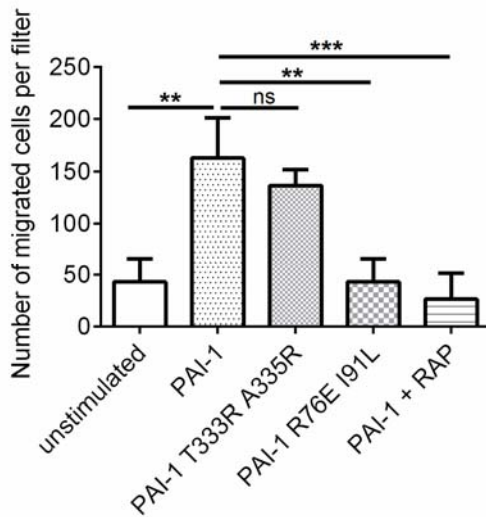
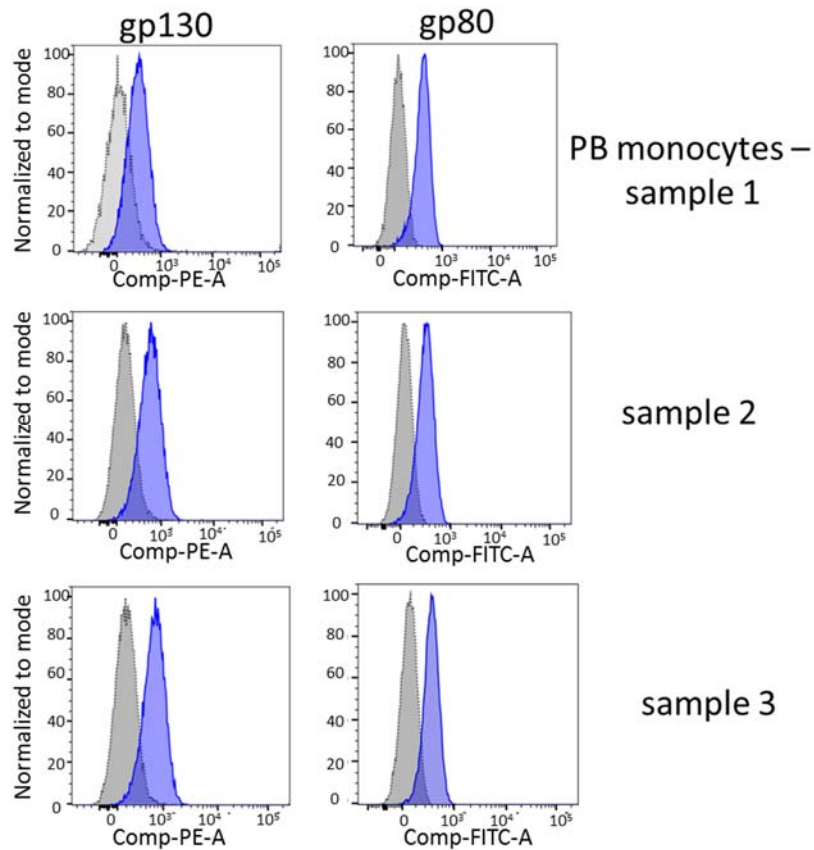


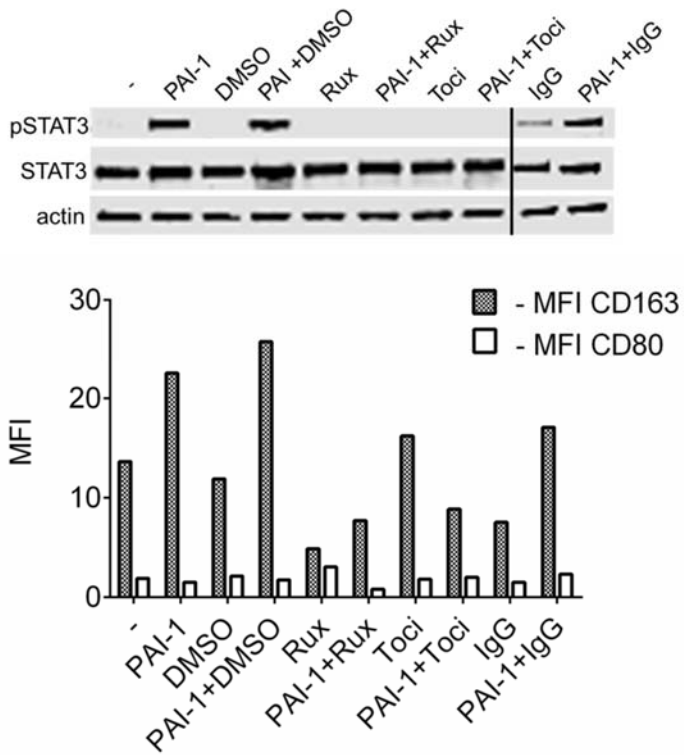
## Supplemental Items



**Figure S1. Migration of human monocytes towards rPAI-1, rPAI-1 R76E I91L, rPAI-1 T333R A335R and in presence and absence of RAP. Related to Figure 2.** Migration of human monocytes toward rPAI-1 and rPAI-1 mutants and in presence and effect of RAP. Data represent the mean number ( $\pm$  SD) of migrated cells in 9 random fields per filter in triplicate samples. Analysis of variance was applied for comparisons between the groups. \*\*  $p < 0.01$  \*\*\*  $p < 0.001$

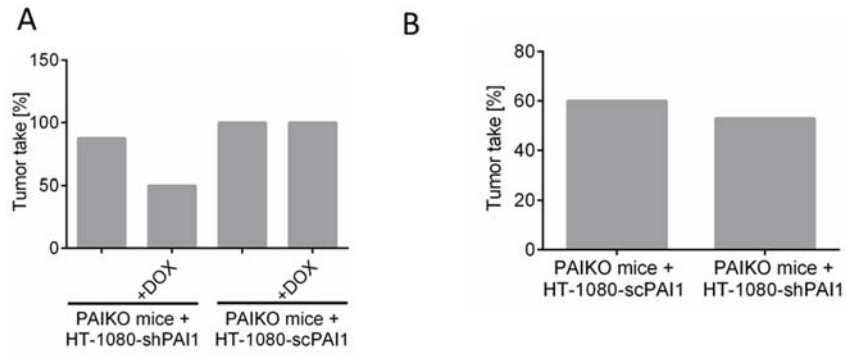


**Figure S2. Expression of gp130 and gp80 on PB monocytes. Related to Figure 4.** Expression of gp130 and gp80 was measured on three preparations of PB monocytes by FACS as described in Materials and Methods. Grey – isotype control, blue – cells stained with anti-gp130 or anti-gp80 antibody.



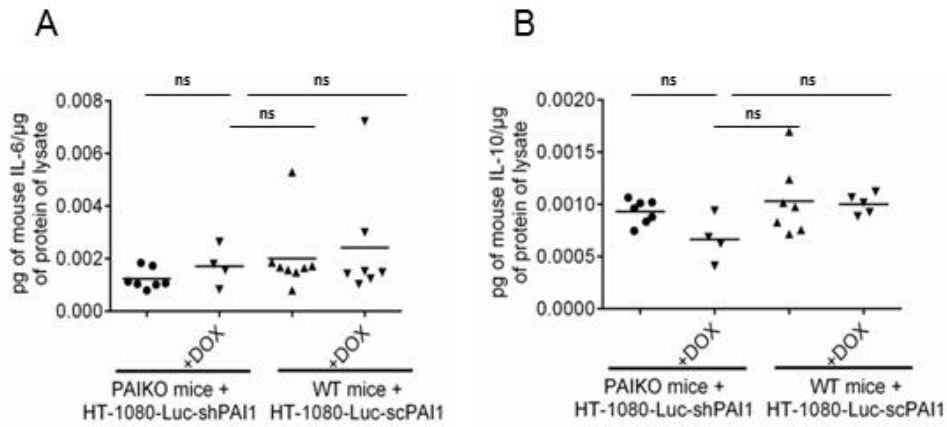
**Figure S3. PAI-1-mediated macrophage polarization is IL-6- and STAT3-dependent. Related to Figure 4.**

Western blot analysis of STAT3 phosphorylation in lysates of PB monocytes obtained after 6 days of treatment with rPAI-1 (40 nM), ruxolitinib (1  $\mu$ M), tocilizumab (20  $\mu$ g/mL), IgG (20  $\mu$ g/mL) or DMSO or their combination. Lower panel: CD163 MFIs of PB monocytes treated as in the upper panel. Lower and upper panels represent two separate experiments.

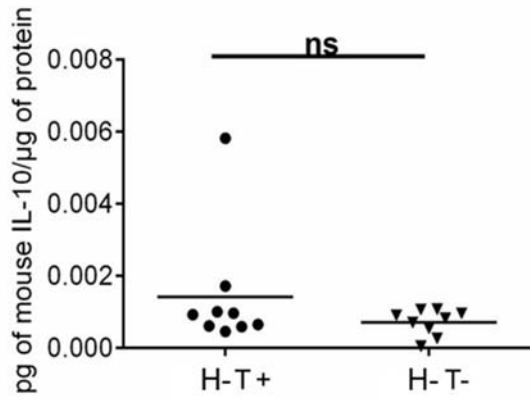


**Figure S4. Tumor Engraftment in *in vivo* experiments. Related to Figure 7.**

Percent of tumor engraftment in *in vivo* experiment: (A) Rag1<sup>-/-</sup> PAI-1<sup>-/-</sup> mice were injected with HT-1080-Luc-shPAI1 and Rag1<sup>-/-</sup> PAI-1<sup>+/+</sup> mice with HT-1080-Luc-scPAI1 tumor cells and half of the mice received doxycycline in drinking water for 35 days as described in Figure 7, panel F. The data represent the per cent of mice with engrafted tumors at day 35. (B) Rag1<sup>-/-</sup> PAI-1<sup>-/-</sup> mice were injected with HT-1080-shPAI1 and HT-1080-scPAI1 tumor cells as described in Figure 7 panel K. The data represent the per cent of mice with engrafted tumors at day 40.



**Figure S5. IL-6 and IL-10 expression in the tumors from the experiment described under Figure 7 panel F.** Quantitative analysis of IL-6 (A) and IL-10 (B) levels measured by ELISA in tumor lysates of tumors from experiment described under Figure 7, Panel F. Each data-point represents a technical duplicate and has been expressed as pg of cytokine per  $\mu$ g of protein in tumor lysate.



**Figure S6. IL-10 expression in the tumor lysates from the experiment described in Figure 7K.**

Each data-point represents a technical duplicate and has been expressed as pg of IL-10 per μg of protein in tumor lysate.

**Table S1**

Sample Number	rPAI-1 variant	EU/ $\mu$ g of protein	EU/mL of medium supplemented with 100 nM of rPAI-1
1	rPAI-1	0.0056	0.0214
2	rPAI-1	0.0027	0.0103
3	rPAI-1	0.0227	0.0872
4	rPAI-1 T333R A335R	0.0051	0.0393
5	rPAI-1 T333R A335R	0.0017	0.0065
6	rPAI-1 R76E I91L	0.0068	0.0261
7	rPAI-1 R76E I91L	0.0018	0.0069

**Table S1. Endotoxin levels in commercially purchased recombinant Plasminogen Activator Inhibitor – 1 (rPAI-1) protein preparations. Related to Figure 3.** Endotoxin levels were measured in commercially purchased rPAI-1 protein preparations using Endolisa assay.