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## Abstract Submission No.: A-0852

# Establishment of a rapidly progressing ADPKD model and verification of the effect of an AMPK activator (HL156A)

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**Objectives :** Autosomal dominant polycystic kidney disease (ADPKD) is the most common genetic kidney disease. Metformin has been found to inhibit cyst growth in animals with ADPKD through AMPK activation, but it is not effective in humans due to its low potency. In this study, the effect of the AMPK activator HL156A, which is over 10 times more potent than the existing Metformin, was confirmed in the ADPKD KO mouse model.
**Methods :** We created PKD1-KO mice by crossing two types of B6 mice ($PKD1^{flox/flox}$ and AQP2-Cre). The effects on cyst inhibition and BUN preservation were observed in the PKD1 KO mice models using Sham as the control and 15 mg and 25 mg of the AMPK activator from D2 to D28.
**Results :** In the PKD1-KO mice, a rapid increase in the number of renal cysts was confirmed from the P7 period. When a PKD1 female and an AQP2 male or a PKD1 male and an AQP2 female were crossed, there was no difference in the number of litters between the two groups (mean number of litters = 5.6+-1.5, P<0.584). In the PKD1-KO model the cyst inhibition effect was observed in a dose-dependent manner in the early model (TKV/BW reduction rate: 15 mg, 16%; 25 mg, 32%). Also, the preservation effect of BUN was observed (130.56±9.36, 101.63±6.10 and 102.93±8.03, respectively). The protein level of p-AMPK was increased by HL156A, while α-SMA and pERK1/2 were decreased.
**Conclusions :** HL-156A was identified as a drug capable of preserving the kidney function by inhibiting cyst proliferation.

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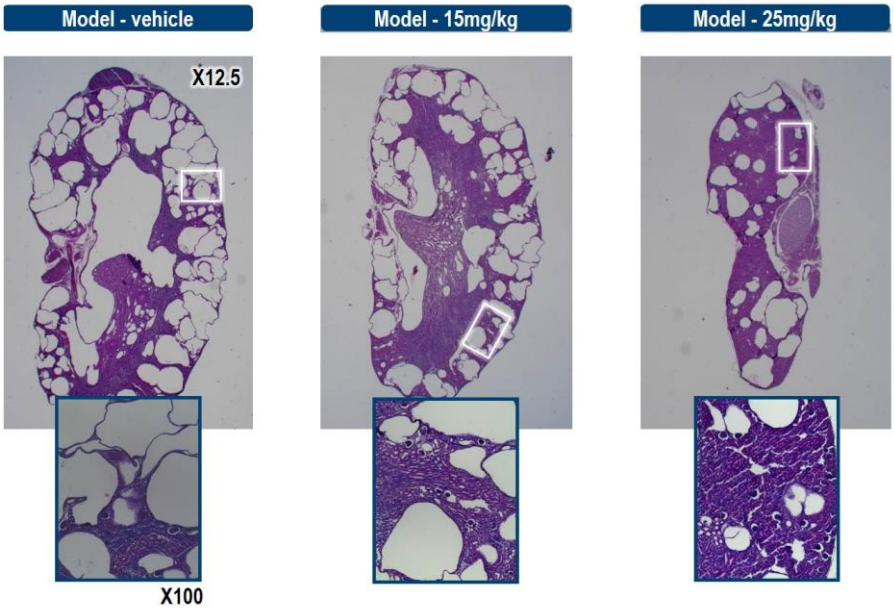

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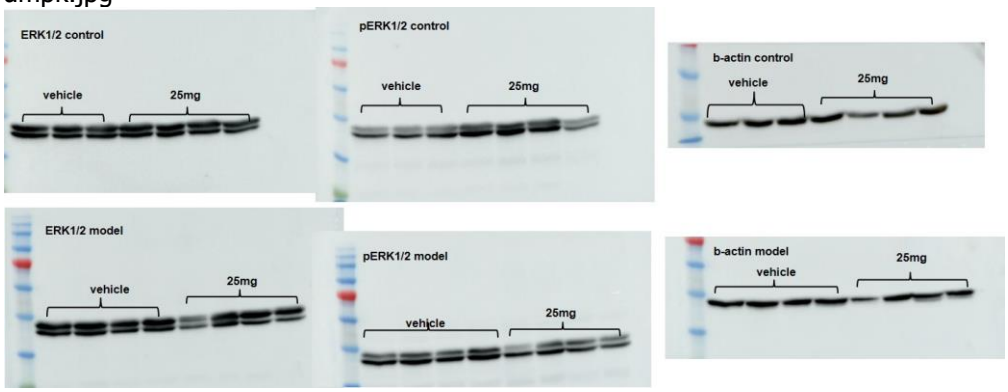
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