Supplemental materials

Note

Role of CYP3A in isoniazid metabolism in vivo

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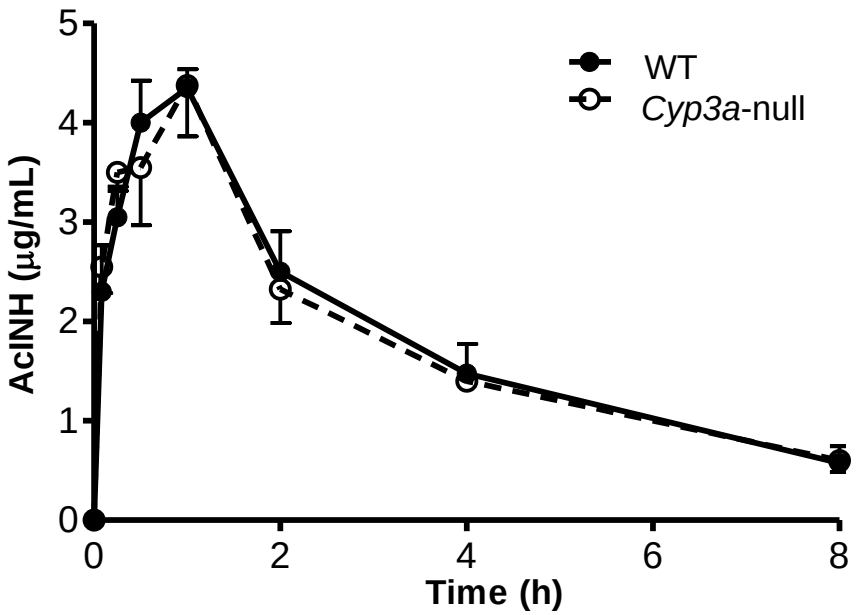
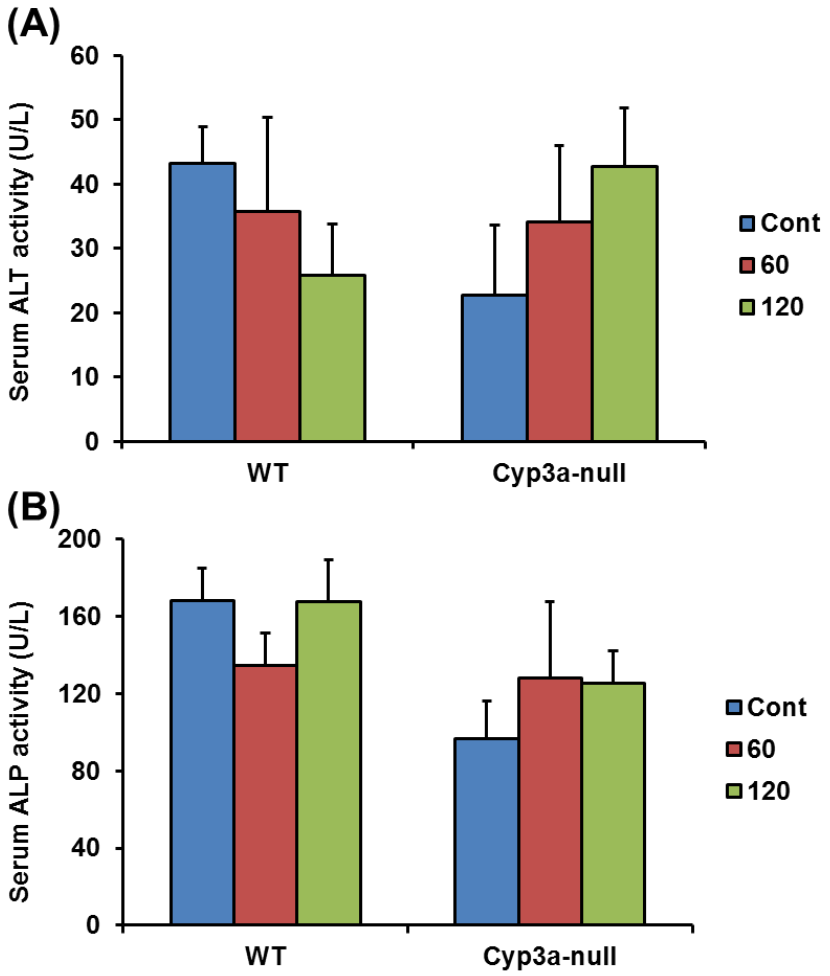
Supplemental table 1. Pharmacokinetic parameters of INH and AcINH. WT and *Cyp3a*-null mice were treated with 50 mg/kg INH. Blood samples were collected after INH treatment and analyzed by UPLC-QTOFMS. Pharmacokinetic parameters were generated by WinNonlin. Data are expressed as mean ± S.D., n=4.

	INH		**AcINH**	
	WT	***Cyp3a*-null**	**WT**	***Cyp3a*-null**
T_{max} (h)	0.2 ± 0.2	0.2 ± 0.1	0.9 ± 0.3	1.0 ± 0.0
C_{max} (µg/ml)	63.0 ± 6.8	70.6 ± 6.5	4.4 ± 0.1	4.4 ± 0.5
$AUC_{0\text{-}8h}$ (h·µg/ml)	94.1 ± 6.1	84.6 ± 8.6	15.0 ± 1.1	14.5 ± 0.7
$T_{1/2}$ (h)	1.0 ± 0.2	1.2 ± 0.2	2.8 ± 0.9	3.2 ± 0.6
CL (ml/h/kg)	533.0 ± 35.0	596.0 ± 65.0	_	_



Supplemental figure 1. Serum concentration-time curve of AcINH. WT and *Cyp3a*-null mice were treated with a single oral dose of 50 mg/kg INH. Blood samples were obtained at 0.083, 0.25, 0.5, 1, 2, 4, and 8 h after administration. AcINH was analyzed by UPLC-QTOFMS. Data are expressed as means ± S.D., n = 4 at each time point.



Supplemental figure 2. **Serum ALT (A) and ALP (B) activities.** WT and *Cyp3a*-null mice were treated orally with 60 or 120 mg/kg INH. Blood samples were obtained at 18 h after administration. The data are expressed as means ± S.D., n = 3 or 4.