**Supplementary Figure S1. IL-6 mRNA expression in macrophages and endothelial cells.** RNAscope 2-plex assay for IL-6 (red) and CD68 (green) **(A)** or IL-6 (red) and CD31 (green) **(B)** indicated that some IL-6 positive cells in the stroma are macrophages or endothelial cells, respectively (arrows).

**Supplementary Figure S2. IL-6 mRNA positive blood vessels in prostate cancer bone metastases.** Example of IL-6 positive endothelial cells and IL-6 negative metastatic tumor cells in prostate cancer bone metastases.

**Supplementary Figure S3. IL-6 Western blot on NCI-H460 cells.** Western blot on protein lysates from NCI-H460 cells grown without (1) or with (2) protein transport inhibition with monensin (Golgi-Stop™). (3) 300 ng recombinant IL-6, positive control.

**Supplementary Figure S4**. **IL-6 CISH assay is more sensitive than IL-6 IHC.** **(A)** Standard curve generated using estimated copies of IL-6 cDNA clone expression vector (Origene, SC125236) used to determine IL-6 mRNA copy number in DU145 and PC3 cells. **(B)** IL-6 CISH on corresponding DU145 and PC3 cells. Note DU145 cells with many copies of IL-6 mRNA (arrow) and cells where lower copy numbers (5-10 dots per cell, arrowhead) can be visualized. Side-by-side IL-6 IHC is negative.