Expanded View Figures

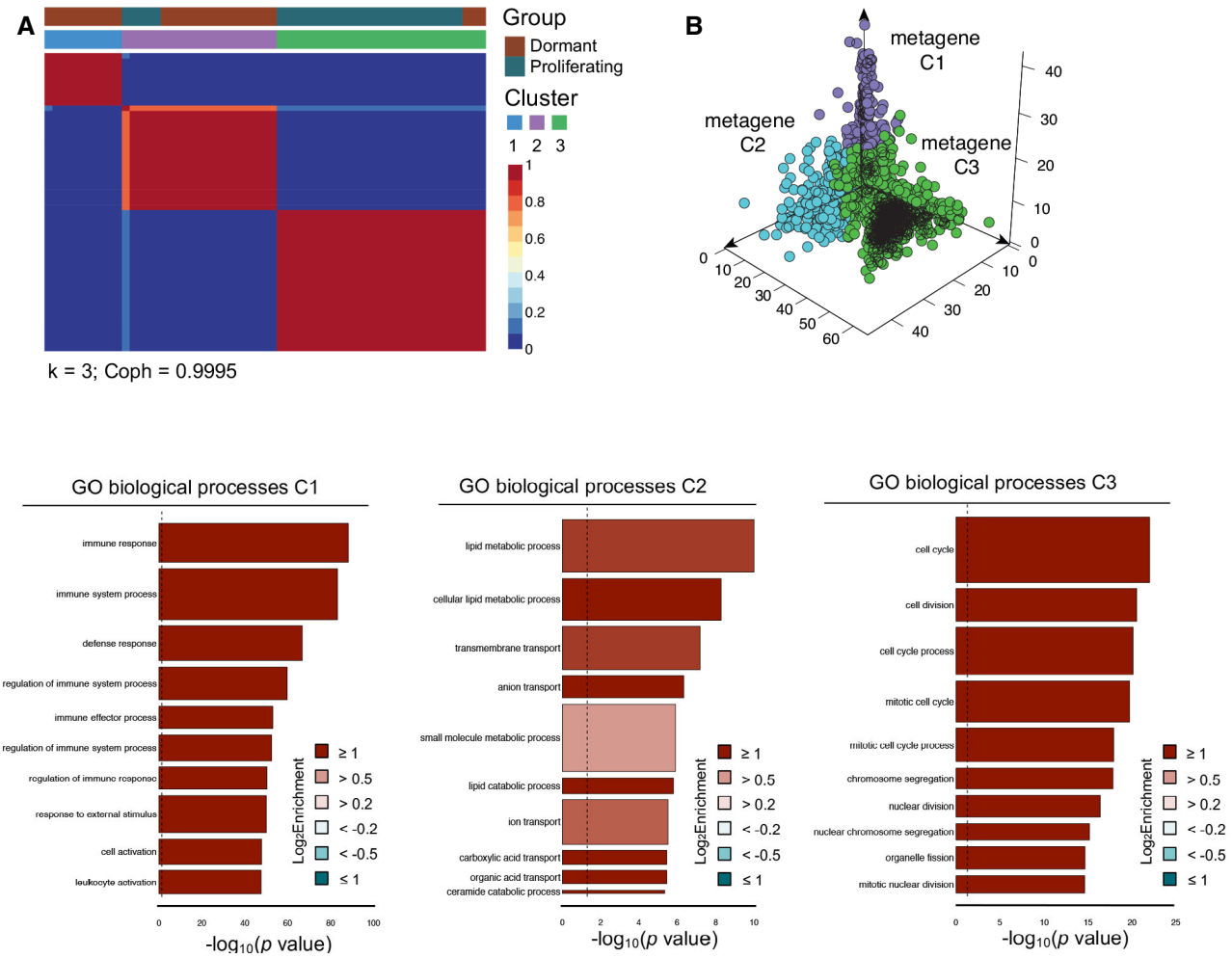

Figure EV1. Type I IFN signaling is retained in dormant PCa cells in bone metastases.

A Consensus matrix of non-negative matrix factorization analysis of all DEGs expressed between dormant and proliferating cells defines two dominant dormant (C1, C2) and one chiefly proliferating (C3) clusters (k = 3; Coph = 0.9995).

B Distribution of all genes contributing to each of the dominant three cluster metagenes (C1–3).

C *goana* gene ontology (GO) analysis (limma) showing the top 10 biological processes for all genes contributing to C1, C2, and C3 in order of fold enrichment. Gene sets appear in order of significance (P-value) with color representing fold enrichment (FE) and bar width indicating the number of genes in each process.

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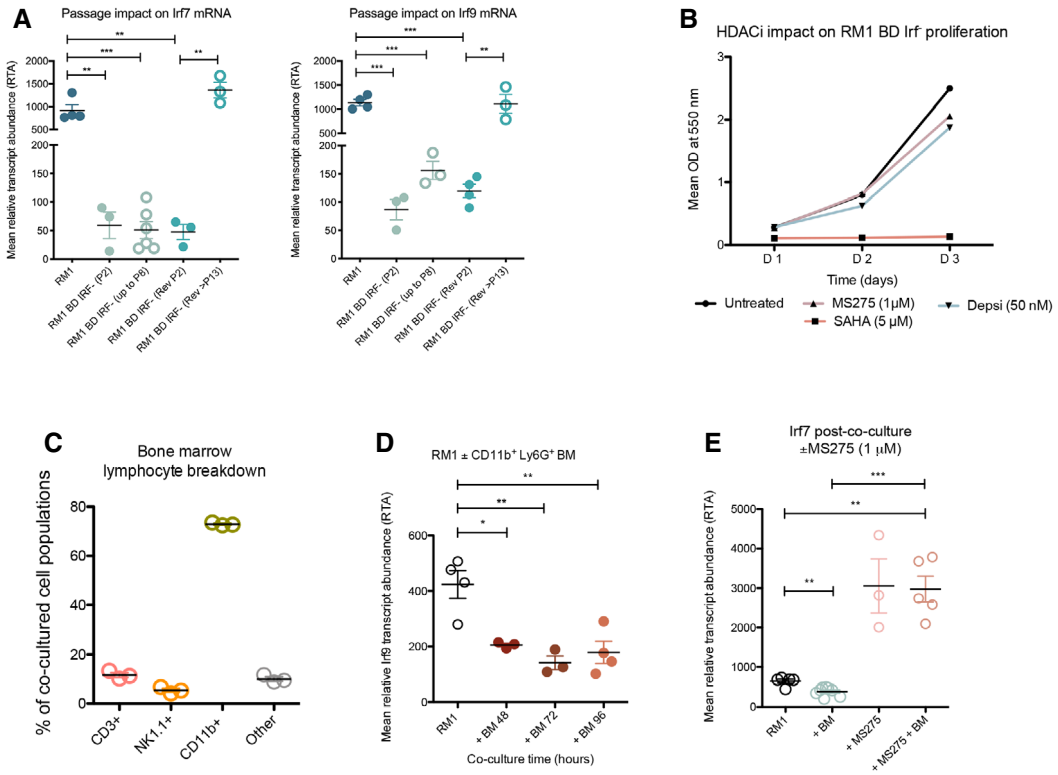

Figure EV2. Loss of tumor-intrinsic type I IFN is inducible by bone marrow cells and is reversed through HDACi modulation.

A Assessment of tumor-intrinsic IFN suppression stability over passage (P; number indicated) in culture by qRT–PCR analysis of mean *Irf7* and *Irf9* mRNA expression in bone-derived RM1 Irf-low (RM1 BD Irf^{-}) cells and a reverted (REV) bone-derived cell line compared to RM1 parental cells. Values are means ± SEM of three independent experiments.

B HDACi impact on RM1 BD Irf^{-} proliferation over time by SRB assay. Mean OD at 550 nm (n = 3).

C Flow cytometry characterization of bone marrow lymphocyte (%) populations (n = 3).

D qRT–PCR of *Irf9* expression in parental RM1 cells 48, 72, and 96 h post-contact co-culture with FACS-isolated naïve CD11b^{+} Ly6G^{+} BM cells (n = 3 mice per time point).

E qRT–PCR of *Irf7* expression in RM1 parental cells ± co-culture with naïve BM ± 48 h treatment with MS275 (n = 3–6). P-values represented as * < 0.05, ** < 0.005, and *** < 0.0005 (Student's t-test). All error bars ± SEM.

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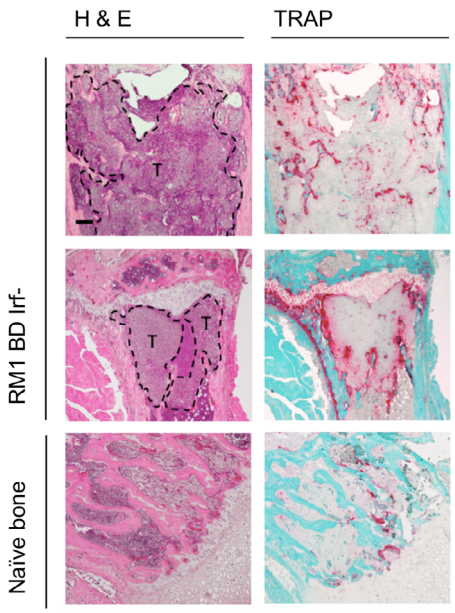

Figure EV3. Impact of differential tumor-intrinsic IFN signaling on metastasis, dormancy and bone remodeling.
Representative H&E- and TRAP-stained bone sections from naïve and RM1 BD Irf^{-} tumor-bearing animals. T indicates tumor regions. Scale bar, 200 μm.

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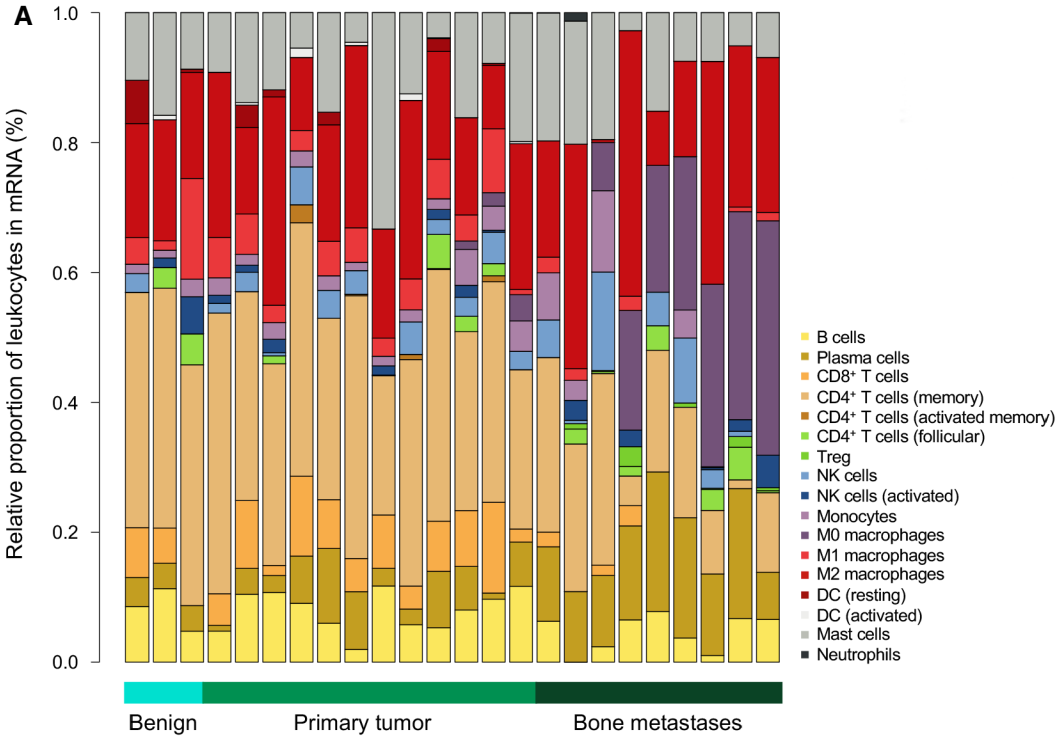

B

Rank	*p* value	FC	Gene	Reporter
147	1.58E-6	-6.39	*Gbp1*	202270_at
415	2.22E-5	-13.84	*Vgll3*	227399_at
531	4.18E-5	-2.46	*Irf9*	203882_at
688	9.41E-5	-43.64	*Ctgf*	209101_at
1208	5.02E-4	-2.13	*Stat1*	200887_s_at
1672	0.001	-3.05	*Tlr3**	206271_at
3329	0.012	-3.02	*Oas2*	206553_at

Figure EV4. IFN signaling is decreased in bone-metastatic PCa.

A Relative proportions (%) of leukocytes in mRNA samples from patient bone metastases (n = 9) compared to primary tumors (n = 12) and benign tumors (n = 3) by CIBERSORT. Cell subsets indicated on graph.

B Oncomine interrogation of the Varambally Prostate dataset using an 8-IRG core signature (data unavailable for *Tslp*; NS for *Oas1* (FC = -1.24; P = 0.214; *Tlr3* additional)) in primary (n = 7) and metastatic (n = 6) tissues derived from Human Genome U133 Plus 2.0 Array analysis (z-score-normalized; log2 median-centered intensity). Fold change (FC) values shown with corresponding P-values (log-rank test).

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