



Animal Model Workshop

Generation and Characterization of a Mouse Model of Papillary Renal Cell Carcinoma (pRCC)

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September 11-13, 2025

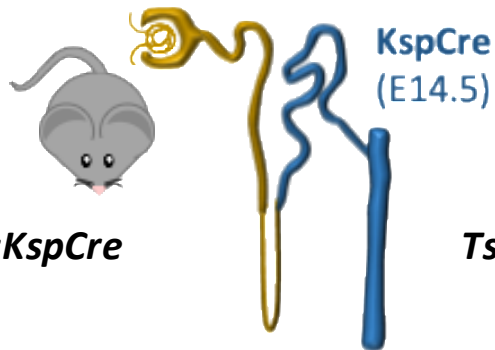
Session #4: GEMMs 2 (nccRCC models)



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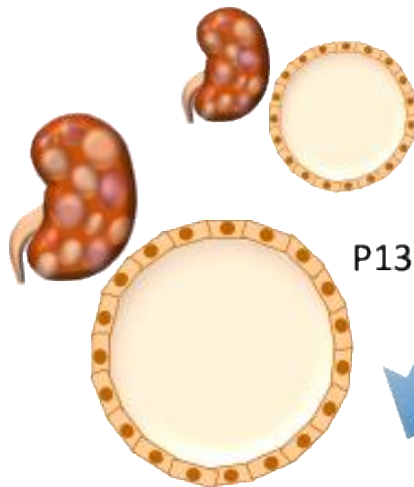
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Is mTORC1 sufficient to drive the PKD phenotype?



Pkd1^{flox/flox};KspCre

Tsc1^{flox/flox};KspCre



P0

P13

Early **cyst** formation highly dependent on PC1 (*Pkd1*) downregulation by mTORC1 (Pema et al., 2016 *Nat. Commun*)

P0



P20

Cyst epithelium transforms to **Renal Cell Carcinoma (RCC)** (Drusian et al., 2018 *Cell Rep.*)



P80



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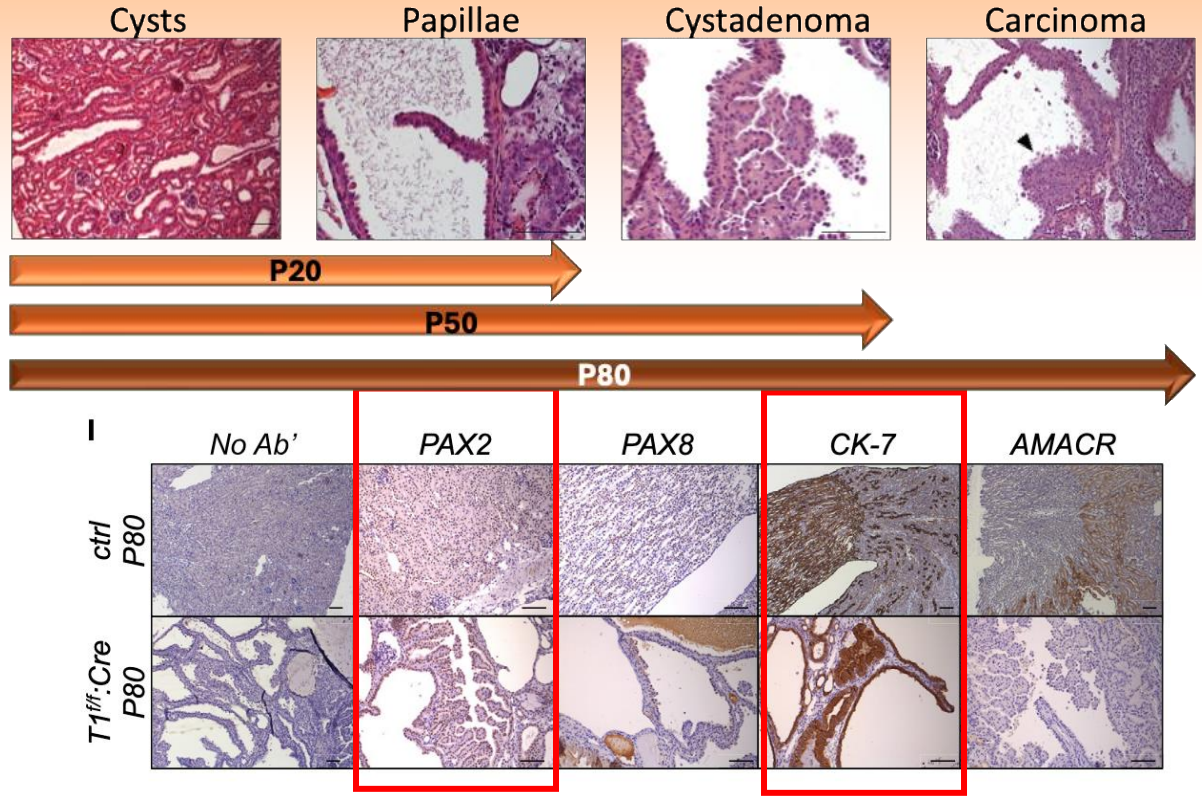
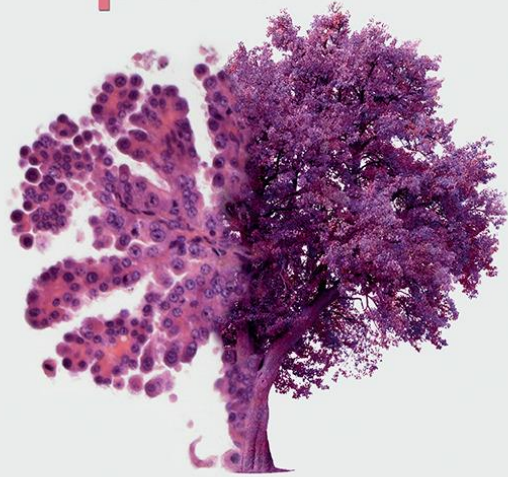
A Mouse Model of pRCC

**Cell
Reports**

Volume 24
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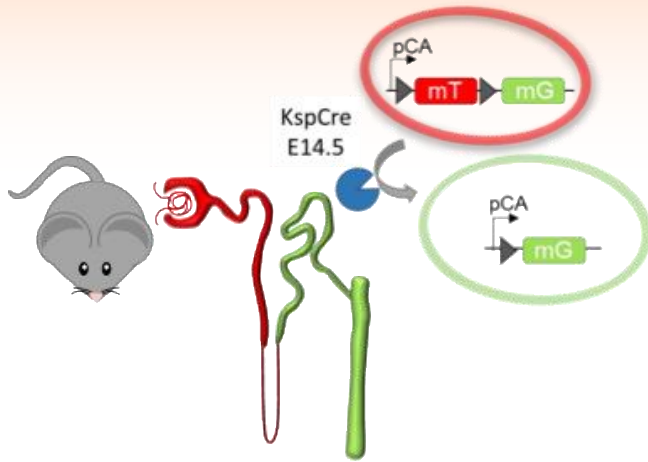


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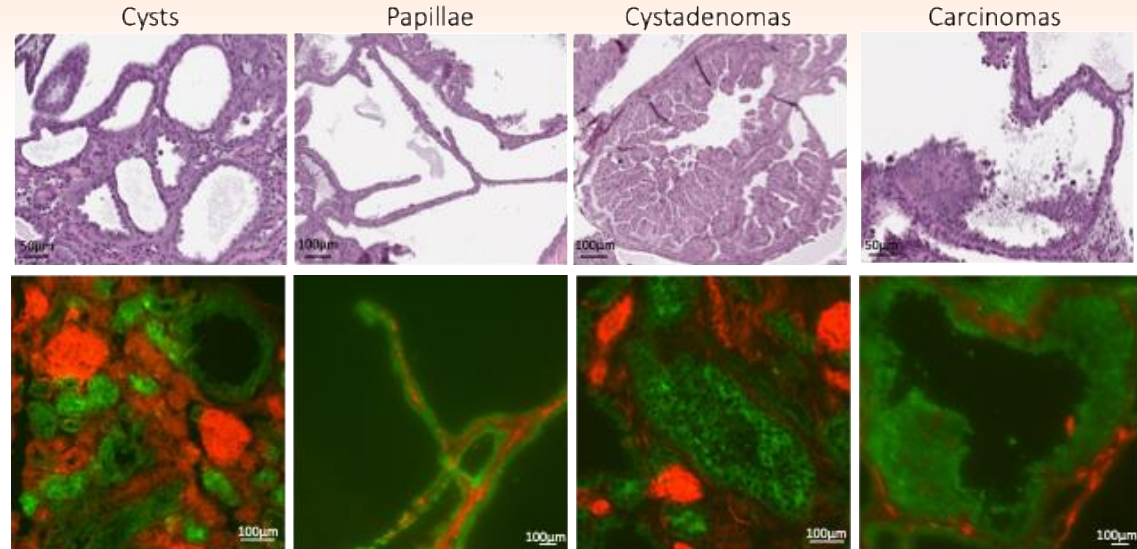
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Drusian et al, Cell Reports, 2018

What drives cyst transformation to pRCC?



Tsc1^{flox/flox};KspCre;mT/mG



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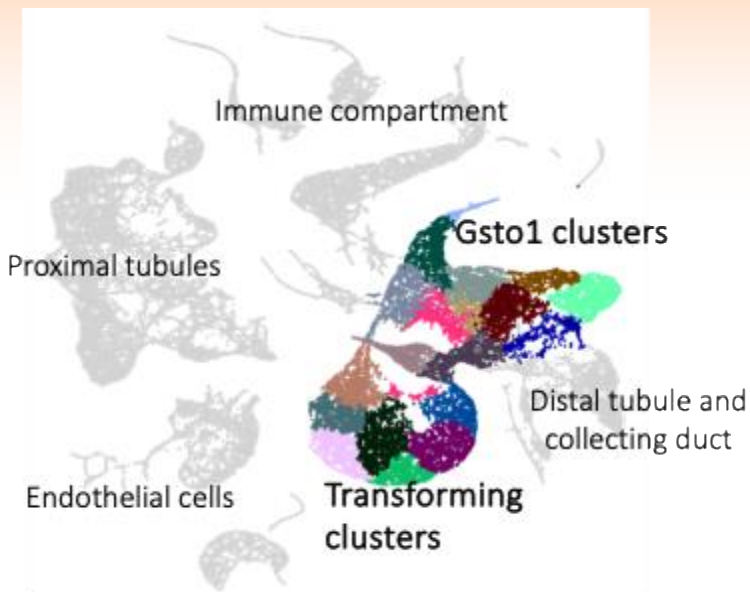
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Clerici, Spies et al, unpublished

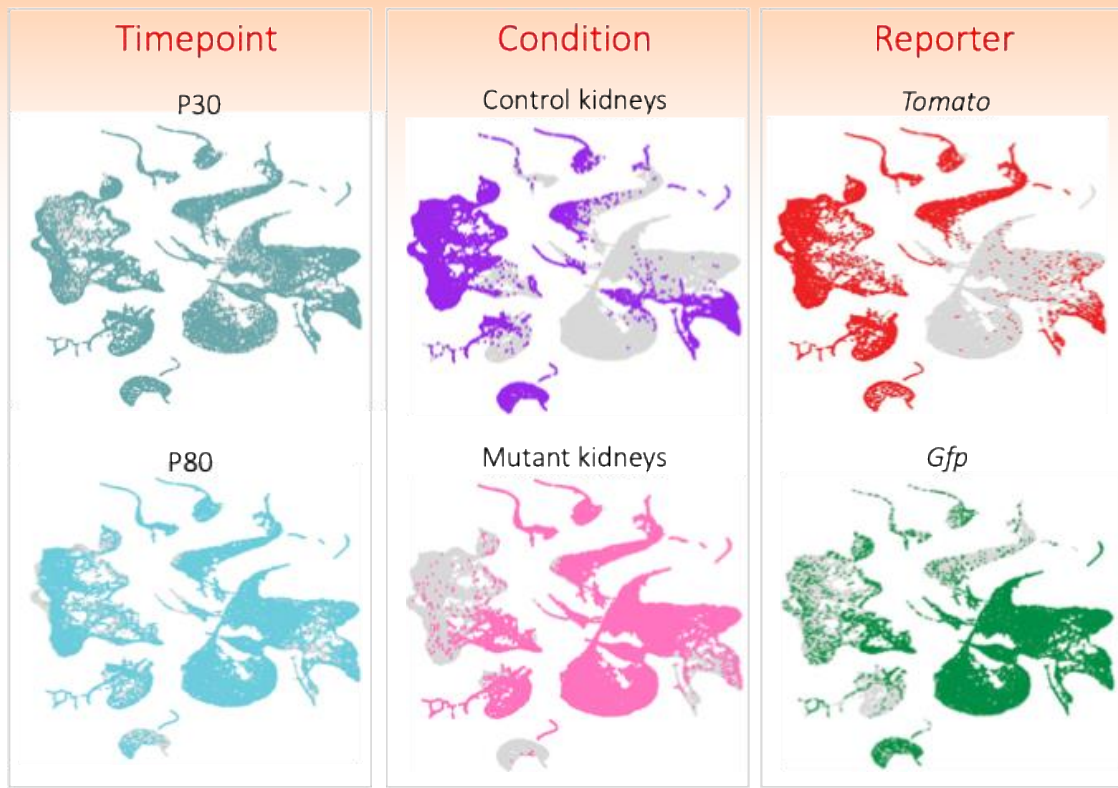
Identification of the transforming clusters

10X Genomics, 68,000 cells



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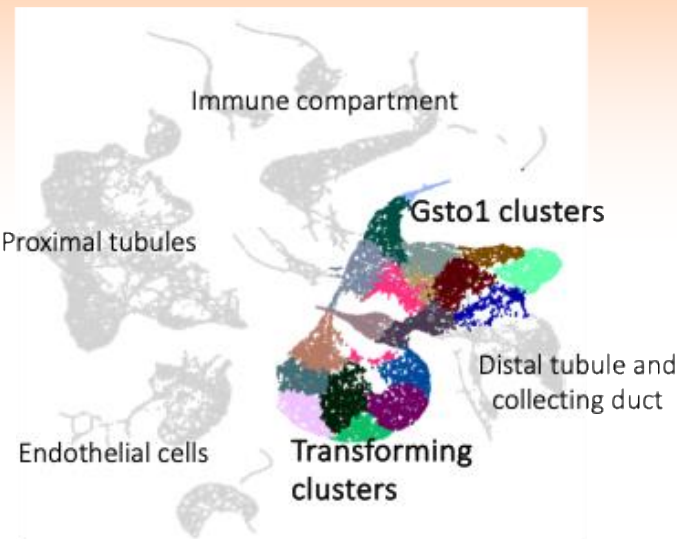


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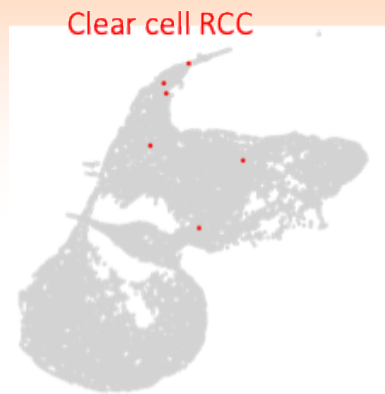
Clerici, Spies et al, unpublished

The transforming clusters carry a pRCC signature

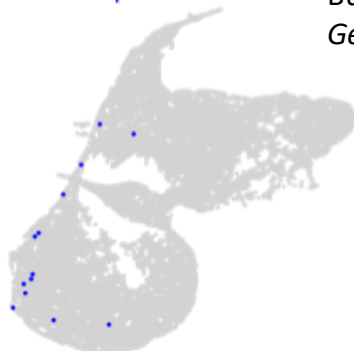


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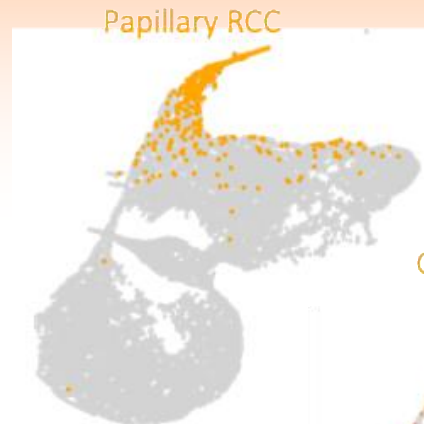


Chromophobe RCC



Clerici, Spies et al, unpublished

Büttner et al., 2022
Genome Medicine



Cystic cells



Barone et al., 2021 PNAS

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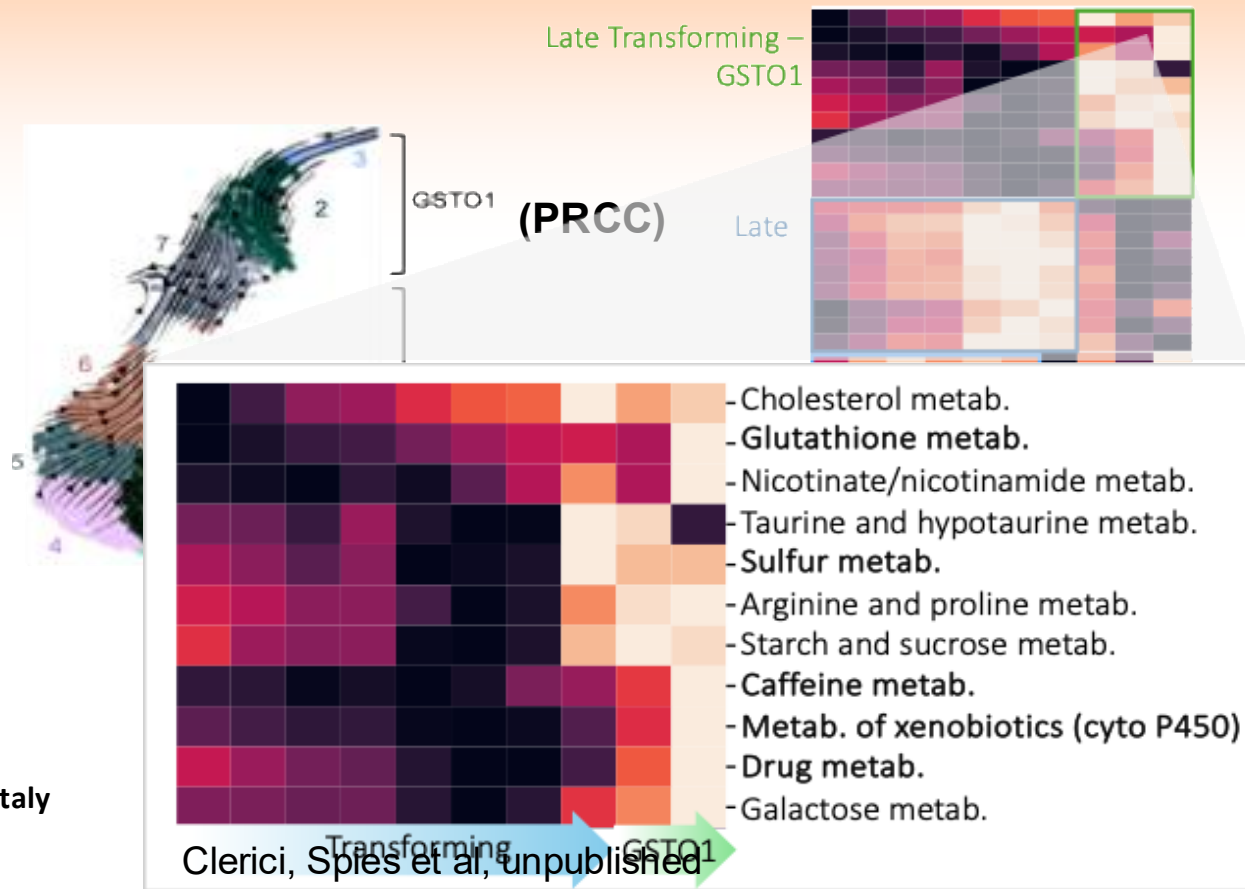
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Searching for drivers of transformation: metabolic rewiring

Papillary RCC



Cystic cells



Summary and Conclusions

- Inactivation of the **Tsc1 gene** using the kidney-specific cadherin16 minimal promoter results in **papillary RCC**
- The **phenotype is progressive** (cysts, cystadenomas, carcinomas) and **fully penetrant**
- Cysts both in Cortex and Medulla, **cancers only in cortex** and show markers of **papillary RCC**
- **scRNAseq** is being used to track the **evolution of cysts to cancer** to identify driving factors
- We are working towards identifying a **minimal signature** of genes that correlates with poor prognosis in KIRP in the TCGA atlas (not shown, in progress)

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Aknowledgements

Current Members

- **Matteo Borella**, Postdoc bioinfo
- **Silvia Caruso**, Technician
- **Laura Cassina**, Staff Scientist
- **Sara Clerici**, Postdoc
- **Francesco Consolato**, Postdoc
- **Melissa Danna**, Junior Technician
- **Gianfranco Distefano**, Senior Technician
- **Alessia Donato**, Postdoc bioinfo
- **Matteo Federici**, Project Manager
- **Martina Migliorero**, Postdoc
- **Kaalindi Misra**, Project Manager
- **Daniel Spies**, Postdoc Bioinfo
- **Davide Stefanoni**, Postdoc

Past Members

- **Christine Podrini**
- **Maddalena Castelli**
- **Marco Chiaravalli**
- **Luca Drusian**
- **Matteo Lampis**
- **Anne K. Nielsen**
- **Monika Pema**
- **Isaline Rowe**
- **Maria Elena Steidl**
- **Claas Wodarczyk**

Collaborators, Metabolism

- **Giovanna Musco**, OSR
- **Christian Frezza**, Cologne, Germany
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- **Angelo D'Alessandro**, Univ Colorado, USA
- **Ton Rabelink**, Leiden University, NL

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