Supplement figures:

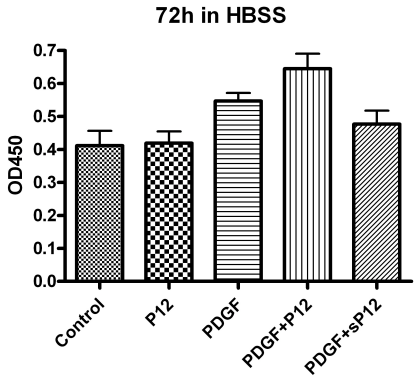

Figure S1. P12 by itself does not stimulate cell metabolism. AHDFs were treated with 1nMPDGF-BB±10μMP12 (sP12) in HBSS for 72 h. Cell metabolism was measured by the XTT assay (asterisk, $P<0.05$ compared to PDGF alone, n=6), Mean +/- SD.

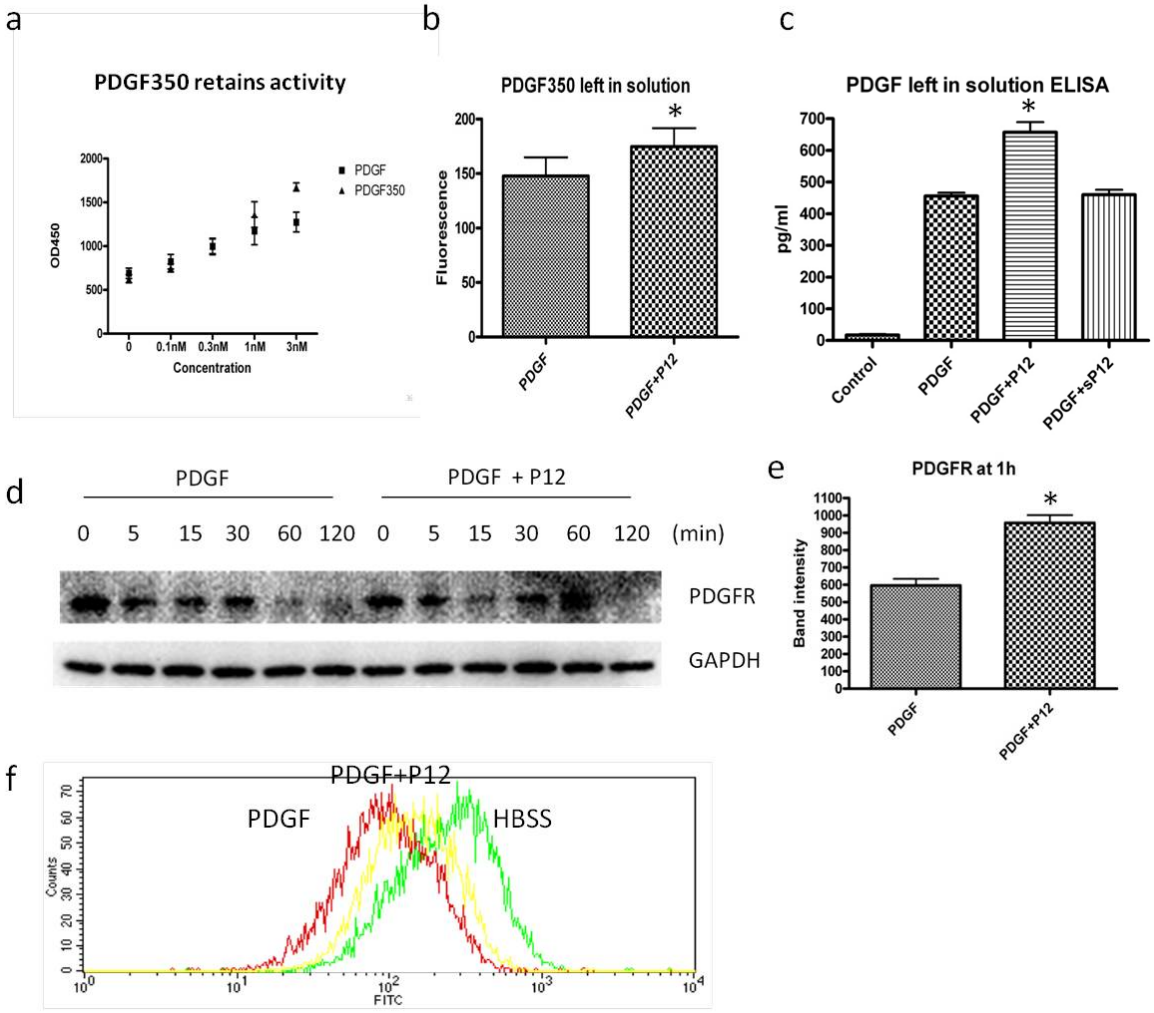

Figure S2. P12 slowed PDGF-BB/PDGFR-β internalization/degradation under nutrient deprivation. **a)** AHDFs were treated with PDGF-BB or PDGF-BB-Alexa350 for 5 days in DMEM. Cell metabolism was measured by the XTT assay. **b)** AHDFs were treated with 1nM PDGF-Alexa350 ± 10μM P12 for 1 h at 37°C. PDGF left in the medium was measured by fluorescence. Control = no additions (asterisk, P>0.05 compared to control, n=6). Mean +/- SD. **c)** AHDFs were treated with 1nM PDGF ± 10μM P12 (sP12) for 1 h at 37°C. PDGF left in the medium was measured by PDGF ELISA. Control = no additions (asterisk, P<0.05 compared to control, n=6). Mean +/- SD. **d)** AHDFs were treated with 1nM PDGF-BB ± 10μM P12 in HBSS for the indicated times. Western blots were performed with an antibody against PDGFR-β. GAPDH was used as a loading control. **e)** Digital quantification of PDGFR band intensity using Kodak IM ver4.0.3. Data from 3 independent experiments (asterisk, P<0.05 compared to PDGF alone, n=3). Mean +/- SD. **f)** AHDFs were treated with 1nM PDGF-Alexa350 ± 10μM P12 for 1 h at 37°C. PDGFR-β was immunostained and analyzed by flow cytometry. Red: PDGF-BB, Yellow: PDGF+P12 and Green: HBSS.

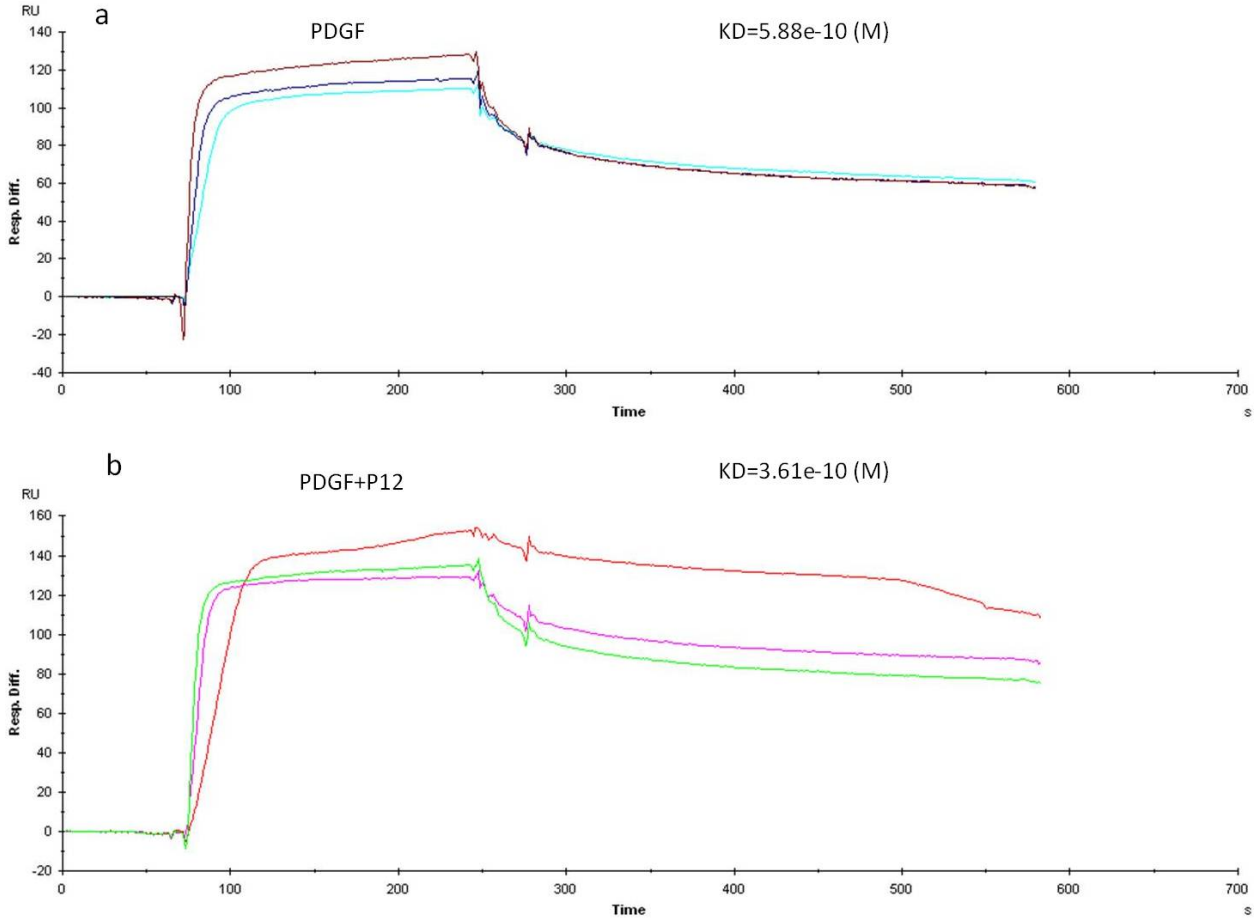

Figure S3. PDGF-BB receptor recognition is not affected by the presence of P12. PDGFR extracellular domain was fixed to CM5 chip through amine coupling. Real-time interaction of PDGF-BB with PDGFR was determined by plasmon surface resonance (BiaCore 2000) with or without 10μM P12. Chip cell without PDGFR was used as a reference. **a)** PDGF-BB was injected at 12.5nM (teal line), 25nM (blue line) or 50nM (brown line). **b)** PDGF-BB was injected at 12.5nM (green line), 25nM (purple line) or 50nM (red line) in the presence of 10uM P12. Dissociation constants (KDs) were derived from the ratio of kinetic dissociation constants (kd) divided by kinetic association constants (ka). RU is resonance unit.

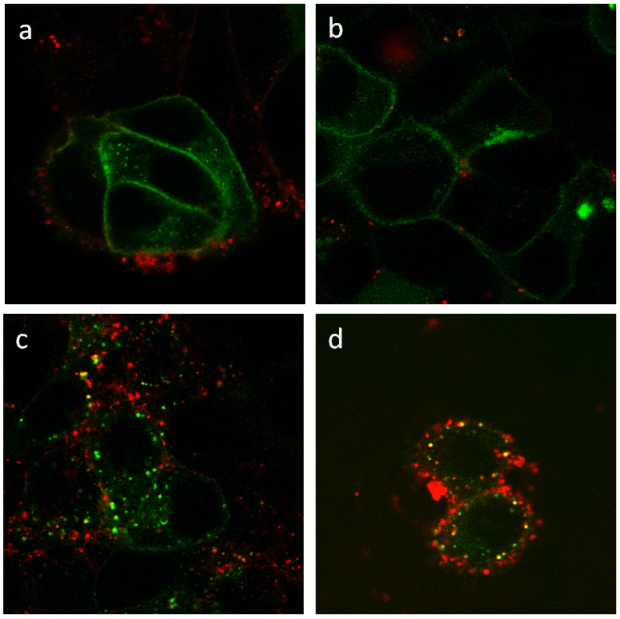

Figure S4. P12 does not stimulate macropinocytosis. MCF-7 cells expressing GFP-PDGFR-β were treated with 10μM P12, 1nM PDGF-BB or both for 15 min in HBSS, stained with TR-dextran and then analyzed by confocal microscope. **a)** MCF-7 cells in HBSS as control. **b)** MCF-7 cells treated with P12 for 15min. **c)** MFC-7 cells treated with PDGF-BB for 15min. **d)** MCF-7 cells treated with PDGF+P12 for 15min. Representative figures from 3 independent experiments.

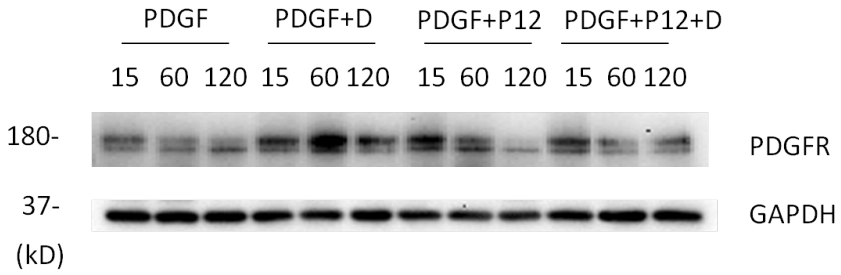

Figure S5. P12 slowed PDGFR degradation and bypassed dynamin blockage of PDGFR internalization/degradation. AHDFs were put pre-incubated for 1h in serum-free condition with 80uM dynasore and then treated with 1nM PDGF-BB ± 10μM P12 for the indicated time in HBSS. Western blots on total cell lysate were performed with an antibody against PDGFR. GAPDH was used as a loading control. Data is representative of 3 independent experiments.

Figure S6. Clathrin heavy chain knockdown in MCF-7 cells. CHC SiRNA was used to knockdown CHC expression in MCF-7 cells. The protein level dropped significantly after 2 consecutive transfections (36 hours apart) with Hiperfect transfection reagents according to kit instruction.

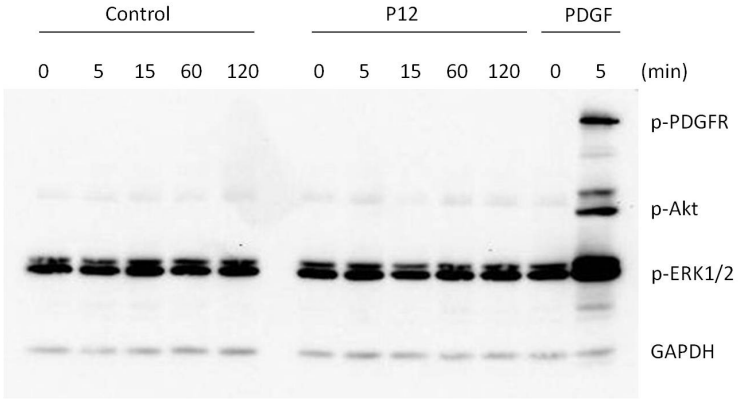

Figure S7. P12 by itself does not affect PDGF signaling. AHDFs were treated with 10μM P12 alone for the indicated time. 5 minutes of 1nM PDGF was used as positive control. Western blots were performed with antibodies against phospho-Akt, phospho-PDGFR, and phospho-ERK1/2. GAPDH was used as loading control. Data is representative of 3 independent experiments.

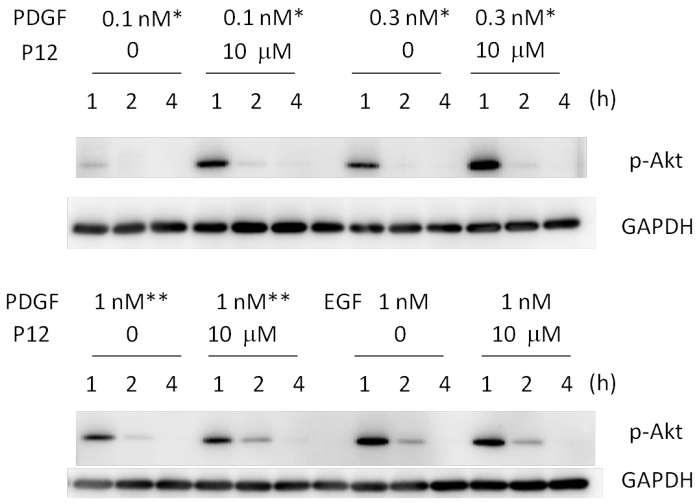

Figure S8. P12 increased p-Akt at various doses of PDGF-BB in acute wound fluid or PDGF-BB in serum. AHDFs were treated with PDGF-BB+/-P12 in HBSS at the doses indicated in the figure. Western blots were performed with an antibody against p-Akt and GAPDH was used as loading control.

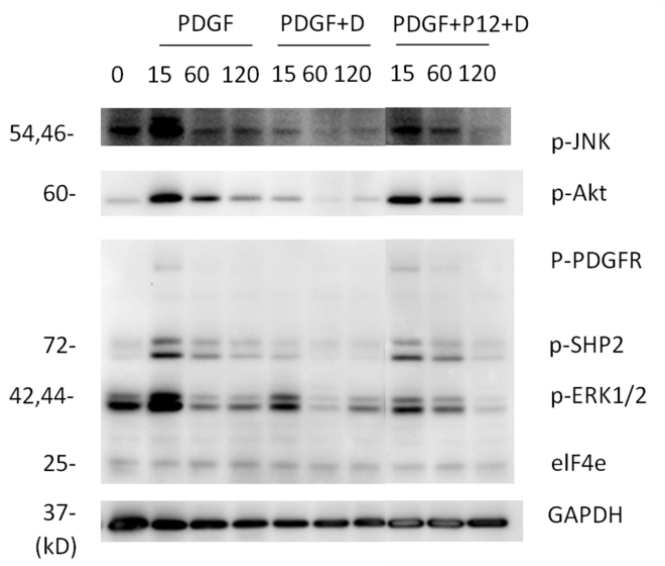

Figure S9. P12 bypassed dynamin blockage to activate the Akt/PI3K pathway. AHDFs were preincubated for 1h in serum-free condition with 80uM dynasore and then treated with 1nM PDGF-BB ± 10μM P12 in HBSS. Western blots were performed with antibodies against phospho-Akt, phospho-JNK, phospho-ERK1/2, phospho-SHP2 and eIF4e. GAPDH was used as loading control. Data is representative of 3 independent experiments.