Supplemental Figure legends

Supplement Figure 1. Lung compliance after inhalation injury. Lung compliance (C) **(A)** and an estimate of inspiratory capacity (A) **(B)**, were increased in C57BL/6 mice 14 and 21 days post Br_2 (400ppm, 30min) gas exposure (n=5-9). Values are means ± SEM. **P* < 0.05 versus air exposed mice by one-way ANOVA followed by Tukey post hoc test.

Supplement Figure 2. Inhibition of ER stress prevents lung hyperinflation after inhalation injury. Lung compliance (C) **(A)** and an estimate of inspiratory capacity (A) **(B)** were measured in C57BL/6 mice 14 days post exposure to either air or Br_2 (400ppm, 30min) and then treated with either DMSO or the ER stress inhibitor, salubrinal. (n=5-6). Values are means ± SEM. **P* < 0.05 versus air + DMSO treated mice and $^{\dagger}P$ < 0.05 versus Br_2 + DMSO treated mice by one-way ANOVA followed by Tukey post hoc test.

Supplement Figure 3. $ATF4^{+/-}$ mice have lower lung volumes after inhalation injury. Lung compliance (C) **(A)** and an estimate of inspiratory capacity (A) **(B)**, were measured in wild type (WT) or ATF4 haplo-deficient ($ATF4^{+/-}$) mice 14 days post exposure to either air or Br_2 (400ppm, 30min). (n=5). Values are means ± SEM. **P* < 0.05 versus WT+air, $^{\dagger}P$ < 0.05 versus WT+Br_2 by one-way ANOVA followed by Tukey post hoc test.

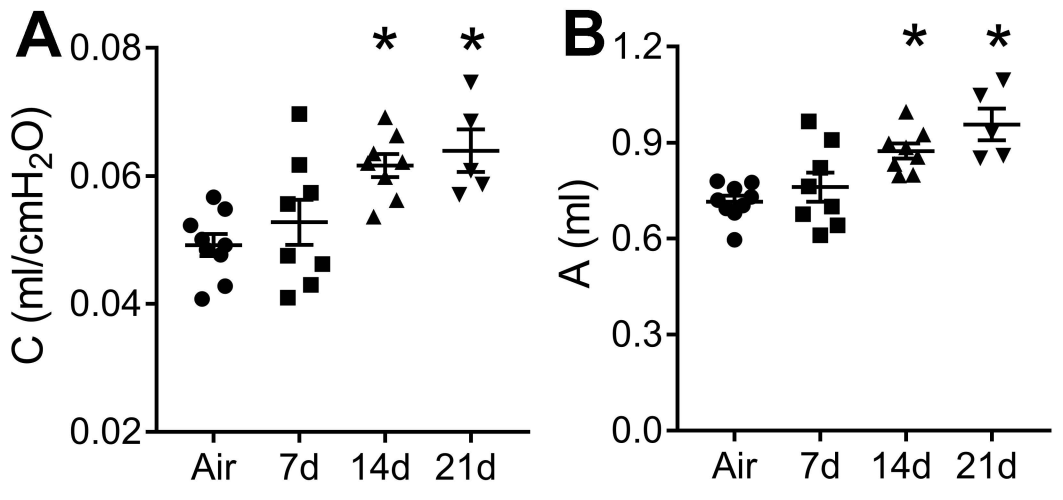
Figure 4. Endoplasmic reticulum stress (ER stress) *in vitro* post Br_2 exposure. Immunoblot analysis showed that exposure of the human bronchial epithelial cells to Br_2

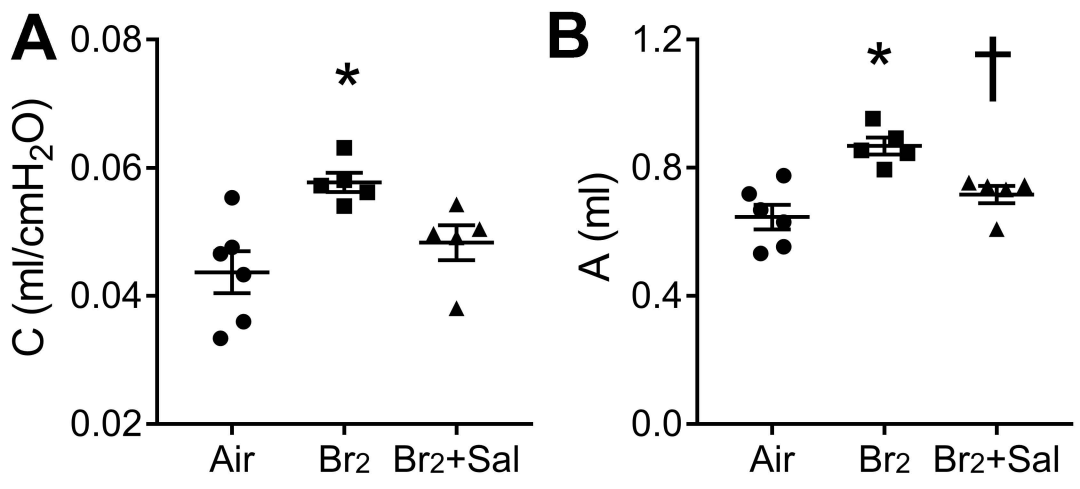
(100ppm, 10 min), increased ER stress marker, ATF4, at 6 and 24 hours post exposure, but did not alter cellular Grp78 or CHOP levels (n=3).

Supplement Figure 5. Plasma hemopexin (Hx) levels in mice. Male C57BL/6 mice were injected with purified human Hx (4μg/g BW for a total of 100μg, IM, BW was 25gm) 1hr post air or Br_2 exposure. Plasma bioavailability of **human Hx** at different times after injection was same after air or Br_2 (n=3) **(A)**. Male C57BL/6 mice were exposed to air or Br_2 gas (400ppm, 30mins) and returned to room air. Plasma levels of **mouse Hx** were measured in mice on days 1, 7, 14, or 21 post Br_2 exposure (n=6-16) **(B)**. Male C57BL/6 mice were exposed to air or Br_2 gas (400ppm, 30mins) and then returned to room air. Some Br_2 exposed mice were given an intraperitoneal injection of purified human hemopexin (Hx) (4μg/g BW) 1 hour post Br_2 exposure. All air exposed mice and some Br_2 exposed mice received saline injection as an appropriate control. Fourteen days post Br_2 exposure, **mouse Hx** levels were measured in the plasma. Endogenous **mouse Hx** levels were elevated in mice that received an injection of human Hx (n=8-16) **(C)**. Values are means ± SEM. $^{*}P < 0.05$ versus Air, $^{\dagger}P < 0.05$ versus Br_2 exposed mice by one-way ANOVA followed by Tukey post hoc test.

Supplement Figure 6. Heme scavenging reduces lung compliance after inhalation injury. Lung compliance (C) **(A)** and an estimate of inspiratory capacity (A) **(B)**, were measured in C57BL/6 mice 14 days post exposure to either air or Br_2 (400ppm, 30min) and then treated with either saline or the heme scavenging enzyme, hemopexin (Hx) 1

hour or 5 days post exposure. (n=6-10). Values are means ± SEM. *$P < 0.05$ versus air + saline; †$P < 0.05$ versus Br_2 + saline; and ‡$P < 0.05$ versus Br_2 + Hx (1h post) by one-way ANOVA followed by Tukey post hoc test.


A
0.08
0.06
0.04
0.02
C (ml/cmH2O)
*
*
Air
7d
14d
21d
B
1.2
0.9
0.6
0.3
0.0
A (ml)
*
*
Air
7d
14d
21d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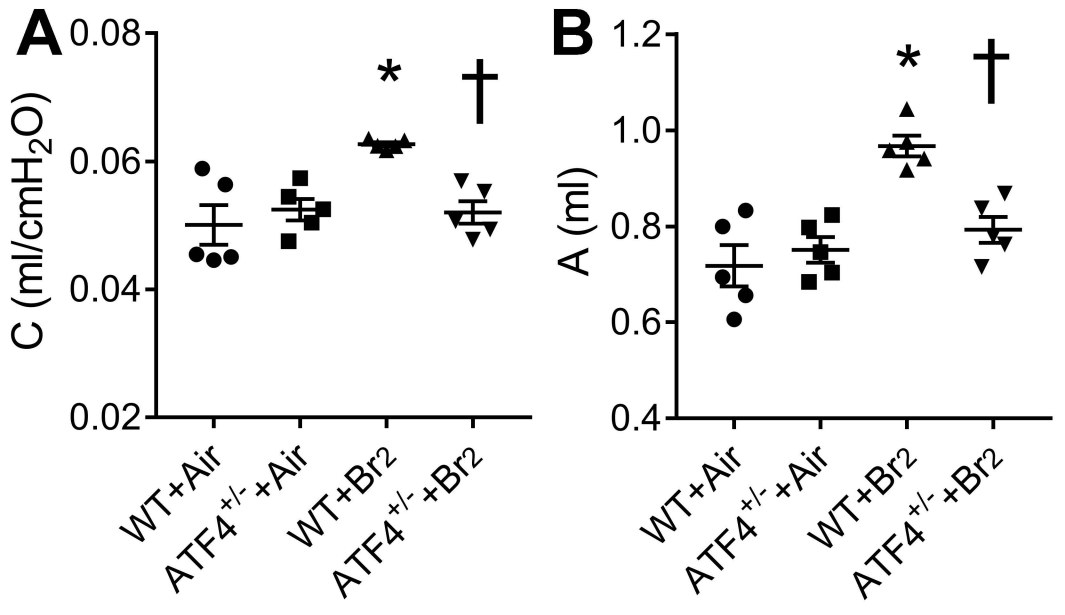
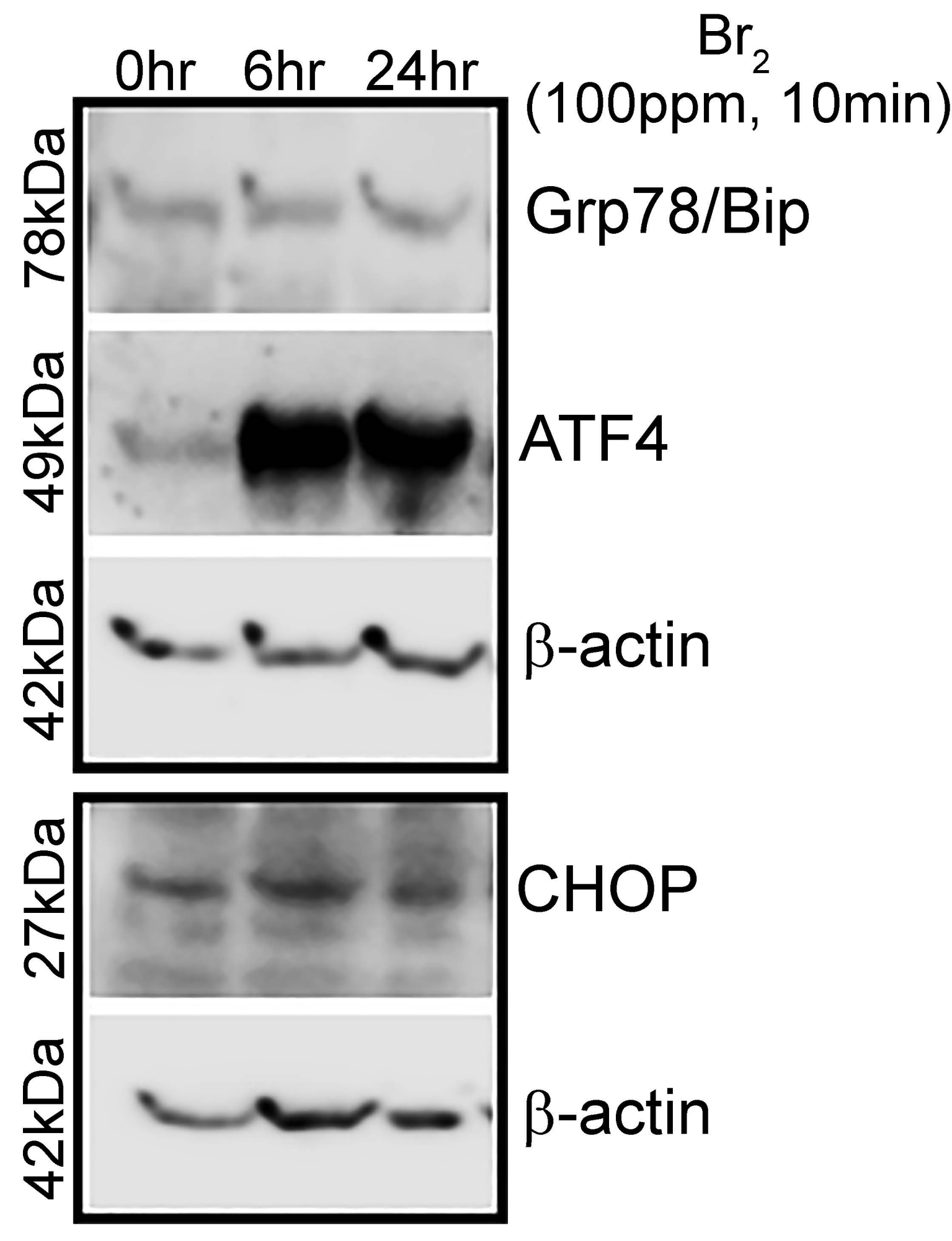
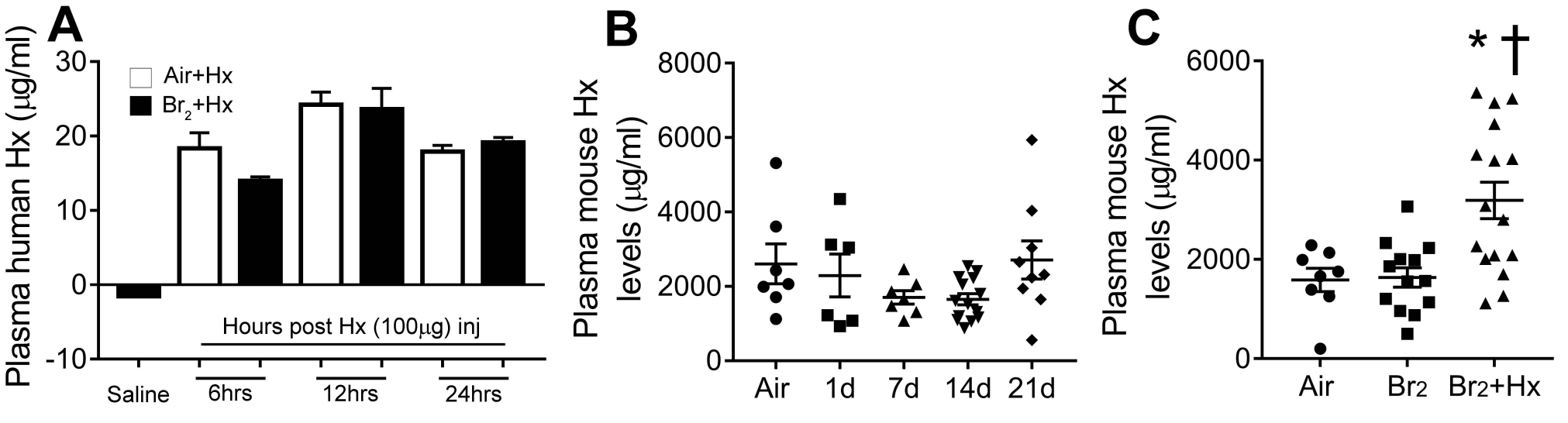
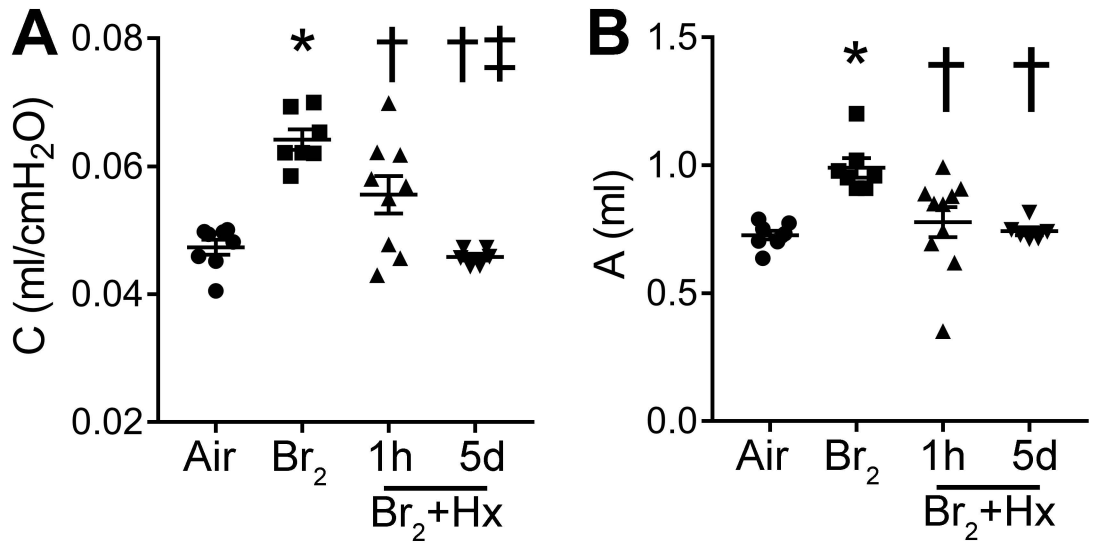
0.06
0.04
0.02
C (ml/cmH2O)
*
Air
Br2
Br2+Sal
B
1.2
0.8
0.4
0.0
A (ml)
*
†
Air
Br2
Br2+Sal


A
0.08
0.06
0.04
0.02
C (ml/cmH2O)
*
†
WT+Air
ATF4+/- +Air
WT+Br2
ATF4+/- +Br2
B
1.2
1.0
0.8
0.6
0.4
A (ml)
*
†
WT+Air
ATF4+/- +Air
WT+Br2
ATF4+/- +Br2


0hr
6hr
24hr
Br2
(100ppm, 10min)
78kDa
Grp78/Bip
49kDa
ATF4
42kDa
β-actin
27kDa
CHOP
42kDa
β-actin


A
Plasma human Hx (μg/ml)
30
20
10
0
-10
Air+Hx
Br2+Hx
Hours post Hx (100μg) inj
Saline
6hrs
12hrs
24hrs
B
Plasma mouse Hx levels (μg/ml)
8000
6000
4000
2000
0
Air
1d
7d
14d
21d
C
Plasma mouse Hx levels (μg/ml)
6000
4000
2000
0
*
†
Air
Br2
Br2+Hx


A
B
C (ml/cmH2O)
A (ml)
0.08
0.06
0.04
0.02
1.5
1.0
0.5
0.0
*
†
†‡
Air
Br2
1h
5d
Br2+Hx