

### **Supplementary Figure 1. Effect of Gs4898 treatment on AKT activity.**

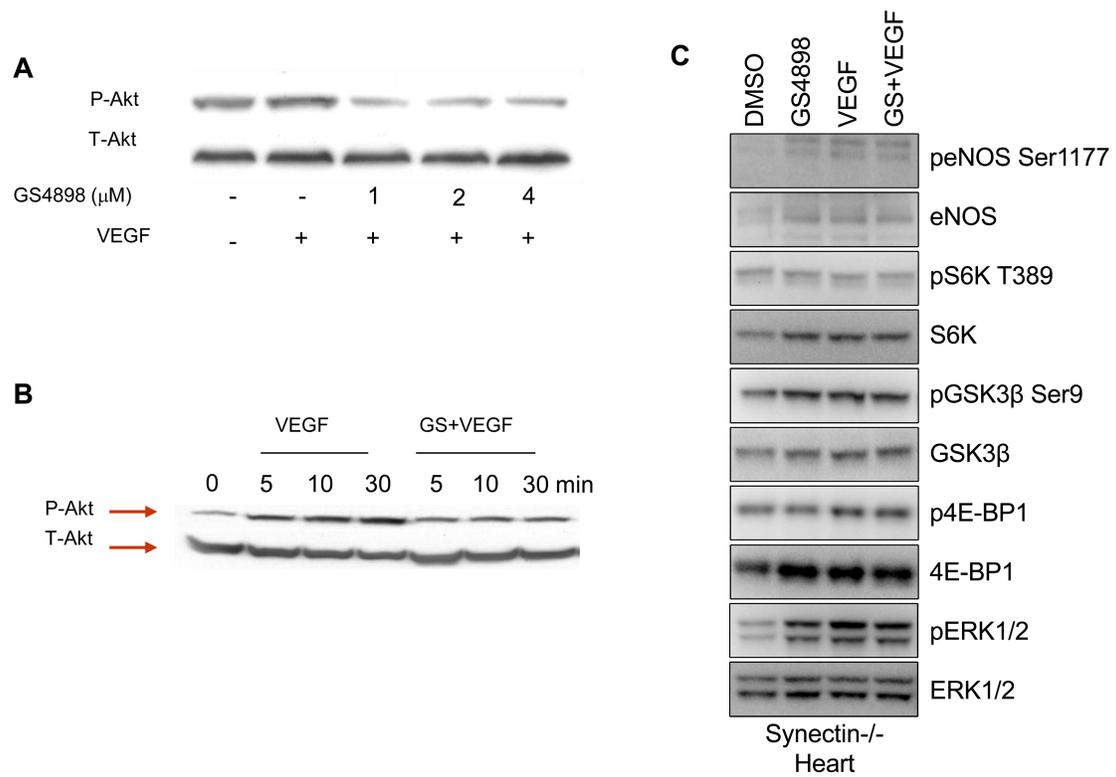
- A.** Wild type AEC were treated with increasing concentration of GS4898 and then exposed to VEGF-A<sub>165</sub> (50 ng/ml) (as indicated on the figure). Western blotting 15 min later demonstrates decrease in Akt activity.
- B.** Wild type AEC were treated with 2  $\mu$ M GS4898 and then exposed to VEGF-A<sub>165</sub> (50 ng/ml). Western blotting was used to determine the time course of Akt activation. Note a prolonged suppression of Akt activation by GS4898.
- C.** Effect of GS4898 treatment on activity of Akt-dependent genes. Synectin null mice were injected with VEGF and sacrificed 15 min later. The heart tissue was used for Western blotting to determine activation of Akt-dependent proteins. Note GS4898/VEGF-induced activation of ERK and the total lack of activation of any downstream Akt target protein, suggesting almost complete inhibition of Akt activity.

### **Supplementary Figure 2. Impaired branching of synectin<sup>-/-</sup> AEC**

Representative wire diagrams of the branching extent of synectin<sup>-/-</sup> AEC plated on growth factor depleted Matrigel. Note increased branching in GS4898/VEGF-treated cells.

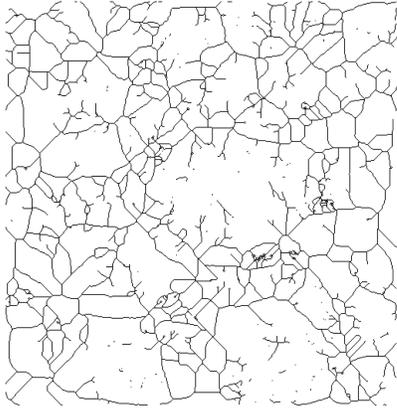
### **Supplementary Figure 3. Laser-Doppler analysis of blood flow**

Representative Laser-Doppler flow images of right and left feet blood flow in synectin<sup>-/-</sup> and <sup>+/+</sup> mice.

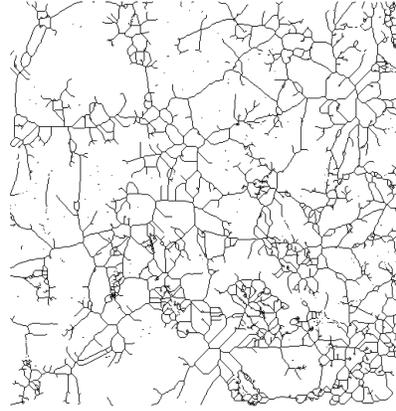


Supplementary Figure 1

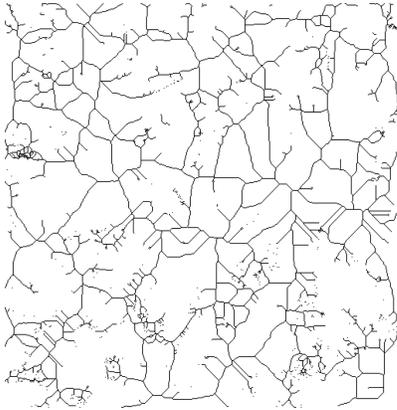
Vehicle



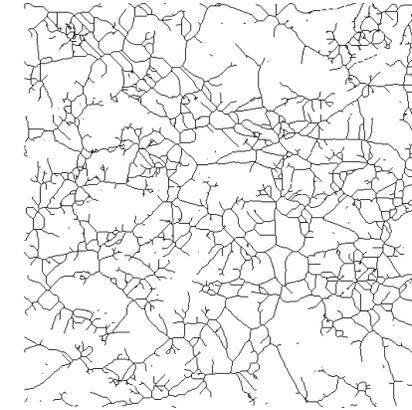
VEGF



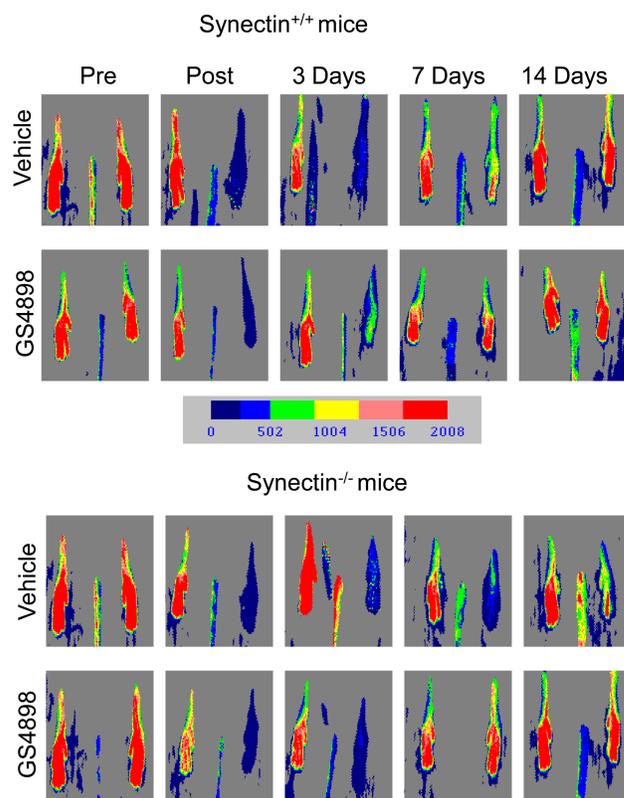
GS4898



VEGF+GS4898



Supplementary Figure 2



Supplementary Figure 3