

## **The role of planar cell polarity in folic acid-induced nephropathy**

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The planar cell polarity (PCP) pathway is critical for kidney organogenesis. However, less is known regarding the role of PCP in renal disease. To explore this, we examined PCP in a mouse model of acute renal injury induced by folic acid (FA). FA administration to wild-type mice resulted in damage to renal tubules within two days and by fourteen days there was incomplete healing of the kidney evidenced by patchy interstitial fibrosis, tubule atrophy and inflammation. Using qRT-PCR we found that mRNA levels of 3 core components of the PCP pathway (*Celsr1*, *Scrib* and *Vangl2*) were significantly ( $p < 0.001$ ) upregulated at 14 days in FA-treated mice compared with vehicle controls. The basal localisation of *Celsr1* and *Scrib* in tubules was also disrupted following FA administration at both 2 and 14 days. Next, we examined whether the severity of folate nephropathy was altered in heterozygous *Looptail* mice that have a point mutation in *Vangl2* (*Vangl2<sup>Lp/+</sup>*) which leads to a general disruption in PCP signalling. Renal function was not different between *Vangl2<sup>Lp/+</sup>* (n=7) or wild-type littermates (n=5) at either 2 or 14 days following FA administration as assessed by blood urea nitrogen and serum creatinine levels. However, there was a significant ( $p = 0.017$ ) increase in renal fibrosis in *Vangl2<sup>Lp/+</sup>* mice compared with wild-types as assessed by quantification of Sirius red staining. In conclusion, our data suggests that folate nephropathy is more severe in *Vangl2<sup>Lp/+</sup>* mice indicating a potentially protective role of the PCP pathway in kidney disease.