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Molecular mechanisms involved in renal injury-repair and ADPKD progression

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Stellingen

Behorend bij het proefschrift getiteld

Molecular mechanisms involved in renal injury-repair and ADPKD progression

Chiara Formica

1. Introduction of injury in the context of ADPKD can help to characterize the mechanisms involved in disease progression, particularly in the early phases of cyst initiation – This thesis.
2. Although the role of the Hippo pathway effector, YAP, in cyst initiation and growth is still controversial, its activation seems to be secondary to cyst expansion more than a driving force in cyst growth – This thesis.
3. Renal injury-repair and ADPKD progression are two extremely intertwined mechanisms, which not only are characterized by activation of similar molecular pathways but are also able to influence each other – This thesis.
4. In order to understand better and to treat PKD successfully, we not only need to identify the genes that are consistently dysregulated in cystic kidneys, but also define their temporal and mechanistic involvement in the different steps of disease progression – This thesis.
5. “Crystal deposition normally triggers a protective mechanism leading to temporary tubule dilation. In PKD, this mechanism acts as a third-hit trigger that causes such dilated tubules to “overshoot” to form cysts” – J.A. Torres *et al.* *J Clin Invest.* (2019) 129(10):4506–4522.
6. “Metabolic reprogramming is a prominent feature of cystic cells and a potentially important contributor to the pathophysiology of ADPKD” – Menezes, L.F., Germino, G.G. *Nat Rev Nephrol* (2019) 15, 735–749.
7. In the study of renal cyst formation and progression, close attention should be given to the role of the cystic microenvironment.
8. Even though cyst growth and cancer share several molecular mechanisms, the characteristic PKD biology seems to promote neoplastic cyst growth while preventing progression to invasive cancer.
9. Systemic changes to research culture are needed if we want the next generation of researchers to thrive – *Nature* (2019) 575, 257-258.
10. We should learn to view a negative result not as a failure but as the sign that we are asking the wrong questions.