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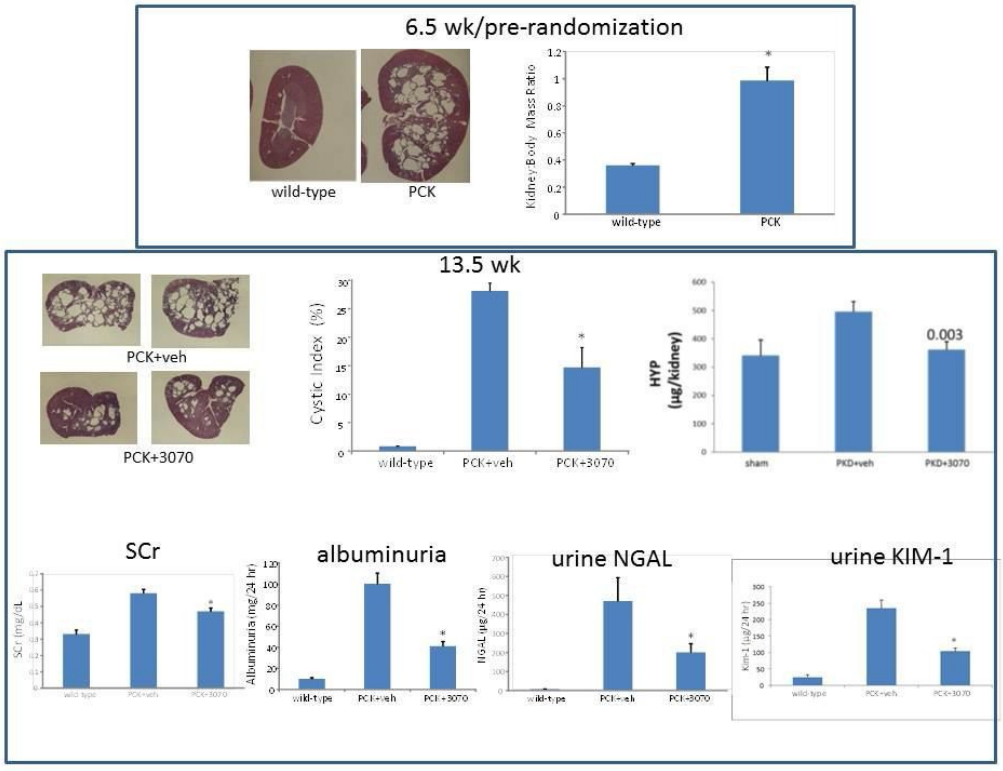
Therapeutic Effects of the Fibrokinase Inhibitor ANG3070 in Polycystic Kidney Disease

Background. Aberrant receptor tyrosine kinase signaling has been implicated in cyst expansion, renal interstitial fibrosis, increased kidney volume and reduced renal function in polycystic kidney disease (PKD). We investigated the effects of a novel, orally bioavailable, small molecule fibrokinase inhibitor, ANG3070, in experimental PKD.

Methods. Male PCK rats (PCK/CrljCrl-pkhd1pck/Crl) were rats were randomized to vehicle or ANG3070 (25 mg/kg, BID, PO) at 6.5 weeks of age following confirmation of frank disease and sacrificed at 13.5 weeks. Age-matched male Sprague-Dawley rats served as wild-type controls.

Results. ANG3070 has no effect on mean arterial pressure. In PCK rats with diseased kidneys (figure1), randomization to ANG3070 treatment was therapeutic, reducing cystic index, renal interstitial fibrosis (hydroxyproline (HYP), albuminuria and other urine biomarkers of renal injury and serum creatinine [figure1].



Conclusions. With ongoing investigational new drug enabling toxicology studies suggesting a large safety index, these data support the continuing development of ANG3070 for PKD, a disease currently without cure. Supported by PR130909 and AR058041-02.