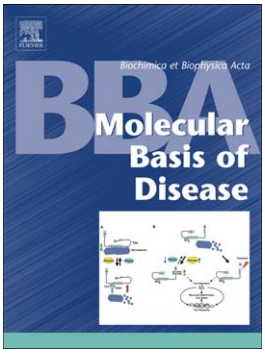

Genetics and mechanisms of hepatic cystogenesis

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Title

Genetics and mechanisms of hepatic cystogenesis

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Abstract

Polycystic liver disease (PLD) is a heterogeneous genetic condition. *PKD1* and *PKD2* germline mutations are found in patients with autosomal dominant polycystic kidney disease (ADPKD). Autosomal dominant polycystic liver disease (ADPLD) is associated with germline mutations in *PRKCSH*, *SEC63*, *LRP5*, and recently *ALG8*, and *SEC61*. *GANAB* mutations are found in both patient groups. Loss of heterozygosity of PLD-genes in cyst epithelium contributes to the development of hepatic cysts. A genetic interaction network is implied in hepatic cystogenesis that connects the endoplasmic glycoprotein control mechanisms and polycystin expression and localization. Wnt signalling could be the major downstream signalling pathway that results in hepatic cyst growth. PLD in ADPLD and ADPKD probably results from changes in one common final pathway that initiates cyst growth.

Abbreviations

AAV – adeno-associated virus

ADPLD – autosomal dominant polycystic liver disease

ADPKD – autosomal dominant polycystic kidney disease

CNN – copy-number neutral

CRISPR/Cas9 – clustered regulatory interspaced short palindromic repeats associated RNA-guided Cas9