INTRODUCTION

Autosomal dominant polycystic kidney disease is an inherited systemic disorder with major renal manifestations and, in some cases, abnormalities in the liver, the pancreas, the brain, the arterial blood vessels, or a combination of these sites.***(Torres and Grantham 2008).***

The disease affects approximately 300,000 to 600,000 Americans of either sex, and without racial predilection. Each child of an affected parent has a 50% chance of inheriting the mutated gene, which is completely penetrant. Autosomal dominant polycystic kidney disease arises as a spontaneous mutation in approximately 5% of cases. However, in about one fourth of newly diagnosed cases, patients report no history of the disease, indicating that many familial cases go undetected.***(Grantham 2008).***

In rare cases, a malignant neoplasm develops, although the incidence of renal cancer among affected patients is not increased, as compared with the incidence in the general population. ***(Igarashi and Somlo 2002).***

Autosomal dominant polycystic kidney disease begins in utero, but signs of the disease may not be detected for several decades. Autosomal dominant polycystic kidney disease is caused by mutations in either of the two genes encoding plasma membrane–spanning polycystin 1 and polycystin 2 *(PKD1* and *PKD2*), respectively.The polycystins regulate tubular and vascular development in the kidneys and other organs (liver, brain, heart, and pancreas) ***(Igarashi and Somlo 2002).***and

interact to increase the flow of calcium through a cation channel formed in plasma membranes by polycystin 2. A mutation of either polycystin can disrupt the function of the other, resulting in similar clinical presentations. However, mutations of *PKD1* are more common than mutations of *PKD2* (accounting for 85% of cases), are likely to be associated with more renal cysts, ***(Grantham et al. 2006)***and lead to renal insufficiency on average 20 years earlier (median ages at the time of death or end-stage failure, 53 and69 years, respectively).***(Hateboer et al.1999).***

In adults with a positive family history, the diagnosis of autosomal dominant polycystic kidney disease is established by radiologic evidence of bilateral, fluid-filled renal cysts. Ultrasonography reliably detects cysts that are 1 cm or larger in diameter and is highly sensitive for the diagnosis in adults. ***(O'Neill et al.2005).***

Autosomal dominant polycystic kidney disease can be caused by hundreds of different intragenic *PKD1* and *PKD2* mutations. Since current genotype testing can identify only approximately 70% of the known pathogenic mutations, it is not a useful screening tool.***(Zhao et al.2008).***

The new kids on the block For more than three decades, autosomal dominant polycytic kidney disease (ADPKD) researchers around the globe, spurned by millions of affected patients, have tried to elucidate the mechanisms that lead to cyst formation and progression of renal failure in this heterogenetic disease. It was not until recently that realistic therapeutic interventions have come within reach. This editorial will briefly summarize the key findings that led the researchers to test vasopressin-2-receptor antagonists (V2RA) and mammalian targets of rapamycin (mTOR) inhibitors in animal models of

polycystic kidney disease, and will highlight why these therapeutic avenues might be more promising and fortunate than their predecessors.*(Gerd Walz 2006).*