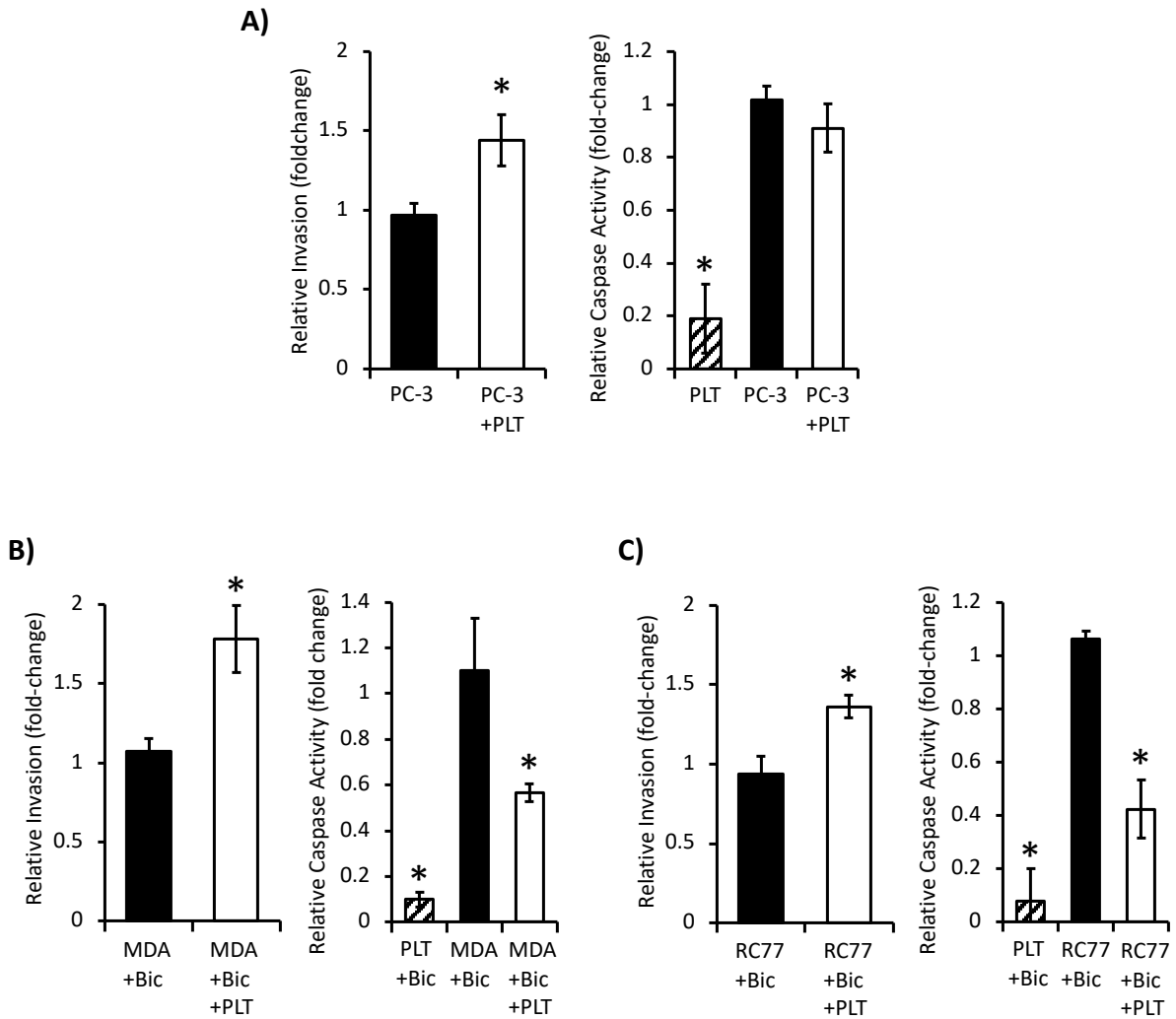
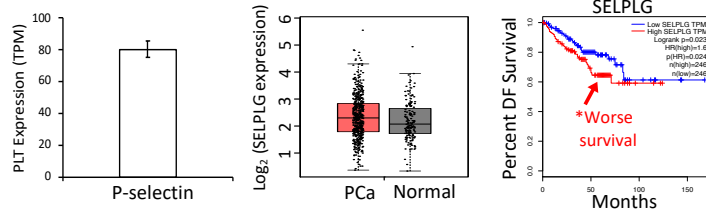


## SUPPLEMENTARY FIGURES

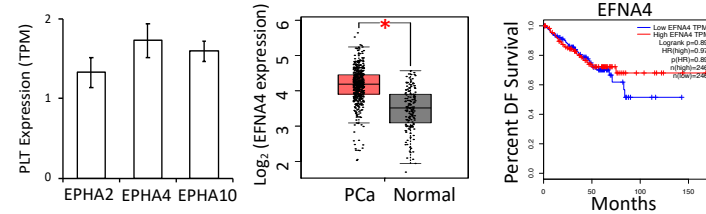


**Supplementary Fig. S1. Platelet-stimulated PCa cell invasion and apoptotic resistance are independent of the androgen receptor.** PC-3 cells are androgen receptor-negative. MDA PCa 2b (MDA) and RC77 T/E (RC77) are androgen receptor-positive cell lines **A)** Platelets (PLT) promote PC-3 prostate cancer cell invasion (left panel) but not apoptotic resistance (right panel). Data presented as the mean  $\pm$  SEM of  $n = 3-4$  independent determinations and analyzed by Student's t-test. \* $P < 0.05$ , significantly different from PC-3 (closed bar). **B)** Effect of androgen receptor blockade with 20  $\mu$ M bicalutamide (Bic) on PLT-stimulated MDA cell invasion and apoptotic resistance. Data presented as the mean  $\pm$  SEM of  $n = 4$  independent determinations and analyzed by ANOVA and Dunnett's *post-hoc* test. \* $P < 0.05$ , significantly different from MDA + Bic (closed bar). **C)** Effect of androgen receptor blockade with 20  $\mu$ M Bic on PLT-stimulated RC77 cell invasion and apoptotic resistance. Data presented as the mean  $\pm$  SEM of  $n = 4-5$  independent determinations and analyzed by ANOVA and Dunnett's *post-hoc* test. \* $P < 0.05$ , significantly different from RC77 + Bic (closed bar). Cell:platelet ratio for all experiments was 1:1000.

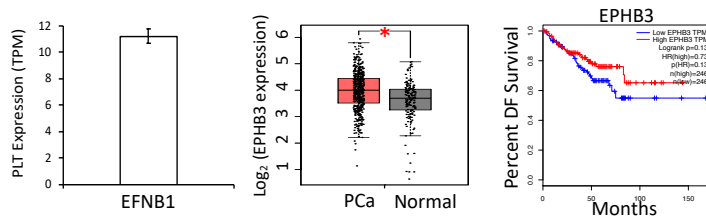
## A) P selectin-SELPLG Axis



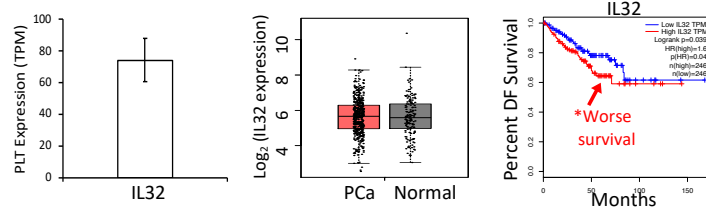
## B) EPHA receptor-EFNA4 Axis



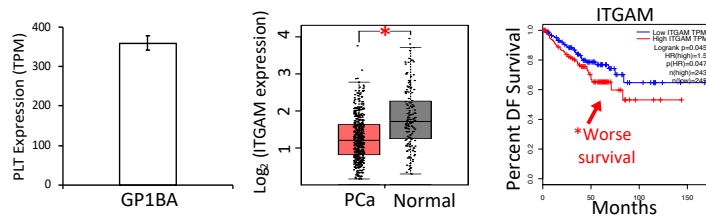
## C) EFNB1-EPHB3 receptor Axis



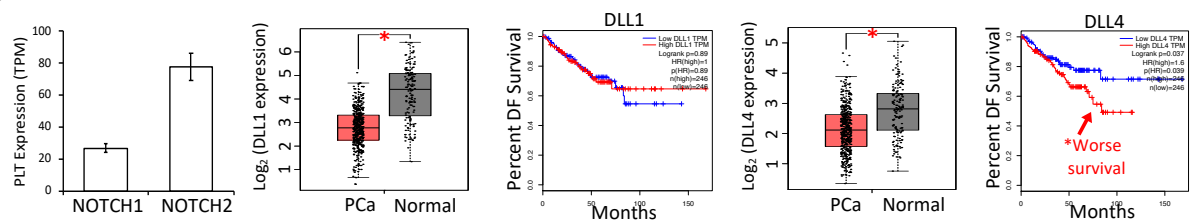
## D) IL32 signaling Axis



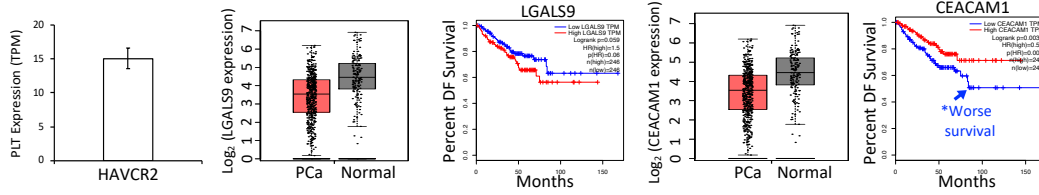
## E) GP1BA (GPIb $\alpha$ )-ITGAM Axis



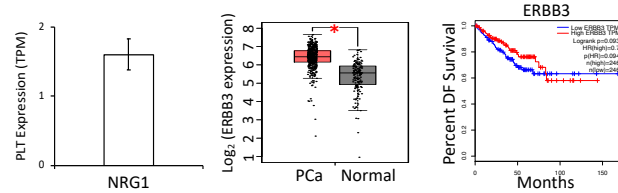
## F) NOTCH-DLL Axis



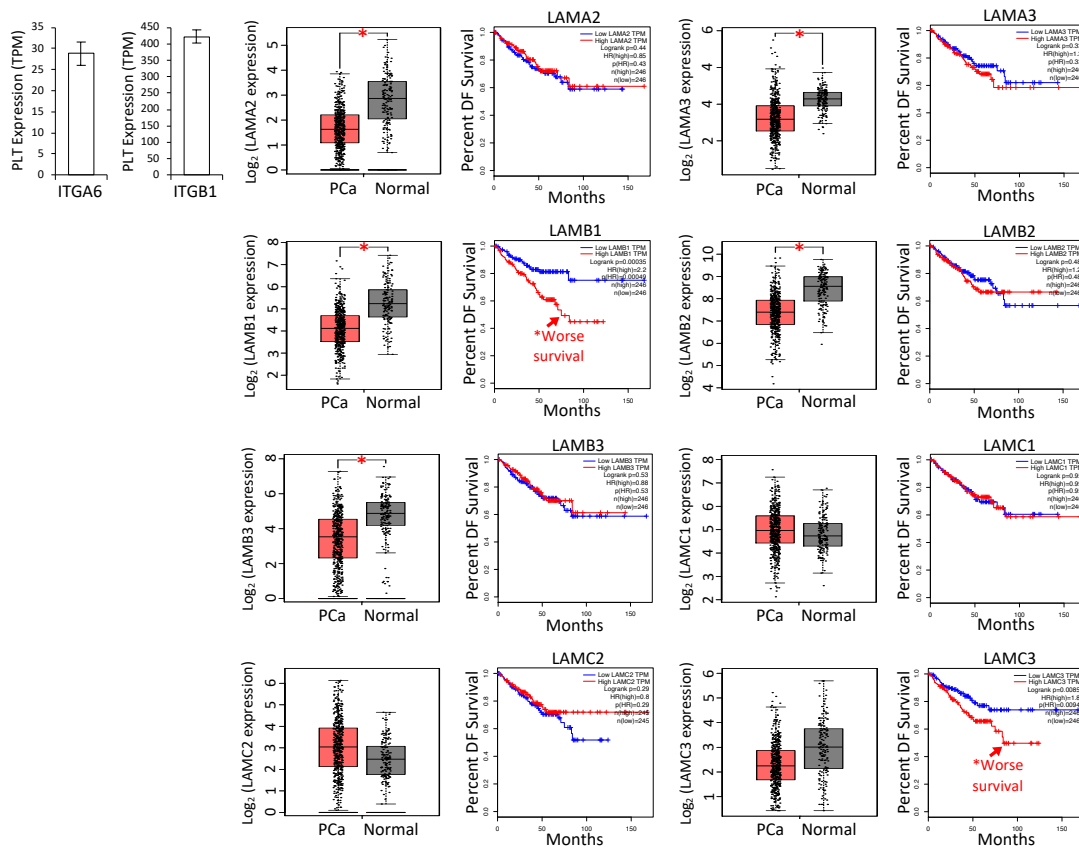
### G) HAVCR2-LGALS9 and HAVCR2-CEACAM1 Axes



### H) NRG1-ERBB3 receptor Axis

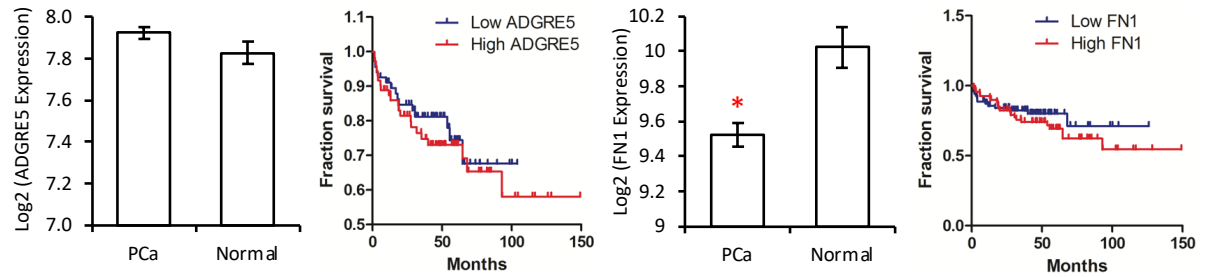


### I) Integrin $\alpha 6\beta 1$ -laminin Axis

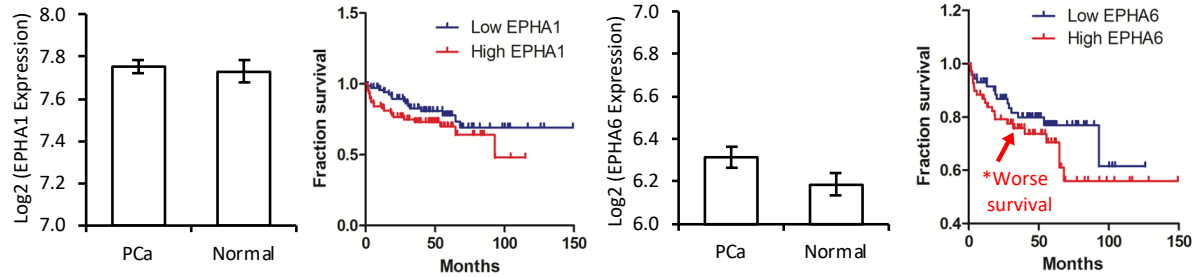


**Supplementary Fig. S2. Candidate platelet-PCa signaling axis partners.** Bar graphs depict expression of platelet signaling partner and corresponding PCa signaling partner based on Garofano et al.<sup>24</sup> and TCGA RNA-Seq data. Disease free (DF) survival plots are depicted for PCa signaling partners based on TCGA data. Signaling axes (platelet component-PCa component) displayed include **A)** P selectin-Selectin P ligand (SELPLG), **B)** EPHA receptor-EPHA4, **C)** EFNB1-EPHB3 receptor, **D)** IL32-IL32 receptor (identity of IL32 receptor remains obscure<sup>48</sup>), **E)** GPIBA-ITGAM, **F)** NOTCH-DLL, **G)** HAVCR2-LGALS9 and HAVCR2-CEACAM1, **H)** NRG1-ERBB3 receptor, and **I)** Integrin  $\alpha 6\beta 1$ -laminin. TPM, transcript per million; \*, Student's t-test or logrank test, \*P < 0.05.

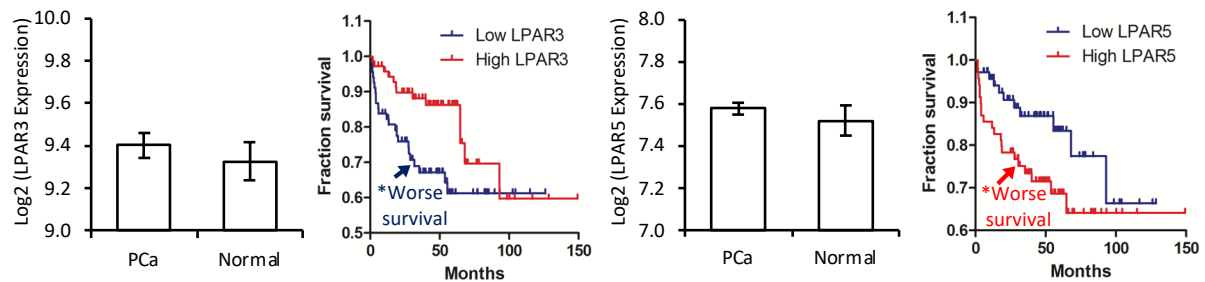
### A) CD55-ADGRE5 and integrin $\alpha_{IIb}\beta_3$ -FN1 Axes



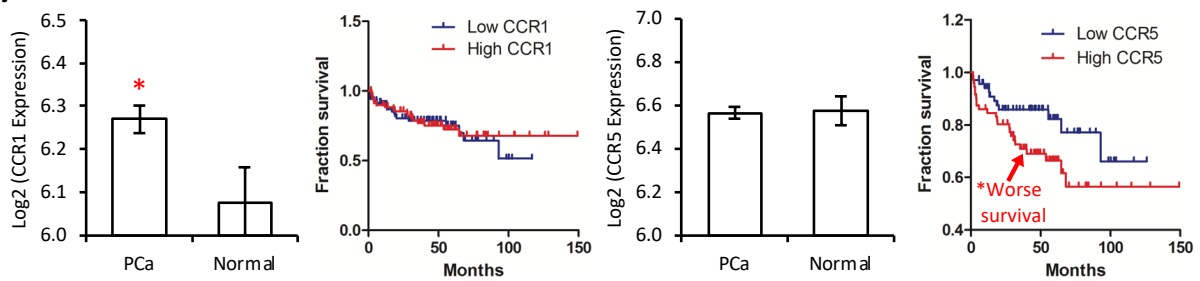
### B) EFNA4-EPHA receptor Axis



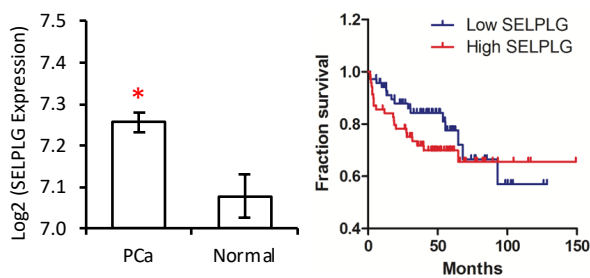
### C) LPA (platelet lipid agonist)-LPAR receptor Axis



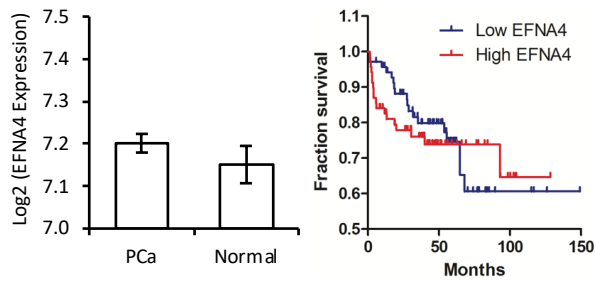
### D) CCL3L1-CCR receptor Axis



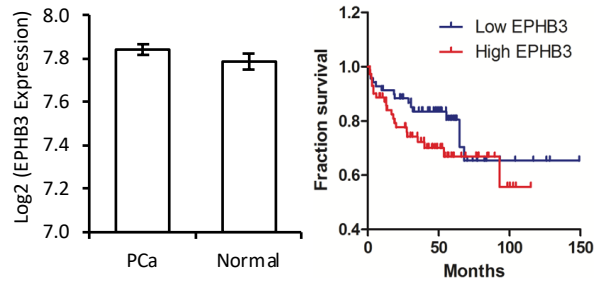
### E) P selectin-SELPLG Axis



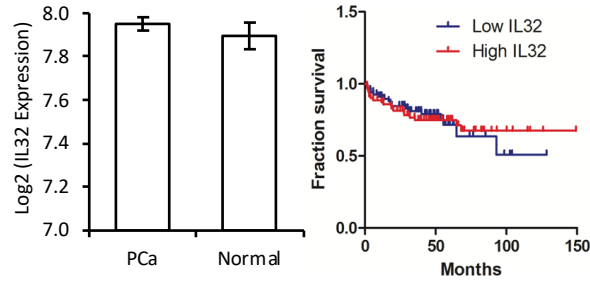
## F) EPHA receptor-EFNA4 Axis



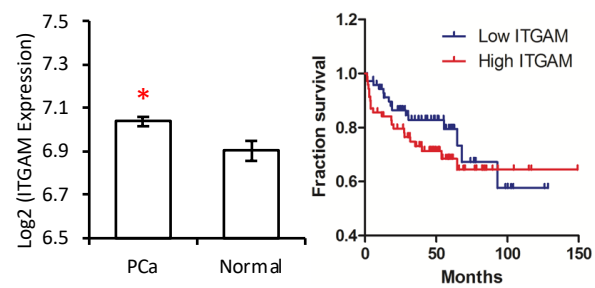
## G) EFNB1-EPHB3 receptor Axis



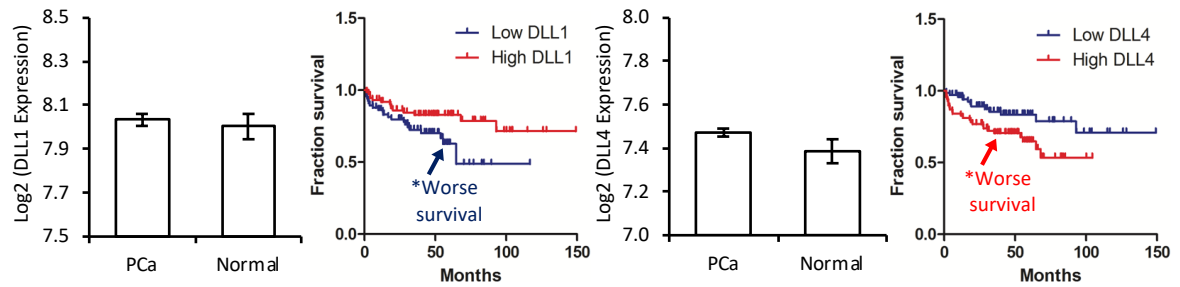
## H) IL32 signaling Axis



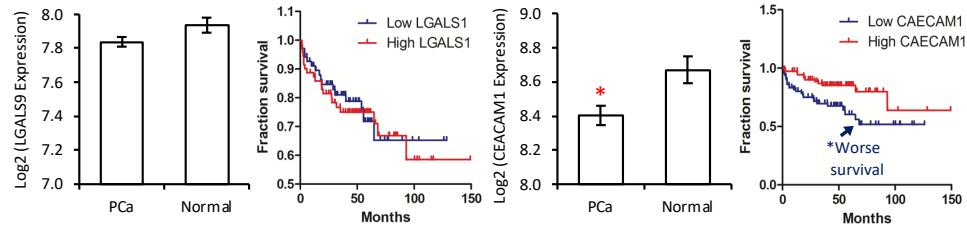
## I) GP1BA (GPIb $\alpha$ )-ITGAM Axis



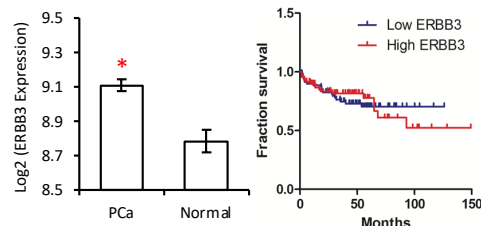
## J) NOTCH-DLL Axis



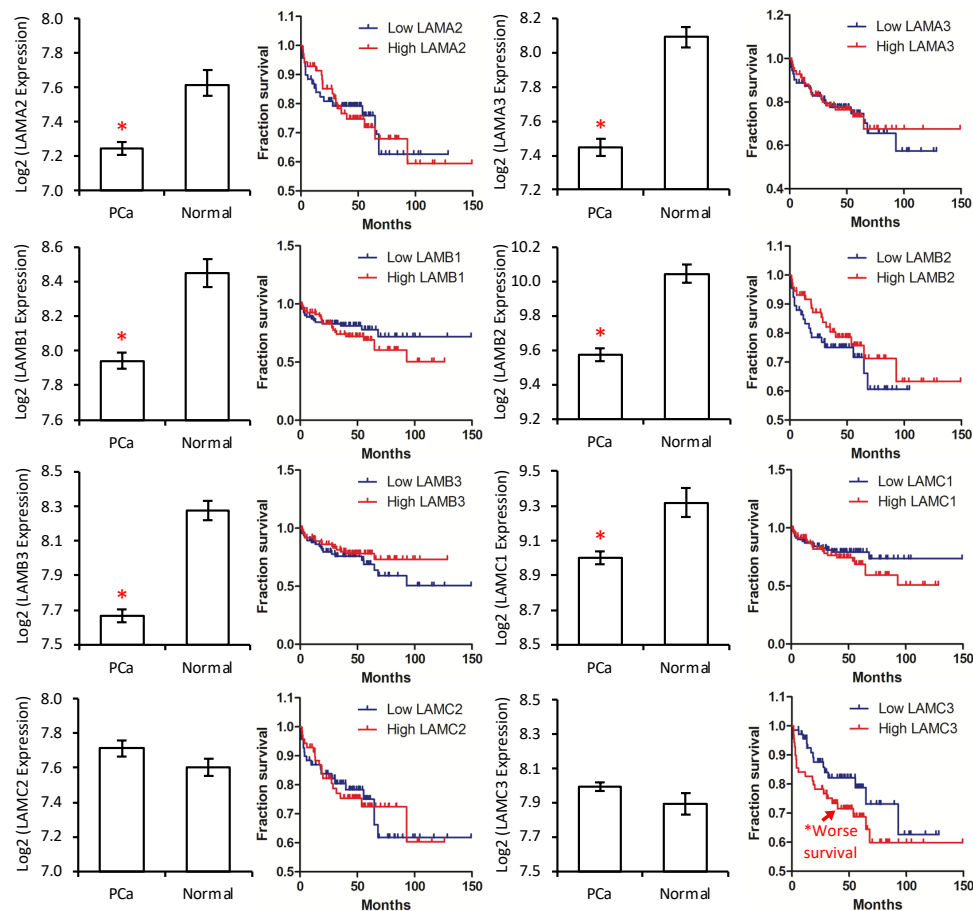
### K) HAVCR2-LGALS9 and HAVCR2-CEACAM1 Axes



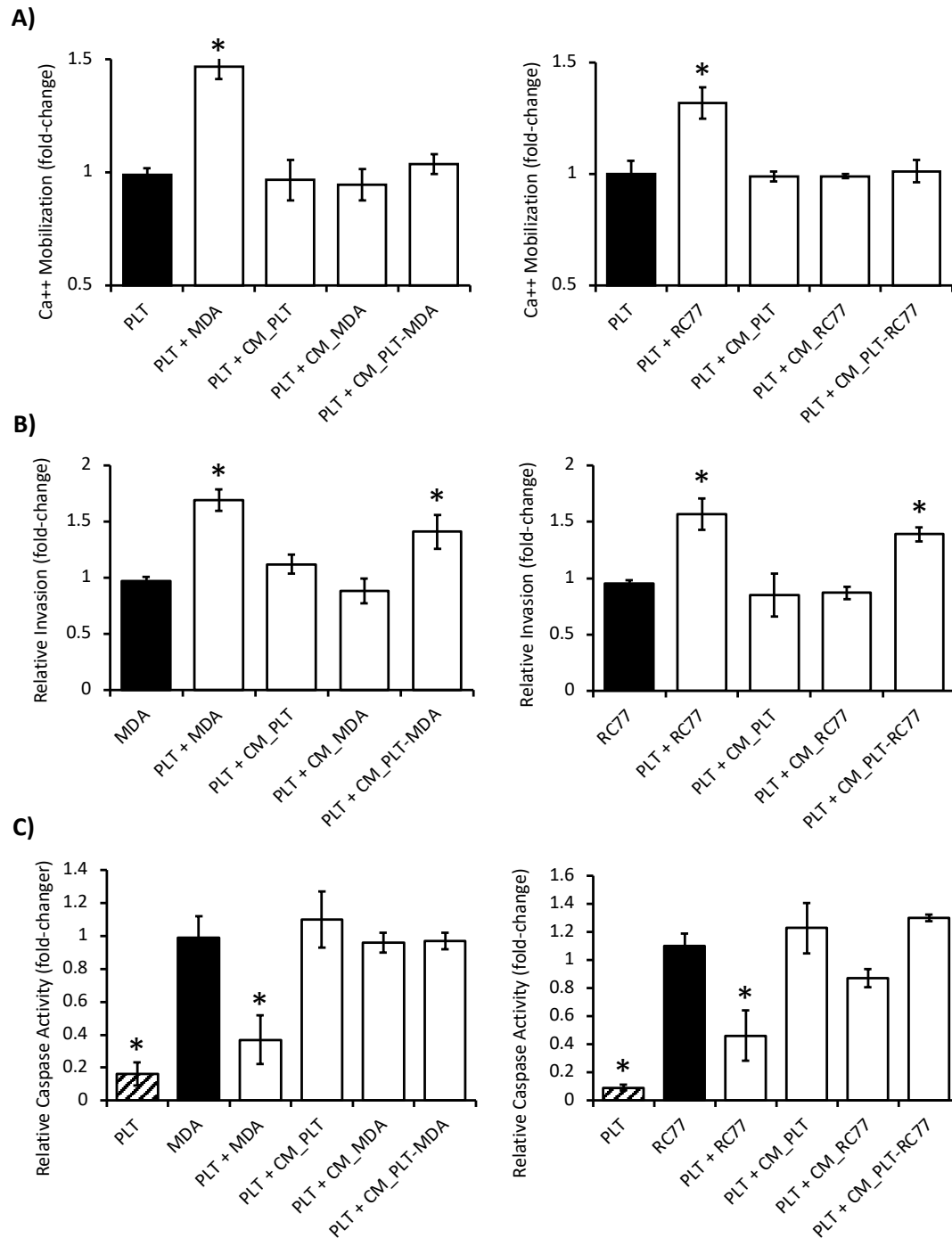
### L) NRG1-ERBB3 receptor Axis



### M) Integrin $\alpha\beta$ 1-laminin Axis

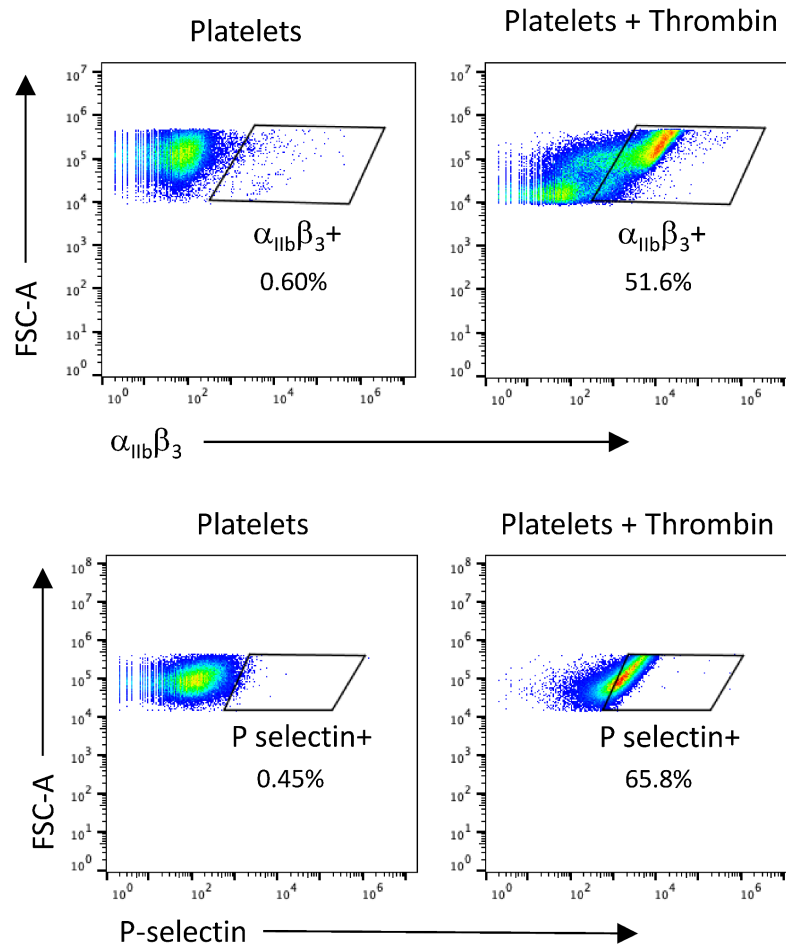


**Supplementary Fig. S3. PCa signaling axis partner expression and survival analyses in separate cohort of PCa patients.** Bar graphs depict expression of PCa signaling partner based on analysis of Taylor et al. Affymetrix Human Exon 1.0 ST array dataset<sup>27</sup>. Disease free (DF) survival plots are depicted for PCa signaling partners based on analysis of Taylor et al.<sup>27</sup> dataset. Signaling axis components are indicated as platelet component-PCa component. For example, CD55-ADGRE5 indicates CD55 component on platelets signaling with ADGRE5 component on PCa cells. \*, Student's t-test or logrank test, \*P < 0.05.

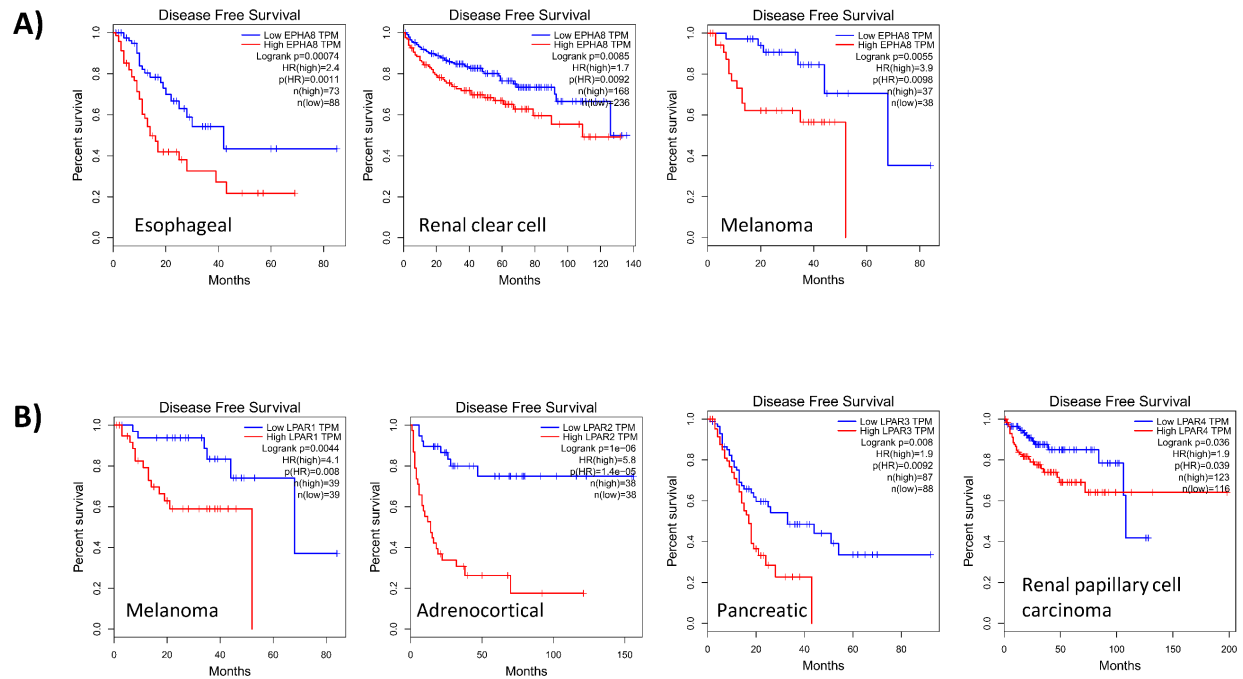


**Supplementary Fig. S4. Effect of conditioned medium on platelets and PCa cells. A)**

Platelets (PLT) were incubated with PCa cells (MDA or RC77), or conditioned media from PLTs cultured alone (CM\_PLT), PCa cells cultured alone (CM\_MDA, CM\_RC77) or PLTs + PCa cells cocultured (CM\_PLT-MDA, CM\_PLT-RC77) for 90 minutes and calcium mobilization in PLTs was measured. **B)** Same as panel A except conditioned medium was collected at 48 hours for invasion assay. **C)** Same as panel A except conditioned medium was collected at 24 hours for caspase activity assay. Data presented as the mean  $\pm$  SEM of  $n = 3-4$  independent determinations and analyzed by ANOVA and Dunnett's *post-hoc* test. \* $P < 0.05$ , significantly different from PLT group (closed bar) in panel A. \* $P < 0.05$ , significantly different from MDA or RC77 cells (closed bars) in panels B and C. Cell:platelet ratio for all experiments was 1:1000.



**Supplementary Fig. S5. Thrombin-stimulated surface expression of P-selectin and activated  $\alpha_{IIb}\beta_3$  in platelets.** Platelets were activated with 0.5 units/ml thrombin for 5 minutes. Representative flow cytometry dot plots for surface expression of two platelet activation markers, P-selectin (CD62P) and activated integrin  $\alpha_{IIb}\beta_3$  (PAC-1). Dot plots are representative of 3 independent assays.



**Supplementary Fig. S6. Survival plots for cancer patients with high and low expression of EPHA8 receptor or LPAR subtypes.** RNA-Seq and disease-free survival data for the indicated cancers were obtained from The Cancer Genome Atlas (TCGA) (<https://tcga-data.nci.nih.gov/tcga/>). P-values for survival curves were determined by the logrank test. **A)** Survival plots for ephrin type-A receptor 8 (EPHA8). **B)** Survival plots for the lysophosphatidic acid receptors (LPAR1, 2, 3 and 4).