

# Cyst Swelling Assays for ADPKD

A unique high content screening platform for  
Autosomal Dominant Polycystic Kidney Disease (ADPKD).



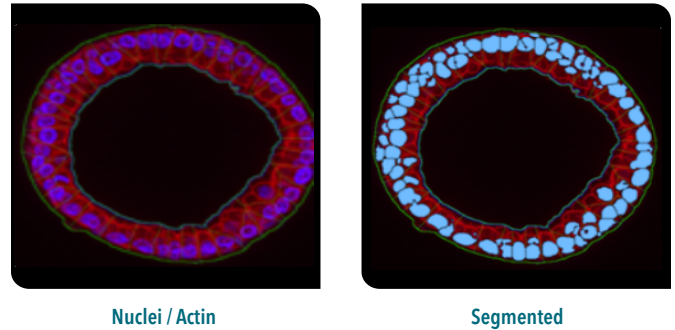
## Autosomal Dominant Polycystic Kidney Disease (ADPKD) and Cyst Swelling

Autosomal dominant polycystic kidney disease is a genetic disorder that causes many fluid-filled cysts to grow in the kidneys. Our ADPKD assays use changes in the cystic phenotype as primary readouts and is able to distinguish between cyst modulatory and toxic compounds in a 3D *in vitro* screening platform. This imaging-based 3D assay has a 384-well plate format which enables the recapitulation of the *in vivo* disease phenotype with robust functional readouts.

### Key Advantages:

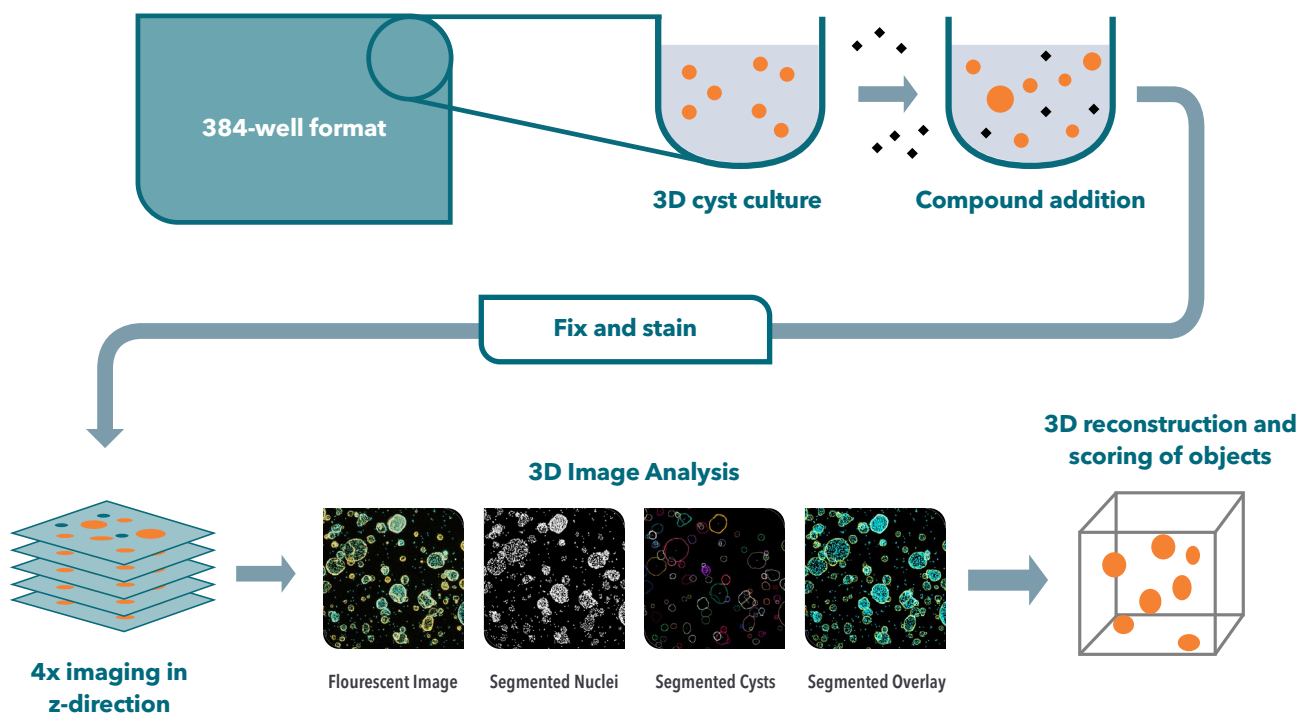
- High content phenotypic evaluation by 3D imaging
- Sensitive and robust functional readouts
- Separation of toxic compounds from effective compounds
- Optimal *in vitro* to *in vivo* translation
- Highly scalable assay format

### Cyst in 3D Culture



### Assay Principle

Following pre-culture, cells are seeded in an extracellular matrix in 384-well plates, where they spontaneously form cysts, typically within 1 to 4 days. Cysts can be stimulated by the addition of compounds that induce swelling, such as vasopressin or forskolin. Simultaneously, treatment to inhibit swelling is added for 48 to 96 hours.



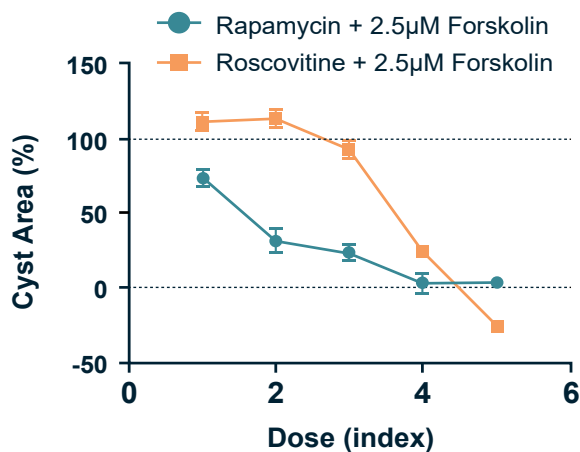
Setup can be customized depending on research questions.



## Models for ADPKD

### Murine Cell Line Model of ADPKD

- mIMCD3 cell line with knockdown of *Pkd1* spontaneously form cysts in 3D culture
- Swelling of these cysts can be stimulated with compounds like forskolin and prostaglandin E2
- Highly robust readout
- Ideal model for large-scale screening campaigns



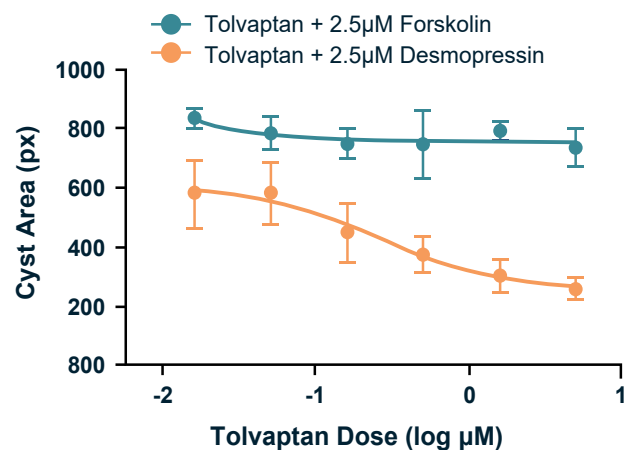
mIMCD3 *Pkd1*<sup>-/-</sup> cells were seeded in 3D and cysts formed after 4 days. These cysts were then exposed to forskolin and test compounds. 72h after exposure, cultures were fixed, stained, imaged and analyzed. Cyst area was normalized between solvent control (0%) and forskolin only (100%) (N = 4). Both rapamycin (teal) as well as roscovitine (orange) are able to inhibit the forskolin induced swelling.

### Discriminating Between Inhibition of Cyst Swelling and Toxicity

Analysis of multiple morphological features associated with inhibition of cyst swelling and cytotoxicity and nuclear toxicity enables the discrimination of compounds with high therapeutic potential (orange arrow) compared to those which are associated with adverse toxic responses (blue arrow).

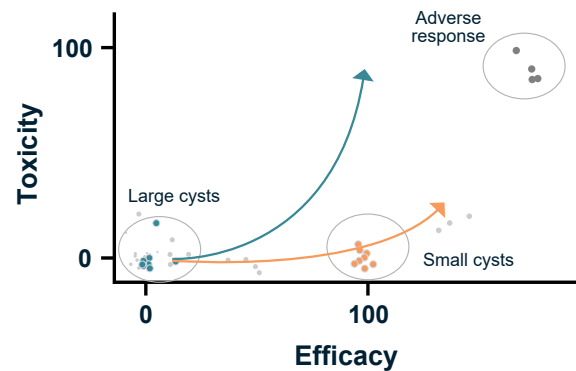
### ADPKD Patient-Derived Ex Vivo Cultures

- Tissue collected directly from the kidneys of ADPKD patients, spontaneously forms cysts in 3D culture
- Swelling of these cysts can be stimulated with compounds like vasopressin or forskolin
- Cultures are biobanked at low passage for compound testing
- Sufficient material available of each patient model for multiple campaigns



ADPKD patient cells were seeded in 3D and formed cysts after 24h. Standard of care tolvaptan was then co-exposed with either forskolin or desmopressin. 48h after exposure, cultures were fixed, stained, imaged and analyzed. Forskolin increased cyst area, however as expected, tolvaptan is unable to inhibit this (teal). Desmopressin similarly increased cyst area however upon increasing concentrations of tolvaptan, this is inhibited (orange). (N = 4, non normalized cyst area). These responses are similar to the *in vivo* situation.

### Swelling versus Cytotoxicity



## Get in touch



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