Supporting Information

Bio-distribution of pharmacologically administered rFVIIa

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Fig. S1. Tissue factor immunostaining of skin tissues of mice administered with pharmacological doses of rFVIIa. Mouse rFVIIa (AF288-FVIIa), 120 µg/kg b.w. was administered into anesthetized male C57BL/6 mice via tail vein. At different time intervals following FVIIa administration, mice were exsanguinated, skin tissue was collected and processed for immunohistochemistry. Skin sections were immunostained with rabbit anti-mouse TF IgG. Panel A, epidermis and upper dermis region; Panel B, lower dermis region. Magnification, 400X. In this and other figures, the times noted in the figure indicate the duration of time following the administration of AF488-FVIIa (or AF488-FIX).

Fig. S2. Immunostaining of bone joint sections for rFVIIa. Bone tissue sections from mice, at different time intervals following AF488-FVIIa, were immunostained with rabbit anti-AF488 antibodies. Magnification, 40X. The calcified cartilage area in the bone joint section, where positive immunostainig of FVIIa was observed, was marked by the oblong shape. Higher magnification (400 X) of this region was shown in Fig. 4 in the main manuscript.

Fig. S3. Immunostaining of bone joint sections with anti-tissue antibodies of mice administered with FVIIa. BM, bone marrow. Magnification, 400X. Note: TF positive immunostaining (red/brown color) in the zone of calcified cartilage in the growth plate region.

Fig. S4. Association of rFVIIa with endothelium immediately following its administration. Serial sections of bone joints of mice received AF488-FVIIa were stained with control IgG, anti-AF488 or anti-TF IgG. Magnification, 400X

Fig. S5. FIX administered to mice does not associate with the endothelium. Serial sections of bone joints of mice received AF488-FIX (120 μg/kg b.w.) were stained with control IgG or anti-AF488 antibodies. Magnification, 400X.

Fig. S6. Immunostaining of bone marrow with anti-tissue factor antibodies. Bone sections (from the joint region) of mice administered AF488-FVIIa were immunostained with anti-tissue factor antibodies. Me, megakaryocyte; AT, adipose tissue. Magnification, 400X.

Fig. S7. rFVIIa administered to mice does not associate with brain tissue. Brain tissue sections of mice administered AF488-FVIIa were stained with anti-AF488 antibodies. bv, blood vessels. Magnification, 400X.

Fig. S8. Tissue factor immunostaining of brain. Brain tissue sections of mice administered AF488-FVIIa were stained with anti-tissue factor antibodies. bv, blood vessels. Magnification, 400X.

Fig. S9. rFVIIa administered to mice does not associate with lung tissue. Lung tissue sections of mice administered AF488-FVIIa were stained with anti-AF488 antibodies. bc, bronchioles; bv, blood vessels. Magnification, 400X.

Fig. S10. Tissue factor immunostaining of lung tissue. Lung tissue sections of mice administered AF488-FVIIa were stained with anti-tissue factor antibodies. bc, bronchioles; bv, blood vessels. Magnification, 400X.

Fig. S1.

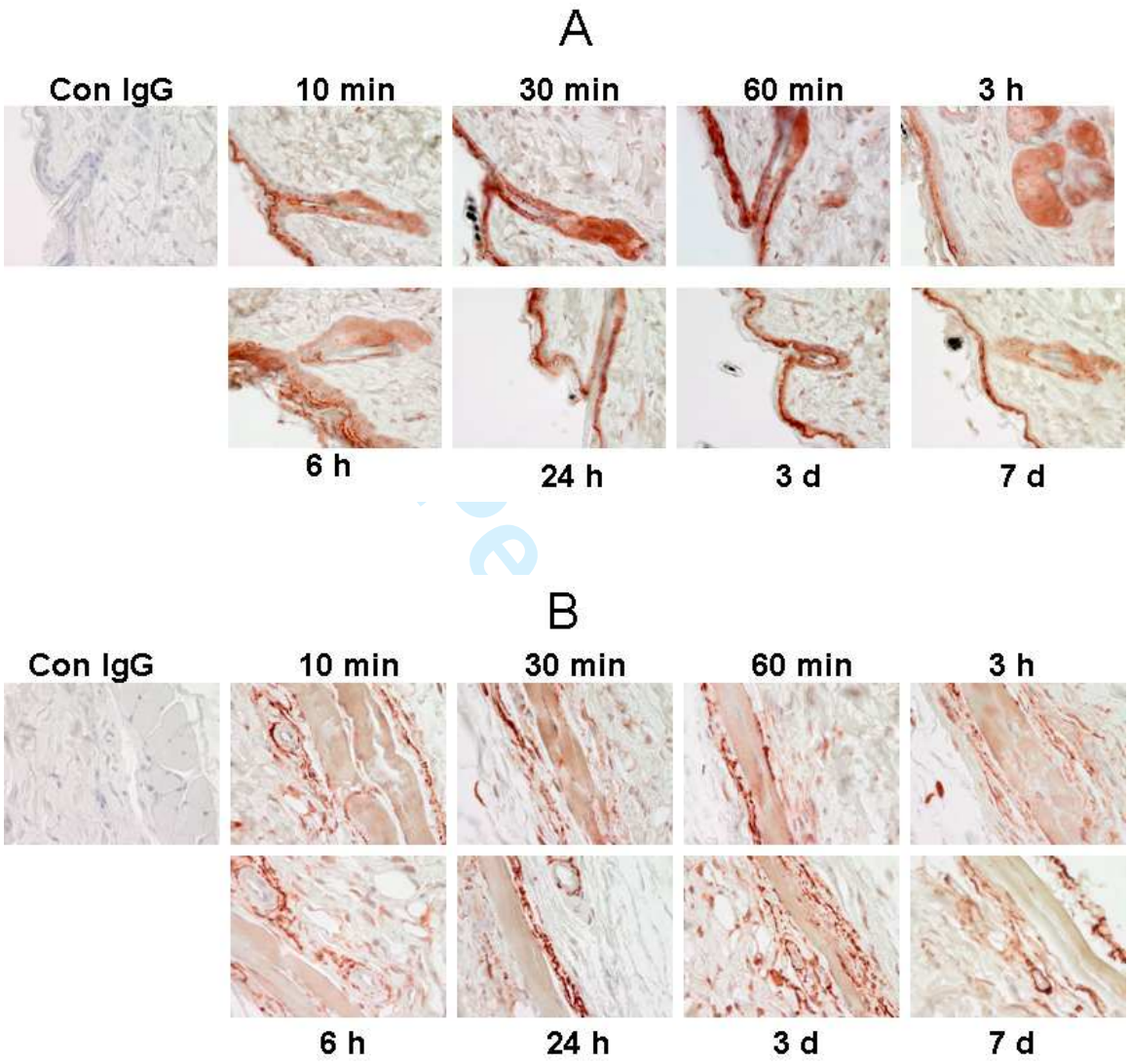

A
Con IgG
10 min
30 min
60 min
3 h
6 h
24 h
3 d
7 d
B
Con IgG
10 min
30 min
60 min
3 h
6 h
24 h
3 d
7 d

Fig. S2

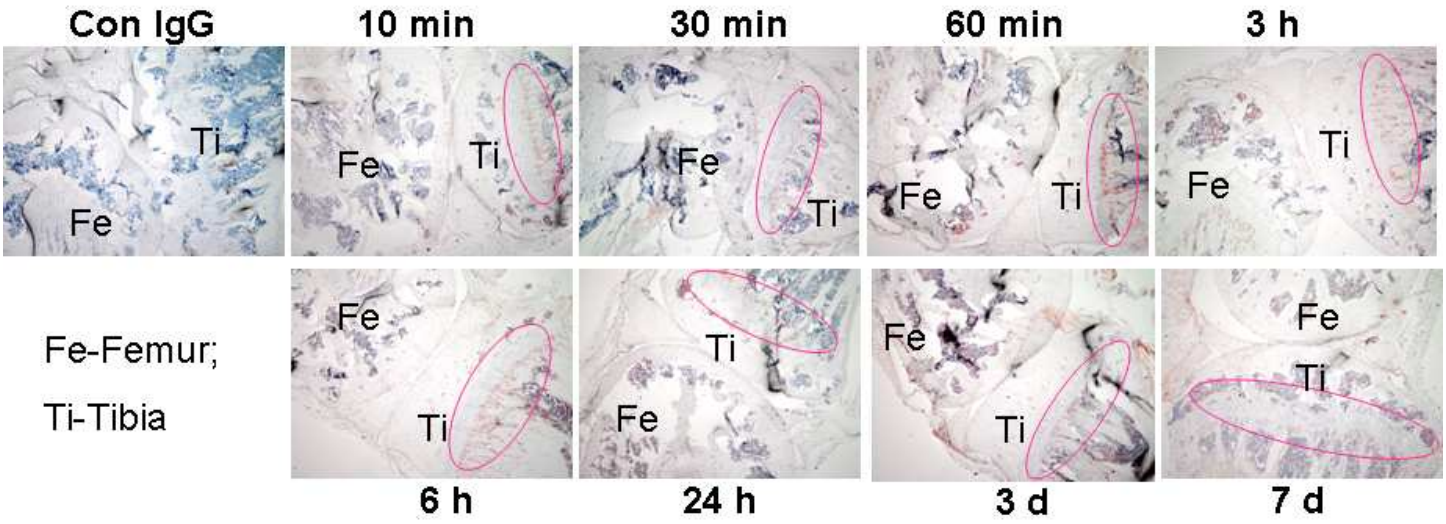


Fig. S3

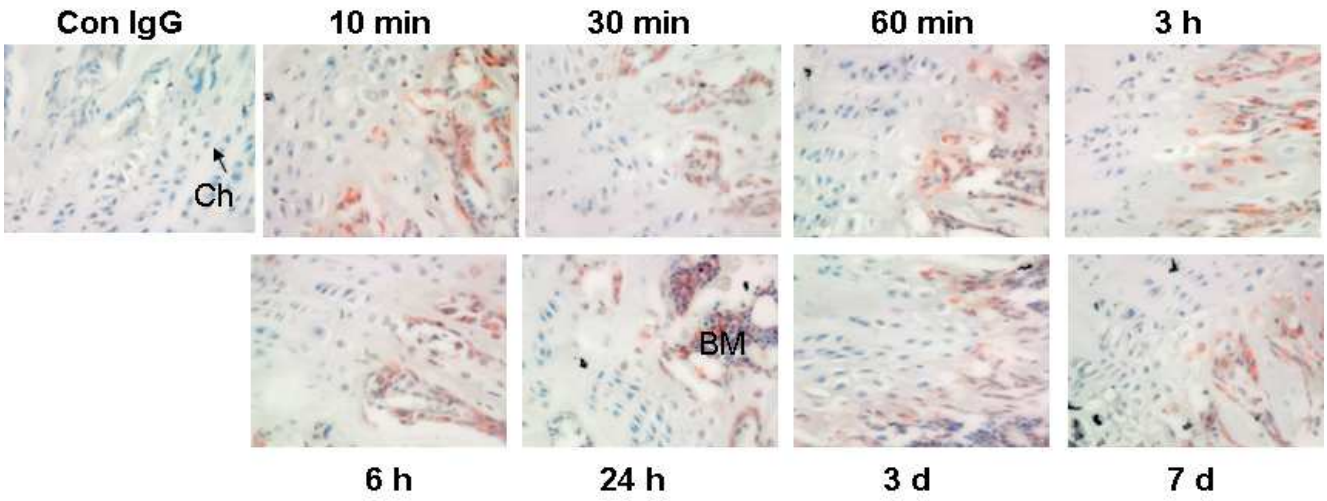


Fig. S4.

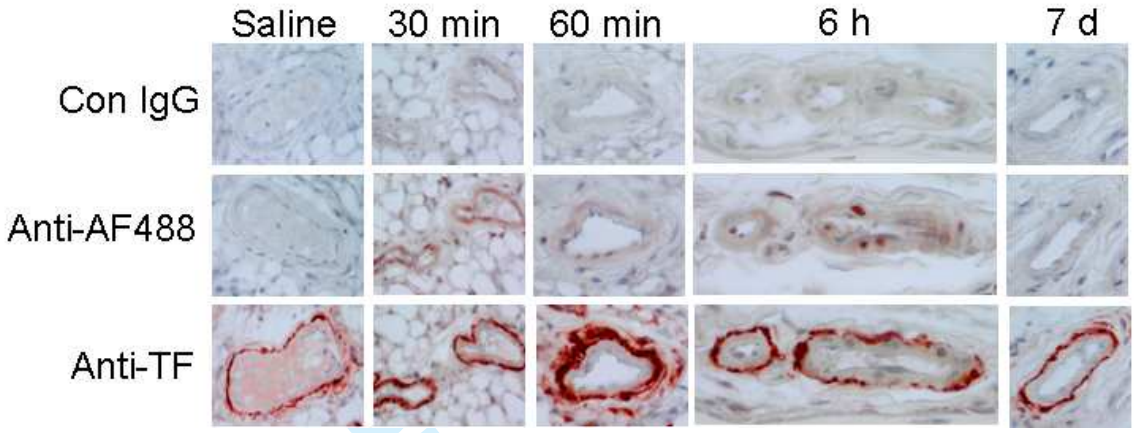
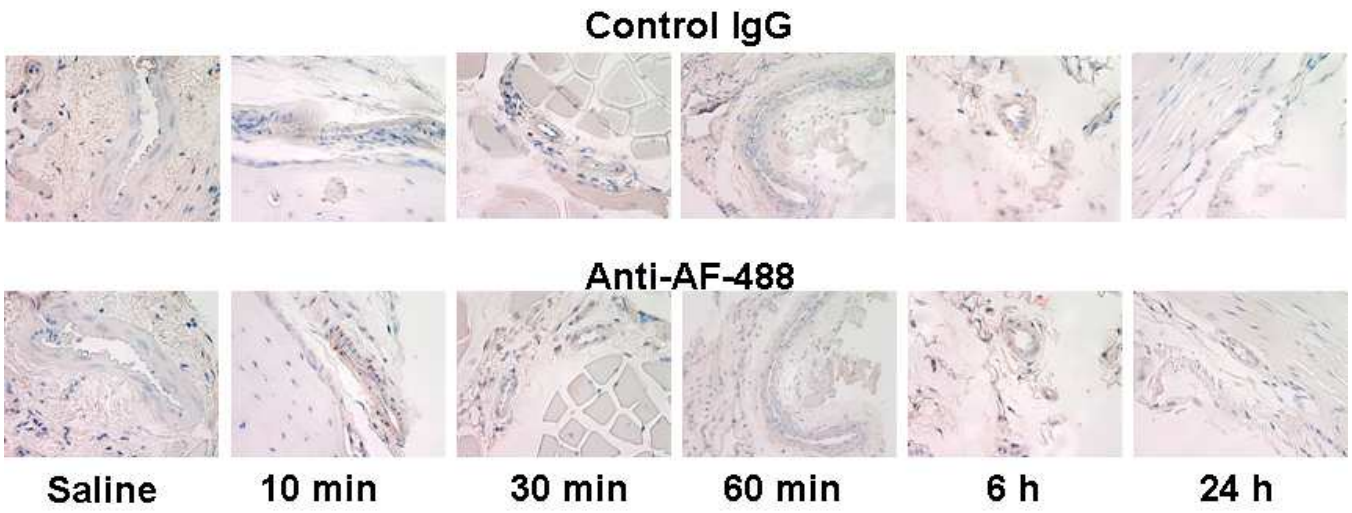


Fig. S5



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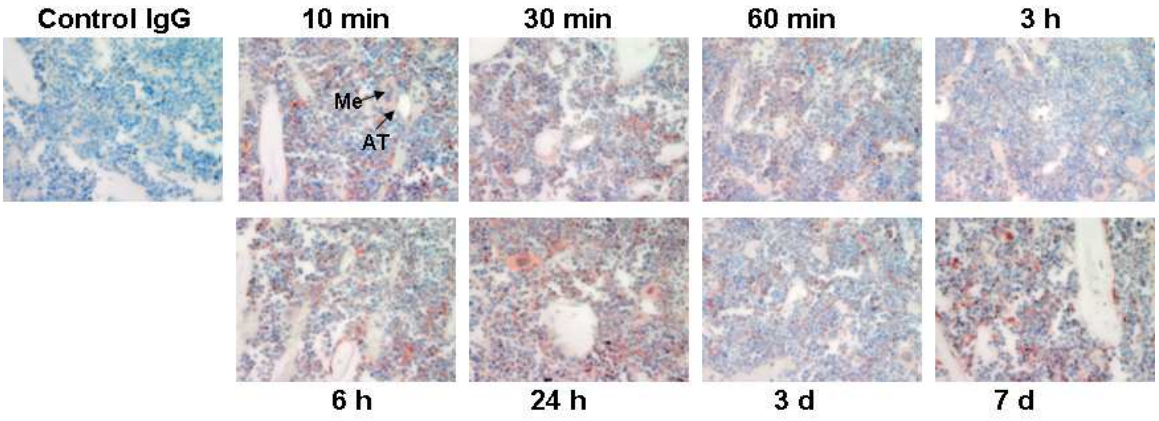

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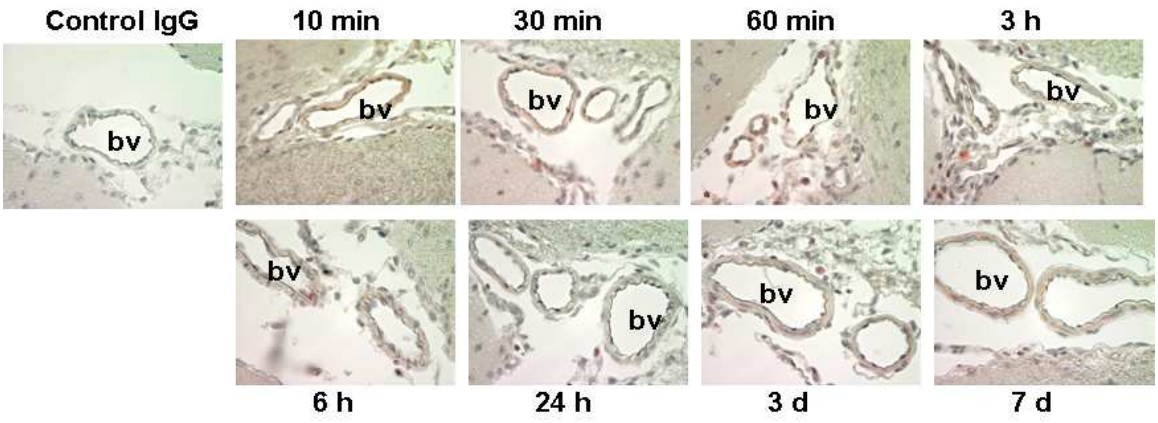

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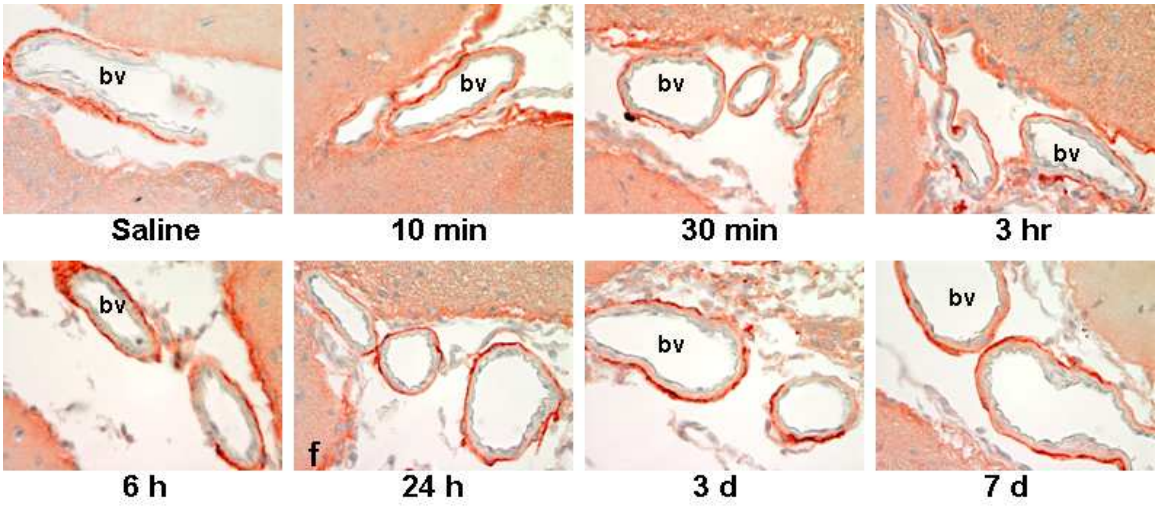

Fig. S9.

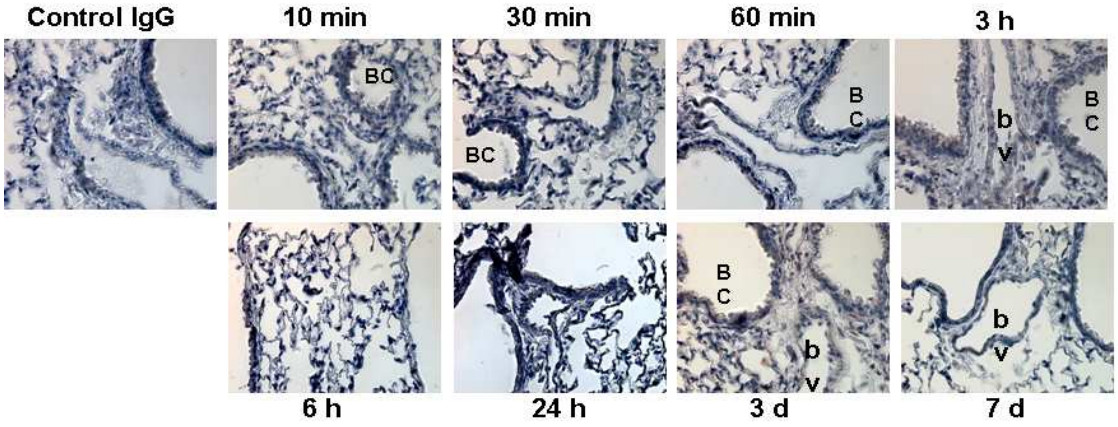

Fig. S10.