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**Man – Midge – Molecule: Studying the pathogenic mechanisms of uric acid urolithiasis and ADTKD-SEC61A1 at the organismal and cellular level**

Putting emphasis on the pathogenesis of different kidney diseases, we study the molecular mechanisms that cause kidney stone formation (urolithiasis) or autosomal dominant tubulointerstitial kidney disease (ADTKD). Regarding urolithiasis and its multifactorial etiology, we employ a top-down approach based on the invertebrate model Drosophila melanogaster to search for genetic and pharmacological components modulating the ectopic biomineralization of uric acid. In addition, we aim to identify the underlying pathological feature of a monogenetic kidney disease called ADTKD-SEC61A1. Two heterozygous mutations in the SEC61A1 gene are known to cause ADTKD. The SEC61A1 gene is ubiquitously expressed and encodes a polytopic membrane protein of the endoplasmic reticulum called Sec61α. In this case, we use a bottom-up approach based on renal cells carrying one of the heterozygous SEC61A1 mutations to characterize aberrant functionality of the mutant Sec61α protein that could explain the renal manifestation and the ADTKD-SEC61A1 phenotype.