Supplemental Figures

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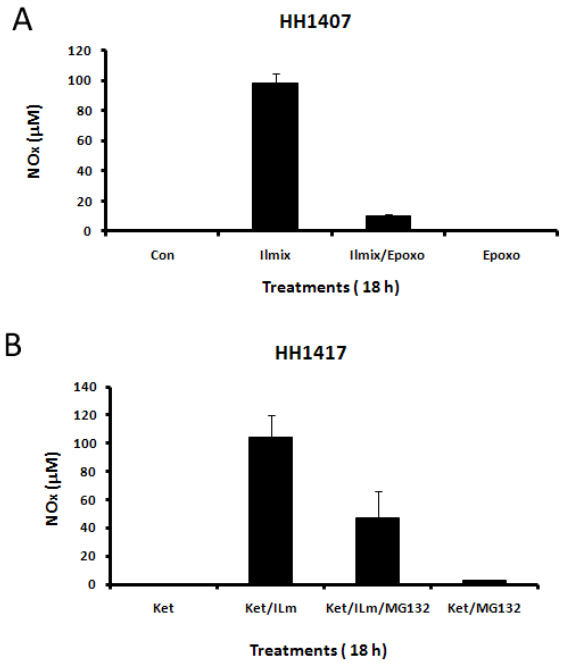
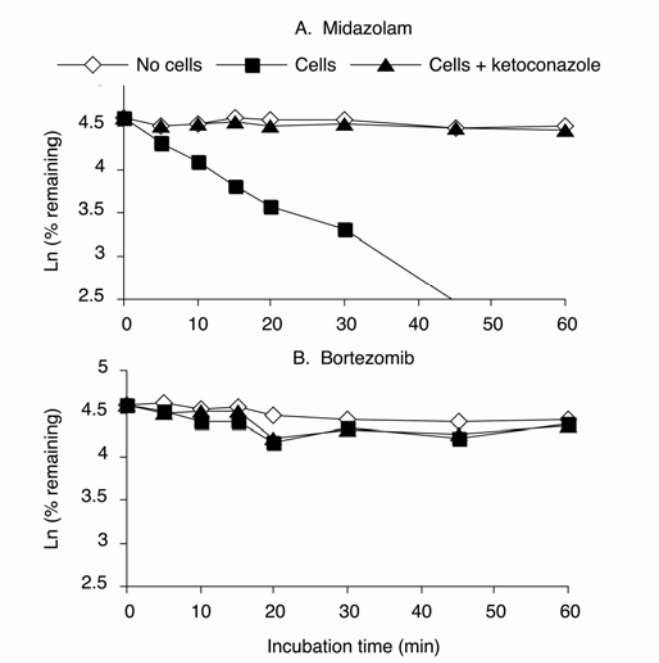
Metabolism and Action of Proteasome Inhibitors in Primary Human Hepatocytes
Drug Metabolism and Disposition



Supplemental Fig. 1. NOx production of primary human hepatocytes and its inhibition by proteasome inhibitors. Primary human hepatocytes were cultured for 3 days after delivery, and treated with 1 mM PB for an additional 2 days. PB was maintained in the media during treatments. A. Hepatocytes (HH1407) were treated with ILmix, epoxomicin (Epoxo, 10 mM), or both for 18 h, and NOx was measured in the media. B. HH1417 cells were treated with ketoconazole (ket, 10 mM) and indicated combinations for 18h and media were collected for NOx measurement.



Supplemental Figure 2. Metabolic stability of midazolam (A) and bortezomib (B) using cryo-preserved primary human hepatocyte cultures. Aliquots of the media were taken at 0, 5, 10, 15, 20, 30, 45 and 60 min for analysis, and the quenched samples were analyzed on LC/MS/MS. Ketoconazole (1µM) was used as a competitive inhibitor of CYP3A4.