Project proposal template
Summer 2015

Project title	Molecular Mechanisms of Polycystic Kidney Disease
First Supervisor	Dr — Paraskevi Goggolidou
Second Supervisor	Dr Mark Carew
School	Life Sciences
Other member of supervisory team (no more than three KU supervisors in total)	
Specific requirements beyond 2:1 degree	Experience in Molecular Cell biology techniques would be advantageous.

Project summary

(max 4,000 characters)

Cystic renal diseases are a common cause of end-stage renal disease and organ failure. They may be genetic or epigenetic in origin and are characterized by dilation of renal tubules, cyst formation and progressive loss of renal function with patients requiring renal replacement therapy (dialysis or transplantation). Autosomal Recessive Polycystic Kidney Disease (ARPKD) is a genetic disorder with an incidence of 1:20,000-1:40,000 and is a common cause of perinatal death. It manifests as extreme bilateral enlargement of cystic kidneys in utero, associated with hepatic ductal plate abnormalities and pulmonary hypoplasia. ARPKD is caused by mutation in *PKHD1* which encodes Fibrocystin, which is required for normal ureteric bud and liver ductal plate branching morphogenesis. Another form of polycystic kidney disease, autosomal dominant polycystic kidney disease (ADPKD) is caused by mutations in *PKD1* or *PKD2* that encode PC-1 and PC-2. PC-1, a membrane receptor that localizes to primary cilia in renal epithelial cells, interacts with β-catenin. PC -2, a calcium-permeable channel protein, also localizes to primary cilia and interacts with PC-1. Fibrocystin interacts with PC-1 and -2 at the cell and ciliary membranes, putatively acting as a mechanosensory receptor.The proposed project will address the molecular and cellular interactions between the three key proteins whose loss of function leads to polycystic kidney disease, aiming to provide insights into the molecular mechanisms of PKD and eventually lead to better diagnosis, prognosis and treatment.