May 2007 - Knowledge Integration Module

The role of collecting ducts vasopressin V2 receptors in health and disease

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Work by Torres et al. (Torres VE, Wang X, Qian Q, Somlo S, Harris PC, Gattone VH: Effective treatment of an orthologous model of autosomal dominant polycystic kidney disease. Nat Med 10: 363-364, 2004) have suggested that renal cyclic AMP levels (a) and expression of Avpr2 and Aqp2 (b) are increased in polycystic mice and effectively treated with vasopressin V2 receptor non-peptide antagonist OPC 31260 (OPC).

Your goal is to apply these initial findings to human patients with autosomal dominant polycystic kidney disease but you would like to confirm the initial findings of Torres et al. obtained in mice in the PCK rat model.

Tasks

1. Rather than using a V2 non-peptide antagonist, you are proposing to intercross PCK rats with homozygous Brattleboro rats (hereditary central diabetes insipidus rats with a mutation in the AVP gene). Describe the experimental protocol, signaling and microscopic measurements you are planning as well as expected results.

2. In collaboration with pharmaceutical industries developing non-peptide V2 antagonists you are willing to test whether a V2 antagonist will decrease kidney volume progression in polycystic kidney disease. Total kidney volume in relation to age is described by the following graph. Will you choose patients A, B, or C to test your V2 antagonist?

Reference