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miR-21 promotes cyst growth in polycystic kidney disease

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Autosomal dominant polycystic kidney disease (ADPKD) is characterized by the presence of numerous fluid filled cysts in the kidney. MicroRNAs (miRNAs), short non-coding RNAs that regulate gene expression, have emerged as promising new therapeutic targets for many diseases, but the role of these non-coding RNAs in ADPKD pathogenesis is still poorly understood. Here, we investigated the role of miR-21, an oncogenic miRNA, in kidney cyst growth. We found that transcriptional activation of miR-21 is a common feature of murine models of PKD. Furthermore, compared with renal tubules from kidney samples of normal controls, cysts in kidney samples from patients with ADPKD had increased levels of miR-21. cAMP signaling, a prominent pathogenic pathway in PKD, transactivated the miR-21 promoter in kidney cells and enhanced miR-21 expression in cystic kidneys of mice. Furthermore, genetic deletion of miR-21 reduced cyst burden, attenuated kidney injury and prolonged survival of an orthologous model of ADPKD. RNA sequencing analysis and additional in vivo studies showed that miR-21 inhibits apoptosis of cyst epithelial cells, likely through direct repression of its target gene programmed cell death 4 *(Pdcd4)*. Thus, miR-21 functions downstream of the cAMP pathway and promotes cyst growth in a mouse model of ADPKD. Our results suggest that inhibiting miR-21 is a potential new therapeutic approach to slow cyst growth in PKD.

Biography

Ronak Lakhia has completed her MD from University of Texas Southwestern Medical School in Dallas, TX in 2008. She has then completed her Residency in Internal Medicine at Baylor College of Medicine in Houston, TX. In 2012, she came back to University of Texas Southwestern Medical Center in Dallas for Nephrology Fellowship. After her clinical year, she joined Vishal Patel's laboratory where she is working on understanding the role of microRNA's in polycystic kidney disease. She has recently published her findings in the *Journal of American Society of Nephrology.*

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