Abstract

Background: Cystinuria is a debilitating condition that leads to recurrent painful cystine calculi that, when mismanaged, can lead to chronic kidney disease. It is caused by a mutation in the cystine transporter of the proximal convoluted tubule of the kidney. Failure to reabsorb cystine from the glomerular filtrate allows it to crystallise and form calculi. The cystine transporter is made up of two subunits: $b^{0,+}$AT and rBAT, encoded for by the genes SLC7A9 and SLC3A1 respectively.

Objectives: This project investigated the M467T, G458A and T471R mutants of the SLC3A1 gene for rBAT by performing biotinylation, immunoprecipitation and immunofluorescence experiments on human proximal tubular epithelial cells.

Results: The results showed that the M467T and G458A mutations cause trafficking defects in the rBAT protein, meaning the rBAT fails to heterodimerise with $b^{0,+}$AT and traffic to the membrane, hindering the cells ability to take up cystine. This builds on knowledge about the M467T mutant from previous study in *Xenopus Oocytes*, and adds new understanding about the novel G458A mutant. It is likely that the T471R mutant of the SLC3A1 gene also causes a trafficking defect in the rBAT protein, however further biotinylation studies will be needed to confirm this.

Conclusions: The project used a robust molecular model to study cystinuria, bringing the understanding of the disease forward by revealing that the M467T, G458A and T471R mutations of the SLC3A1 gene for the rBAT protein likely cause trafficking defects.