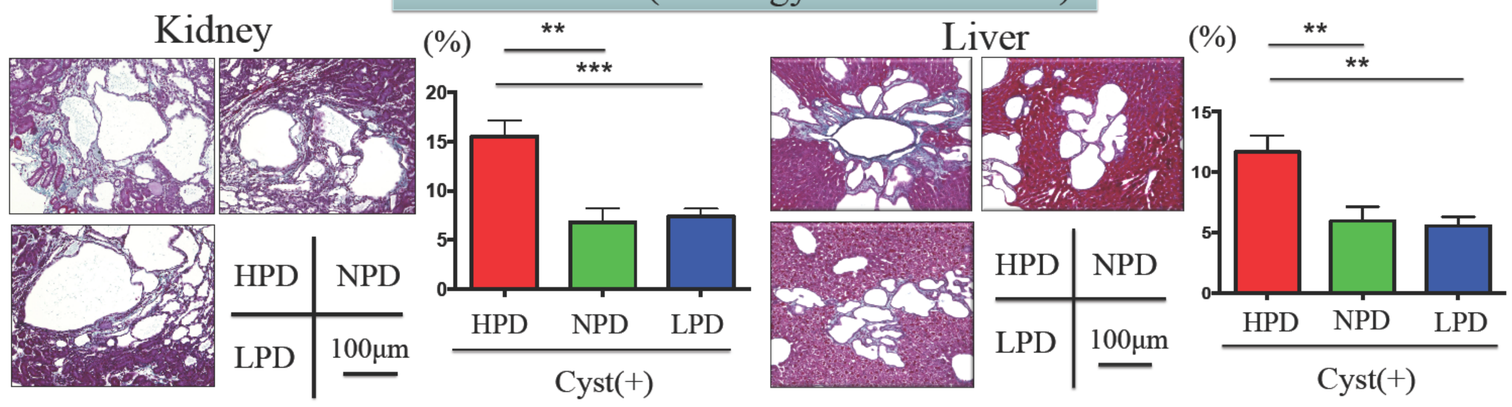


Fig 5. HPD developed more severe fibrosis compared with other groups in both kidney and liver.

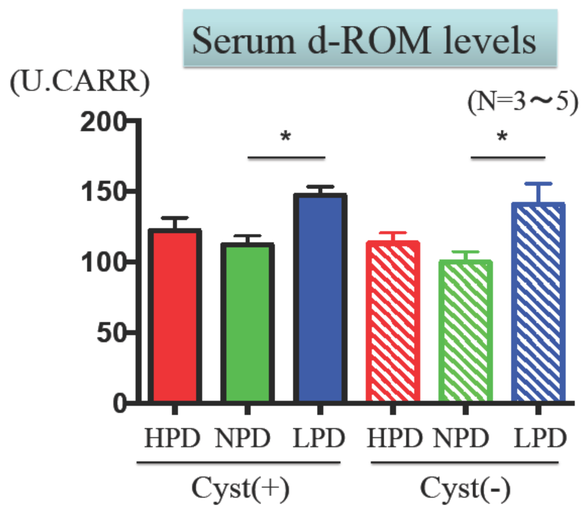


Fig 6. Serum d-ROM levels in LPD were significantly higher than NPD in both cystic mice and non-cystic mice.

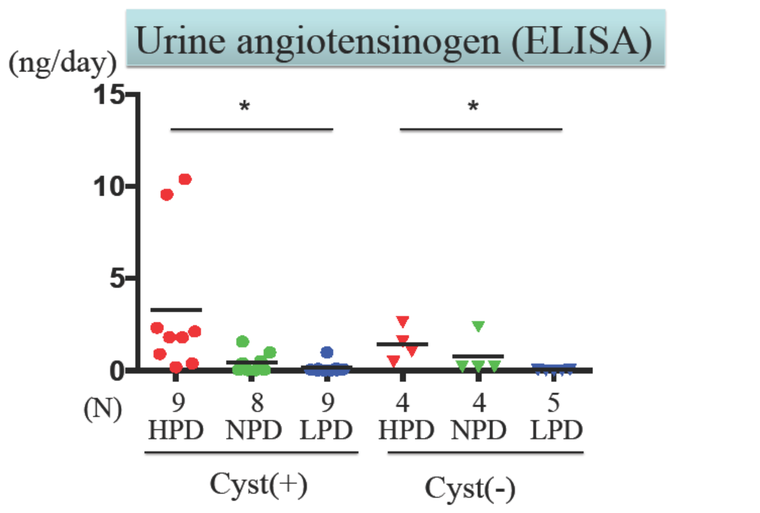
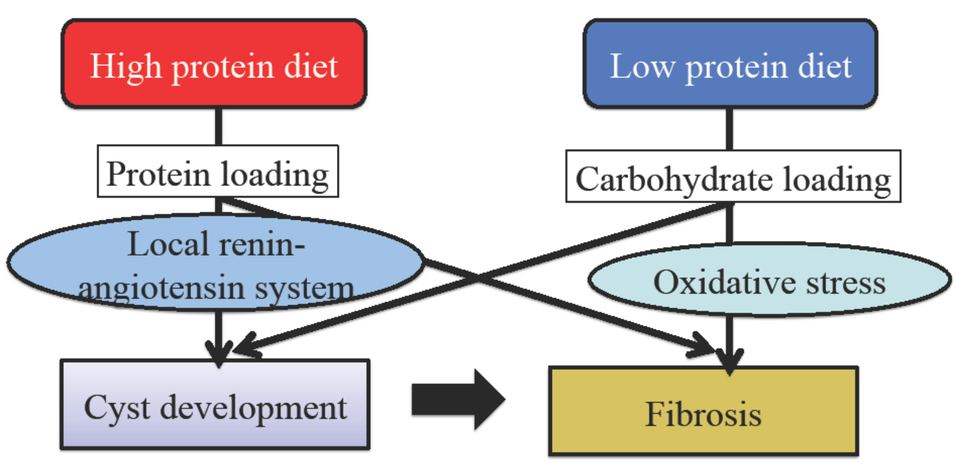


Fig 7. Urine angiotensinogen level was highest in HPD.

Data are expressed as Means ± SEM Unpaired t-test * p<0.05, **p<0.01,***p<0.001,****p<0.0001

DISCUSSION



CONCLUSION

✓ Excessive dietary protein loading accelerates disease progression in ADPKD.
✓ Low protein diet did not prevent disease progression presumably due to carbohydrate loading and elevating oxidative stress.

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52 ERA 48--FP
D) Genetic diseases and molecular genetics.
Junya Yamamoto
DOI: 10.3252/pso.eu.52era.2015
ePosters supported by F. Hoffmann- La Roche Ltd.
52nd ERA-EDTA CONGRESS London2015 UNITED KINGDOM MAY 28th
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