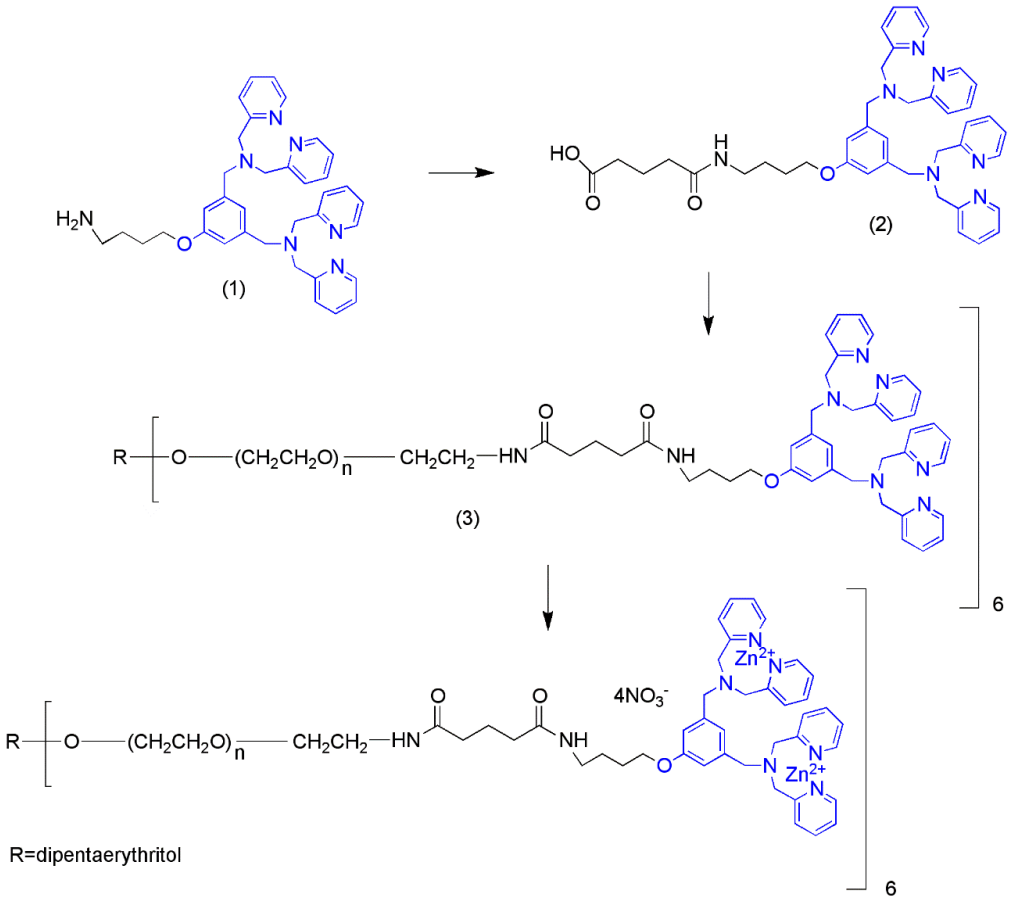

Figure S1: Synthetic scheme to produce $(ZnDPA)_6$-DP-15K i.e. ExoBlock. DPA-amine (1) is prepared from 3,5-dicarboxymethylphenol in 5 synthetic steps according to a literature procedure (Lakshmi, C, Hanshaw RG, Smith BD. 2004. *Fluorphore-linked zinc(II) dipicolylamine coordination complexes as sensors for phosphatidylserine-containing membranes*. Tetrahedron**,** 60, 11307-11315). Reaction of (1) (523mgs, 0.890mmol) with glutaric anhydride (107mgs, 0.940 mmol) in chloroform (20 mL) for 24h at room temperature and concentration of the mixture provides compound (2) in quantitative yield. Treatment of (2) (593mgs, 0.850mmol) with the water soluble coupling agent, 1-ethyl-3(3-dimethylaminopropyl)carbodiimide (189mgs, 0.984mmol) and N-hydroxysulfosuccinimide (234mgs, 1.078mmol) in anhydrous DMF (12mL) for 20h at room temperature gives the activated ester intermediate in situ. Next, 6-arm-PEG-amine (dipentaerythritol), HCl salt, MW=15,000 (450mgs, 29.7 μmoles, Jenkem Technology) in DMF (10mL) containing 50uL of N,N-diisopropylethylamine is added and the mixture stirred at room temperature overnight to provide (3). The DMF is then removed by rotary evaporation and zinc nitrate hexahydrate (630mg, 2.12 mmol) in 40mL of methanol is added and the mixture stirred for 24h. The methanol is then removed by rotary evaporation and the residue taken up in water (30mL) and transferred to three 10mL dialyzer tubes of MWCO=8-10kDa (Spectra-Por Float-A-Lyzer). Bags are placed in 3L of water and stirred with 3 water changes at 2h, 6h and 24h. Solutions from dialysis bags are combined and filtered through a 0.2um PTFE Nalgene filter and the solution is freeze dried overnight to provide 560mgs of ExoBlock as a white solid.

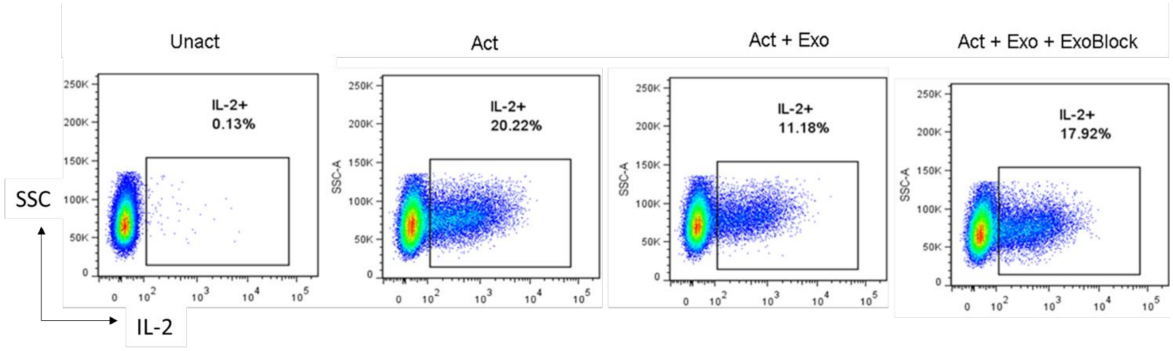

Figure S2: ExoBlock reverses inhibition of IL-2 expression mediated by ovarian tumor-associated exosomes. T cells were either left unactivated (Unact), activated for 6h with immobilized antibodies to CD3 and CD28 without exosomes (Act), with exosomes only (Act + Exo), or with exosomes and ExoBlock (Act + Exo + ExoBlock). Activation was monitored by detecting the intracellular expression of IL-2.

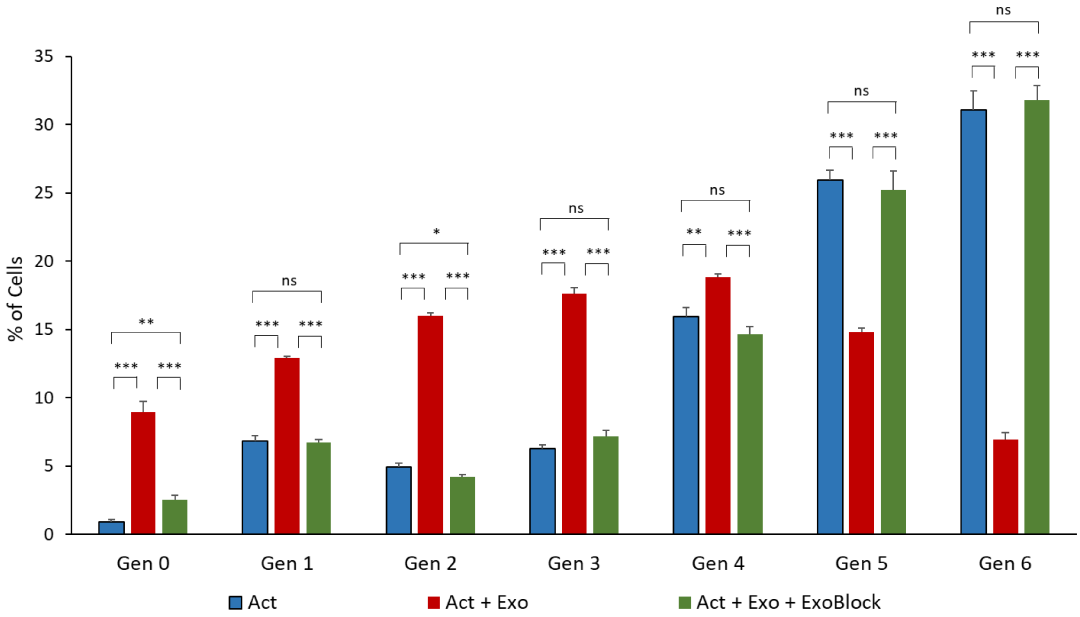

Figure S3: ExoBlock reverses inhibition of T cell proliferation mediated by ovarian tumor-associated exosomes. T cells labeled with CellTrace Violet were activated for 7 days with immobilized antibodies to CD3 and CD28 without exosomes (Act), with exosomes only (Act + Exo), or with exosomes and ExoBlock (Act + Exo + ExoBlock). Proliferative responses were assessed by monitoring dye dilution using flow cytometry. The percentage of undivided cells (Gen 0) as well as in each generation of division (Gen 1-6) was determined using the proliferation platform software (FlowJo). n = 3. Data shown as Mean ± SEM, ns = not significant; *p ≤ 0.05; **p ≤ 0.01; ***p ≤ 0.001.

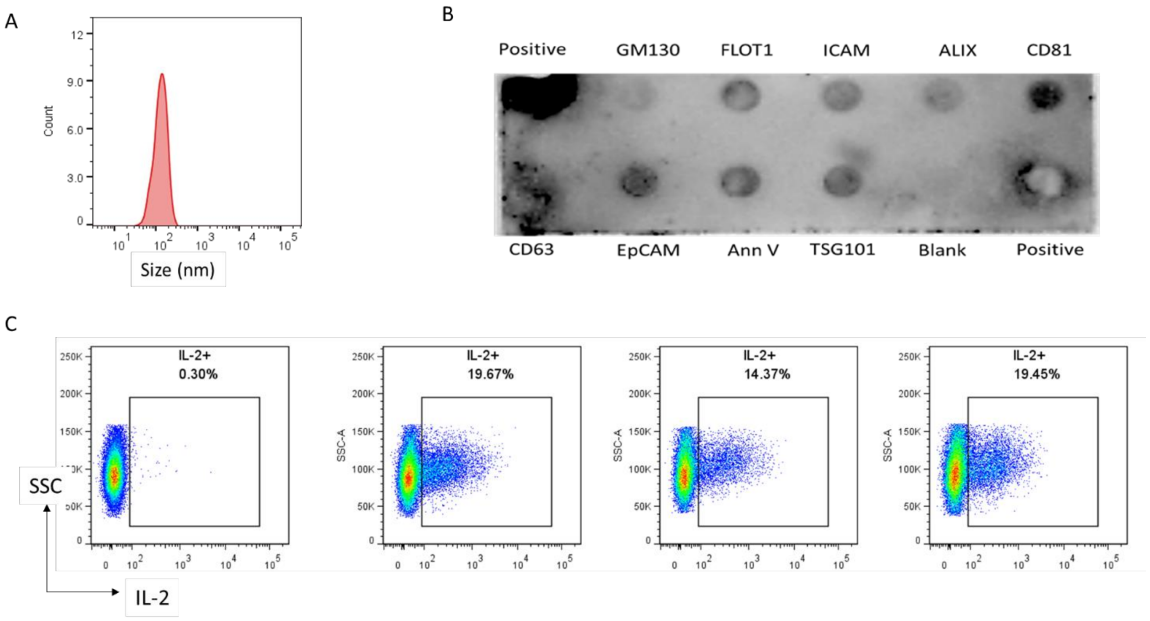

Figure S4: ExoBlock reverses inhibition of IL-2 expression mediated by melanoma-associated exosomes. (**A-B)** Characterization of exosomes derived from DM6-Mut melanoma: **(A)** Size distribution analyzed by Nanoparticle tracking analysis **(B)** Presence of exosomal markers shown by ExoArray **(C)** T cells were either left unactivated (Unact) activated for 6h with immobilized antibodies to CD3 and CD28 without exosomes (Act), with exosomes only (Act + Exo), or with exosomes and ExoBlock (Act + Exo + ExoBlock). Activation was monitored by detecting the intracellular expression of IL-2.

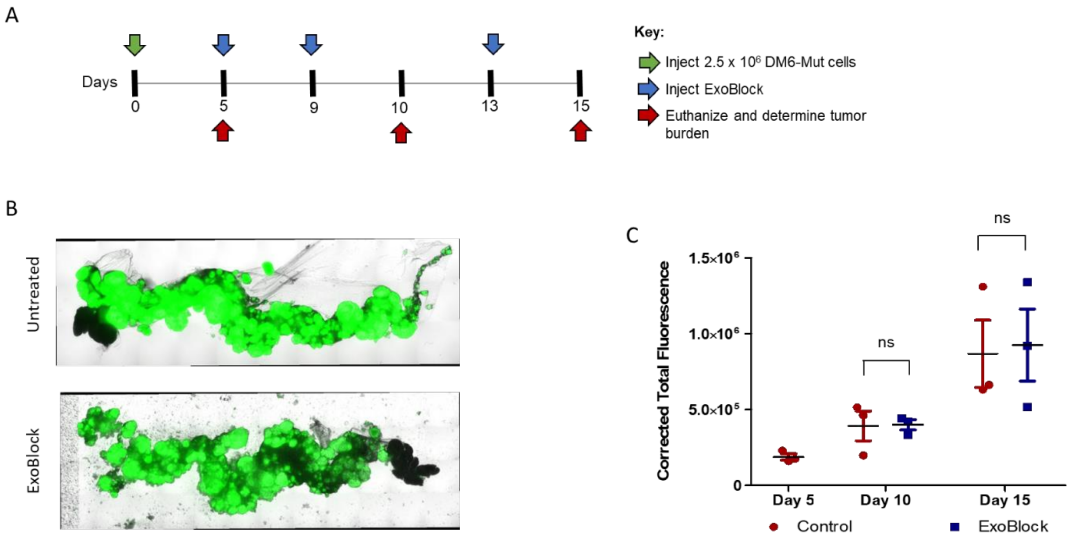

Figure S5: ExoBlock does not suppress tumor growth in the absence of T cells. (A) Experimental scheme indicating the timeline for injection of tumor cells (green arrow), treatment with ExoBlock (blue arrows) and estimation of tumor burden (red arrows). **(B)** Representative images of omental tumor burdens on day 25. **(C)** Tumor burdens were determined by quantifying the GFP signal using ImageJ software and are represented as corrected total fluorescence (CTF). n = 3 mice per group. Data shown as Mean ± SEM, ns = not significant.

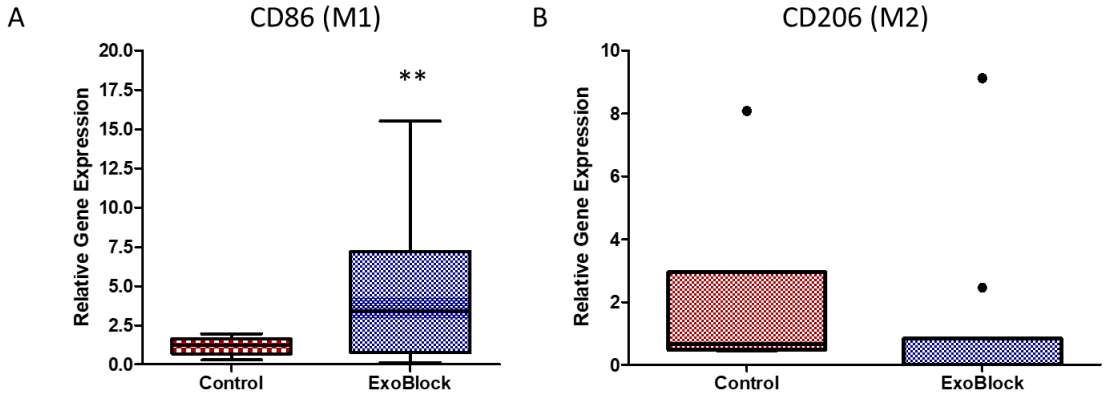

Figure S6: ExoBlock reverses M1:M2 macrophage ratio in the OTX model. The OTX model was established by injecting patient-derived ovarian tumor aggregates into NSG mice. The mice were either left untreated (control) or treated with ExoBlock on days 10, 15 and 20. The expression of CD86 and CD206 in the tumor xenografts on day 25 was determined using qRT-PCR. n = 9 for A and 6 for B. Data shown as Mean ± SEM, **$p \leq 0.01$.

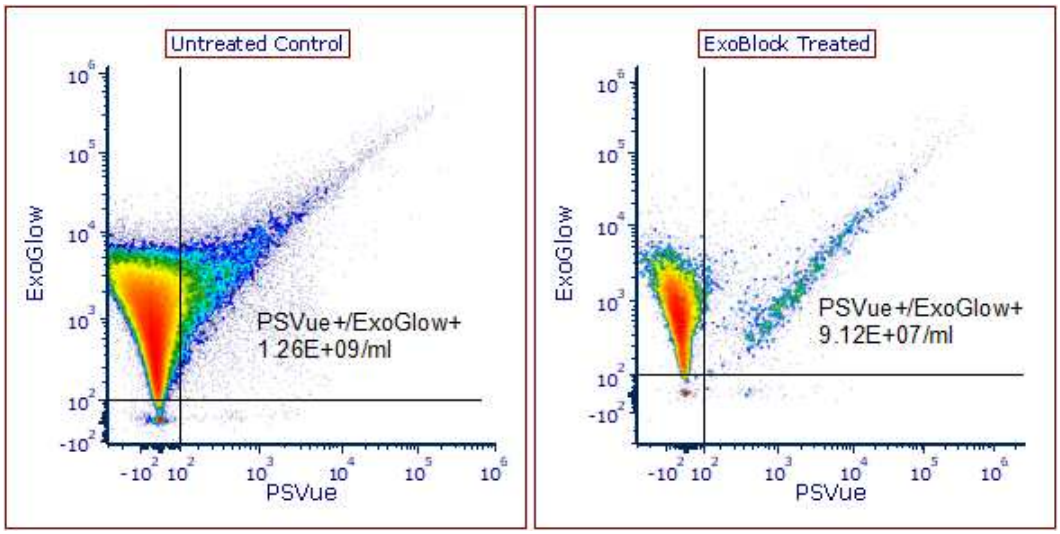

Figure S7: ExoBlock decreases circulating PS+ exosomes in the OTX model. Representative images for the imaging flow cytometric (IFC) determination of PS+ exosomes from day 25 omental tumor xenografts. Exosomes were identified using ExoGlow and PS expression was determined using PSVue binding.