Direct Thrombin Inhibitors Fail to Reverse the Negative Effects of Heparin on Lung Growth and Function after Murine Left Pneumonectomy

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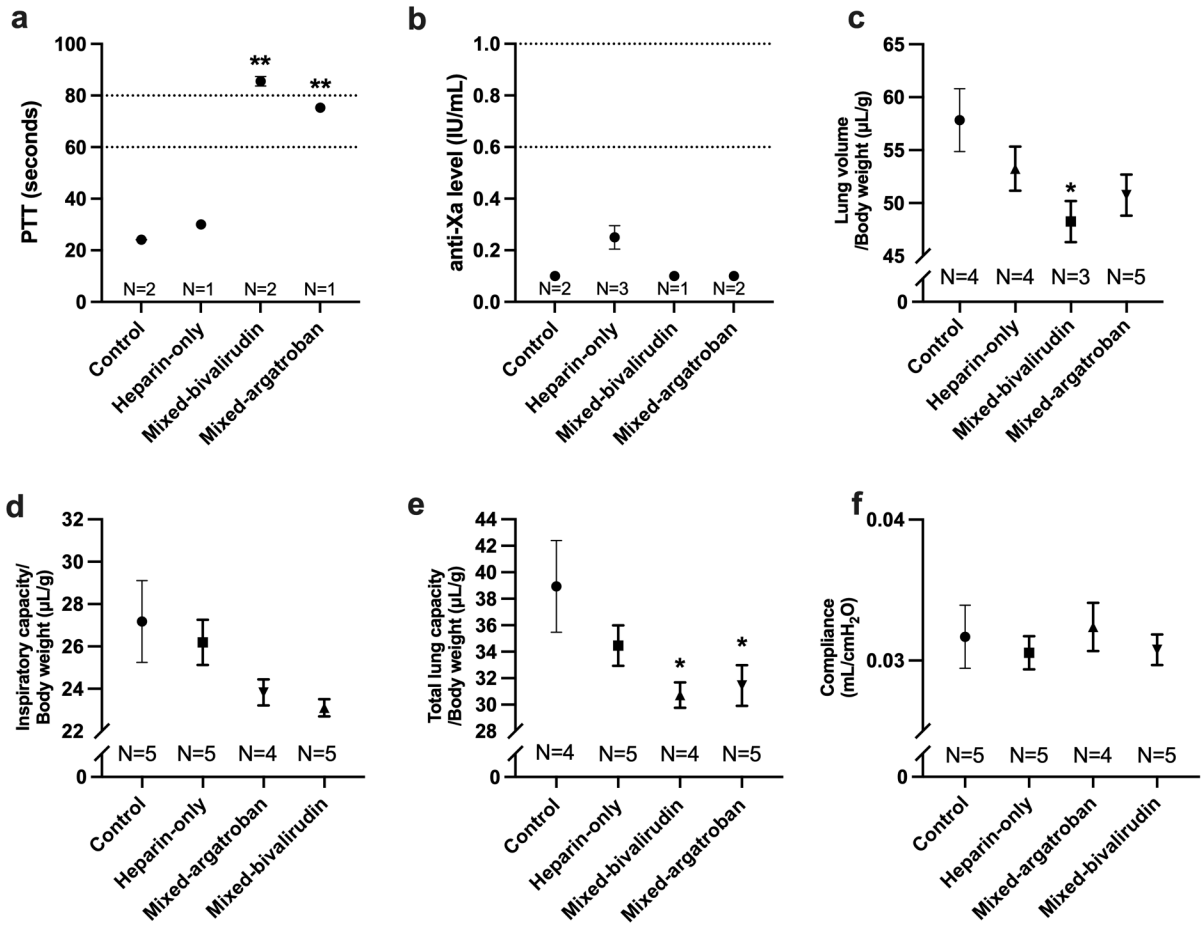
Supplemental Tables, Figures, and Files

Supplemental Table S1. Study groups and anticoagulant dosing

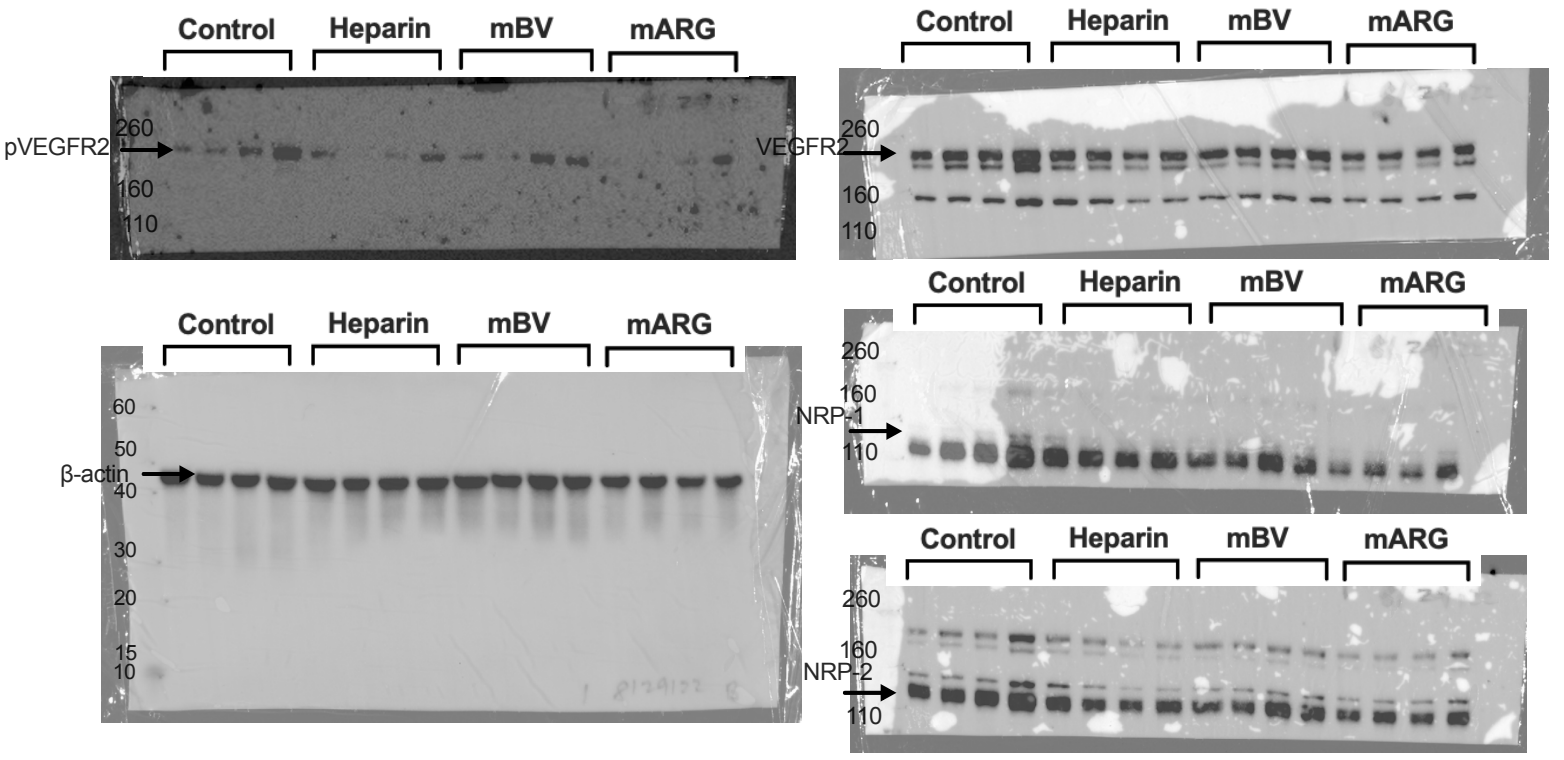
GROUPS	IP INJECTION (ONCE DAILY)		OSMOTIC PUMP INFORMATION		
			Drug (concentration)	Rate	Dose
Control	Normal Saline (10 µL/g)	+	Normal Saline (N/A)	1 µL/hr	**1 µL/hr**
Heparin-only	Heparin (0.25 IU/g)	+	Normal Saline (N/A)	1 µL/hr	**1 µL/hr**
Mixed-bivalirudin	Heparin (0.25 IU/g)	+	Bivalirudin (50 µg/µL)	1 µL/hr	**50 µg/hr**
Mixed-argatroban	Heparin (0.25 IU/g)	+	Argatroban (100 µg/µL)	0.5 µL/hr	**50 µg/hr**

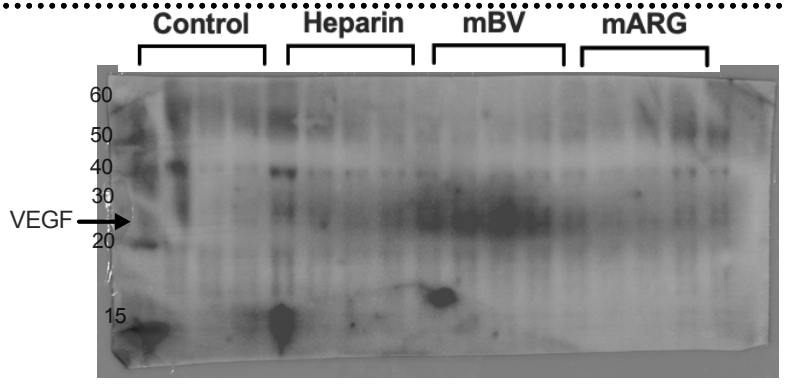
N/A: Not applicable; IP: intraperitoneal; IU: International units

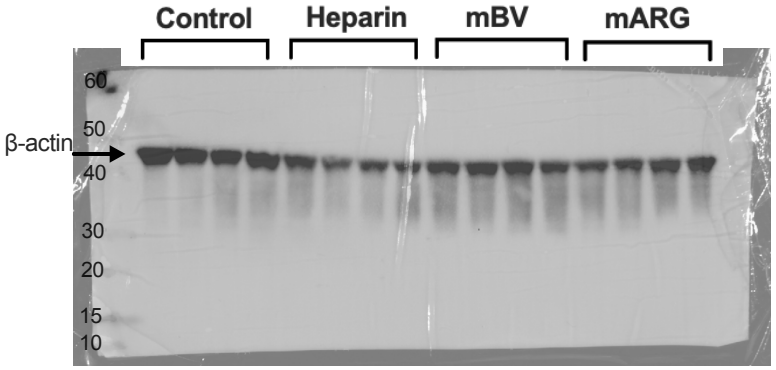


Supplemental Figure S1. **Anticoagulation assessment and pulmonary outcomes in female mice.** Bivalirudin and argatroban-treated mice achieved therapeutic anticoagulation (**a**) as demonstrated by the elevated partial thromboplastin time (PTT) compared to controls. There was no difference in PTT measurement in the low-dose heparin group. Administration of low-dose heparin in the three groups (heparin-alone, mixed bivalirudin/argatroban) did not contribute to therapeutic anticoagulation as demonstrated by the subtherapeutic anti-factor Xa levels in all groups (**b**). All three heparin-exposed groups had decreased lung growth compared to saline-treated controls (**c**). On pulmonary function testing, the mixed-argatroban and -bivalirudin treated mice had decreased inspiratory capacity (**d**). All three groups receiving heparin had decreased total lung capacity (TLC) compared to controls (**e**). There were no differences in pulmonary compliance across all four groups (**f**). Statistical analysis of the experimental groups was done using analysis of variance (ANOVA), with Dunnett's adjustment for multiple comparisons. TLC and lung volumes were normalized to mouse body weight. Shown are mean ± standard error. Typical therapeutic PTT range: 60.0-80.0; anti-factor Xa range: 0.60-1.00 are indicated on the graph. *P<0.05; **P<0.01.

Supplemental File 1. Full length blots correspond to part of Figures 6a, 6b:

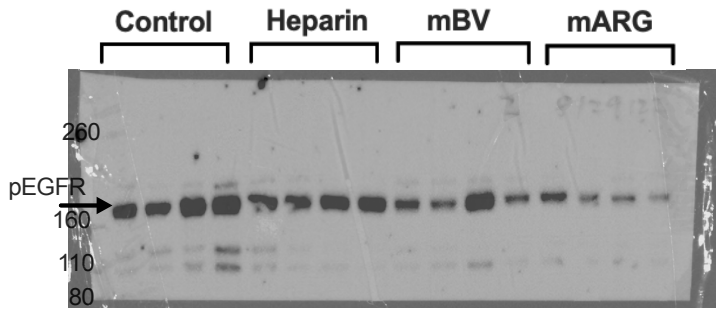


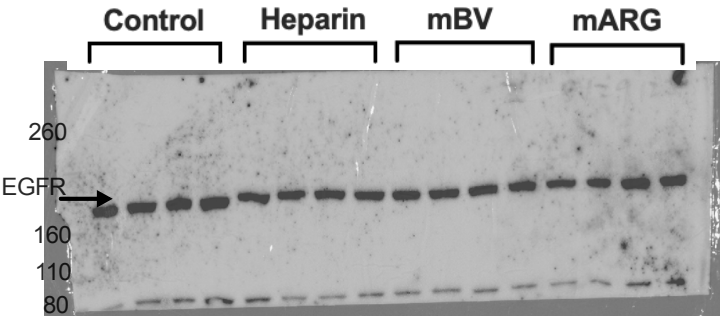


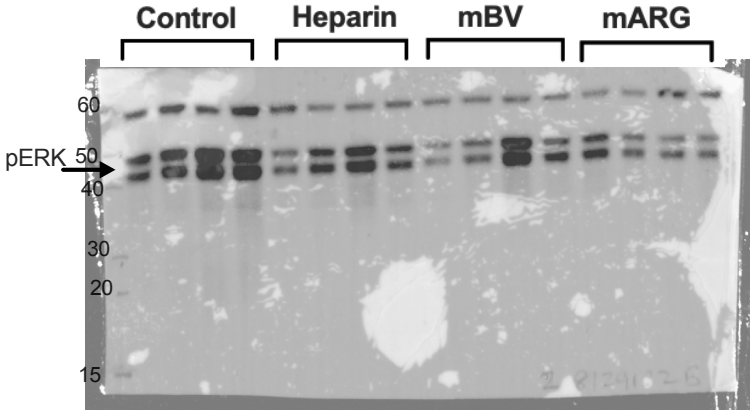


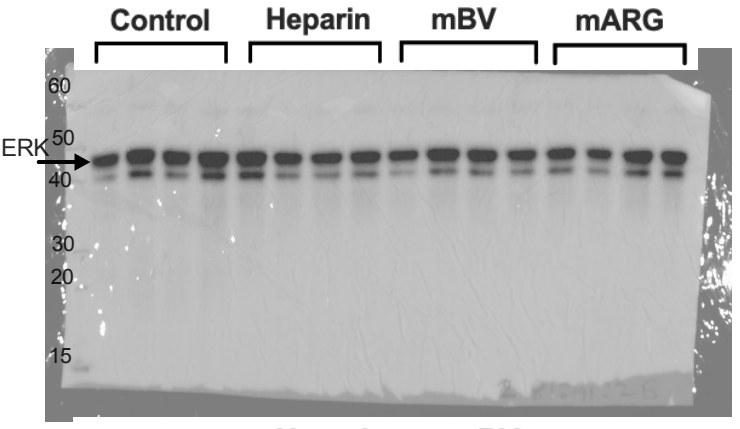
Key:
Control: normal-saline
Heparin: Heparin-only
mBV: Mixed-bivalirudin
mARG: Mixed-argatroban

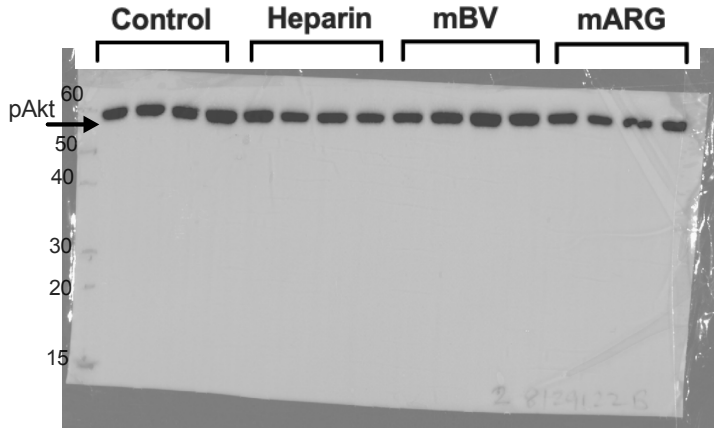
Supplemental File 2. Full length blots correspond to part of Figure 6c, 6d, 6e :

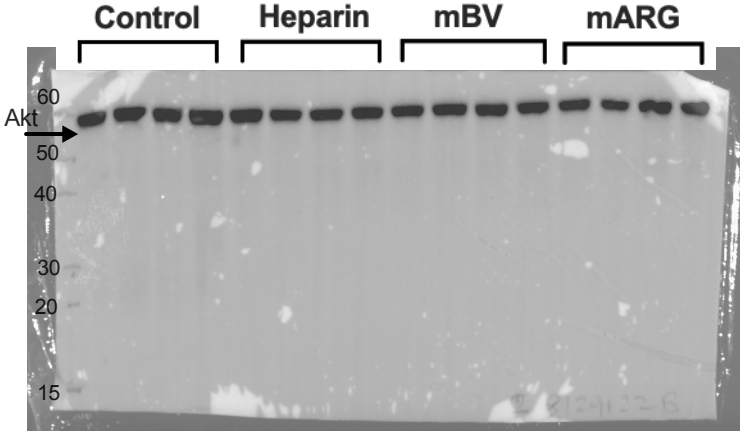


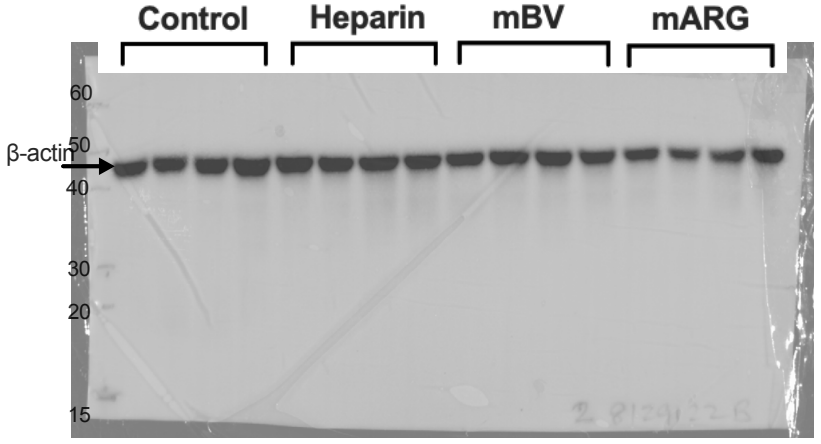












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