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Figure S1: Metastasis by 22RV1 to the humerus in huNOG and huNOG-EXL mice. A, Bioluminescent images taken of huNOG humeri, **B,** Quantified bioluminescence of huNOG humerus metastasis. **C,** Bioluminescent images taken of huNOG-EXL humeri, **D,** Quantified bioluminescence of huNOG humerus metastasis.

Figure S2: Metastasis by 22RV1 to the skull in huNOG and huNOG-EXL mice. A, Bioluminescent images taken of huNOG skulls, **B,** Quantified bioluminescence of huNOG skull metastasis. **C,** Bioluminescent images taken of huNOG-EXL skulls, **D,** Quantified bioluminescence of huNOG-EXL skull metastasis.

Figure S3: Metastasis by 22RV1 to the spleen in huNOG and huNOG-EXL mice. A, Bioluminescent images taken of huNOG spleens, **B,** Quantified bioluminescence of huNOG spleen metastasis. **C,** Bioluminescent images taken of huNOG-EXL spleens, **D,** Quantified bioluminescence of huNOG-EXL spleen metastasis.

Figure S4: Metastasis by 22RV1 to the lung in huNOG and huNOG-EXL mice. A, Bioluminescent images taken of huNOG lungs, **B,** Quantified bioluminescence of huNOG lung metastasis. **C,** Bioluminescent images taken of huNOG-EXL lungs, **D,** Quantified bioluminescence of huNOG-EXL lung metastasis.

Figure S5: Metastasis by 22RV1 to the heart in huNOG and huNOG-EXL mice. A, Bioluminescent images taken of huNOG hearts, **B,** Quantified bioluminescence of huNOG heart

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metastasis. **C,** Bioluminescent images taken of huNOG-EXL hearts, **D,** Quantified bioluminescence of huNOG-EXL heart metastasis.

Figure S6: 22Rv1 growth in huNOG-EXL and NOG-EXL mice. A, Subcutaneous "primary" flank tumor volume growth measured over time in both huNOG-EXL and NOG-EXL mice. **B,** Subcutaneous "primary" flank tumor volume growth measured over time in both huNOG-EXL **C,** Subcutaneous "primary" flank tumor volume growth measured over time in both NOG-EXL.

Figure S7: Immune-profile in huNOG-EXL 22Rv1 xenograft spleen. A, Gating strategy used to determine presence of human CD45+ cells in the NOG-EXL model spleen. **B,** Representitave data showing the abundance of various immune cell populations; human leukocytes, CD19+ cells, CD3+ cells and double negative cells, MDSC and activated myeloid cells and helper t-cells (CD4+) and cytotoxic t-cells (CD8+) (top to bottom). **C,** Quantitated data comparing human CD45, CD3, CD4, and CD11b populations in spleens isolated from testosterone implanted vehicle, intact vehicle, castrated vehicle, and castrated enzalutamide treated mice. **D,** Gating strategy for determining the activation state of MDSCs (CD3-CD19- CD11b+ CD14-). **E,** Representative data showing the activation state of the MDSC cells harvested from spleens under different treatment categories through the presence of the surface markers: CD25, CD44, CD69 and PD-1. **F,** Quantitated data showing the activation state of the spleen MDSCs throughout the different treatments.

Figure S8: Immune-profile of t-cells in huNOG-EXL spleen. A, Gating strategy for determining the activation state of T-cells and regulatory-like T-cells. **B,** Representative data showing the activation state of the CD3+ cells harvested from spleens under different treatment categories through the presence of the surface markers: CD25, CD44, CD69 and PD-1 and regulatory-like cells (CD3+CD25+PD-1+). **C,** Quantitation showing the expression of CD25, **D,** CD44, **E,** CD69, **F,** PD-1, **G,** regulatory-like T-cells (Tregs).

Figure S9: Immune-profile of spleen and tumor B-cell Populations and B-cell activation NK-Cell population in huNOG-EXL spleen. A, Representative data showing the activation state of the CD11b+CD14+ cells harvested from spleens under different treatment categories through the presence of the surface markers: CD25, CD44, CD69 and PD-1. **B,** Quantitation showing the expression of CD25, CD44, CD69, PD-1. **C,** Representative data showing the activation state of the CD19+ cells harvested from spleens under different treatment categories through the presence of the surface markers: CD25, CD44, CD69 and PD-1. **D,** Quantitation showing the expression of CD25, CD44, CD69, PD-1. **E,** Percent total CD19+ cells of the total CD45+ population of TILs. **F,** Percent total CD19+ cells of the total CD45+ population of splenocytes. **G,** Percent total NK cells from the spleen (CD3-CD19-CD16+CD56+).

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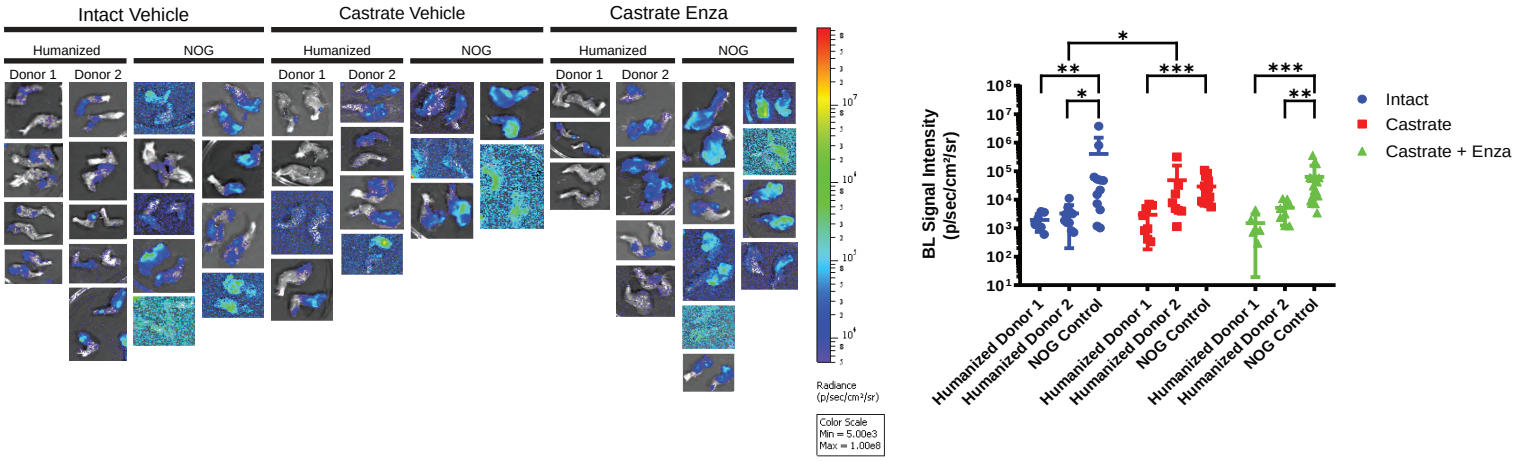
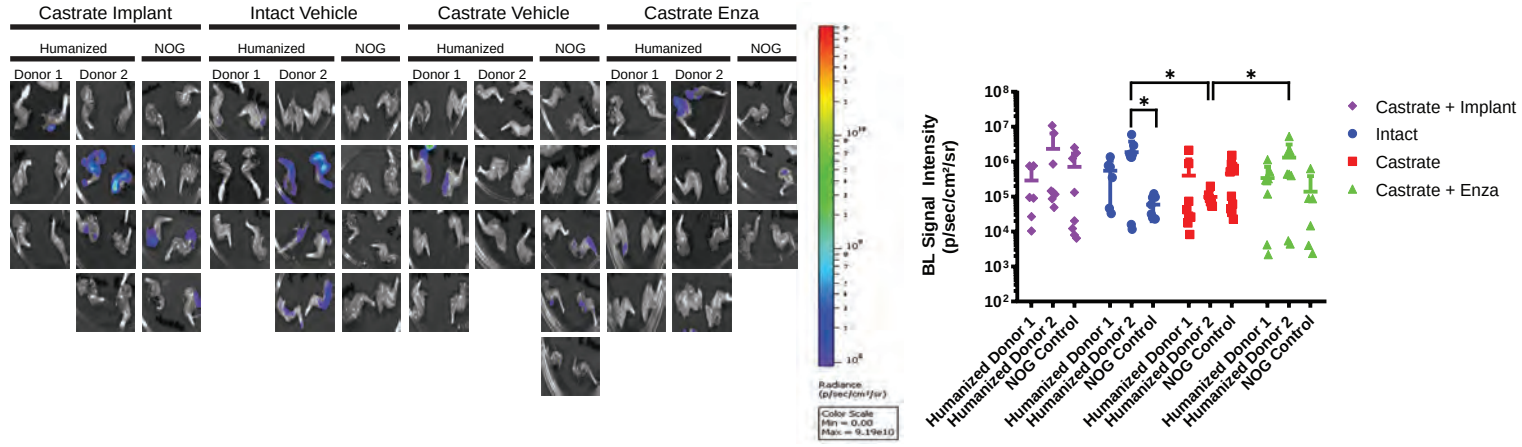
A

Humerus huNOG



B

Humerus huNOG-EXL



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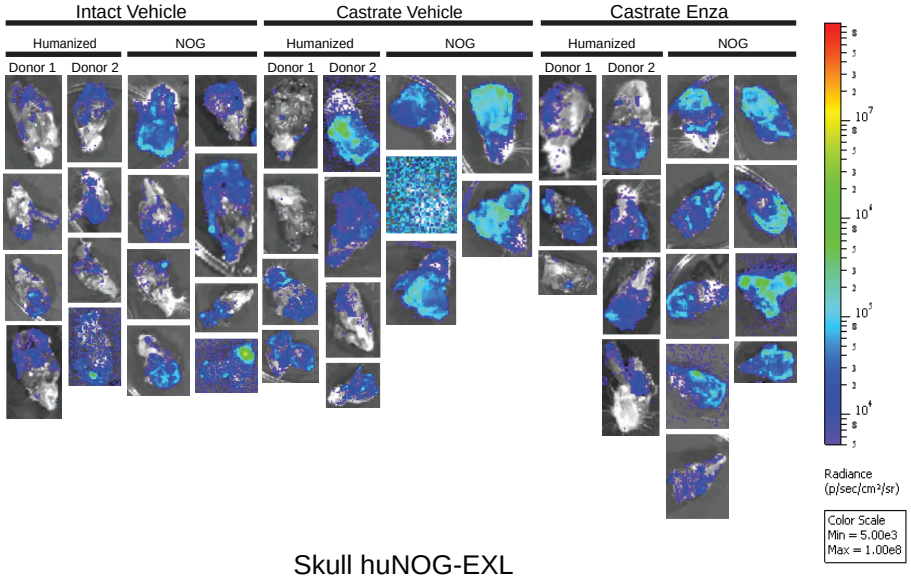
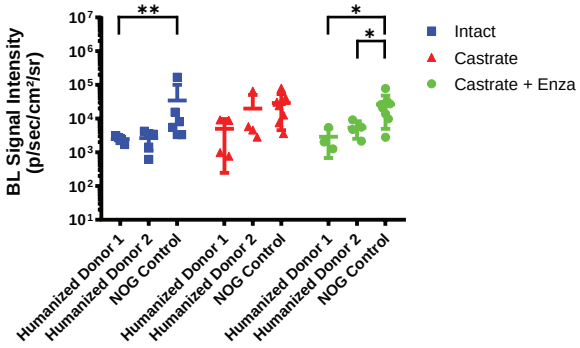
A

Skull huNOG





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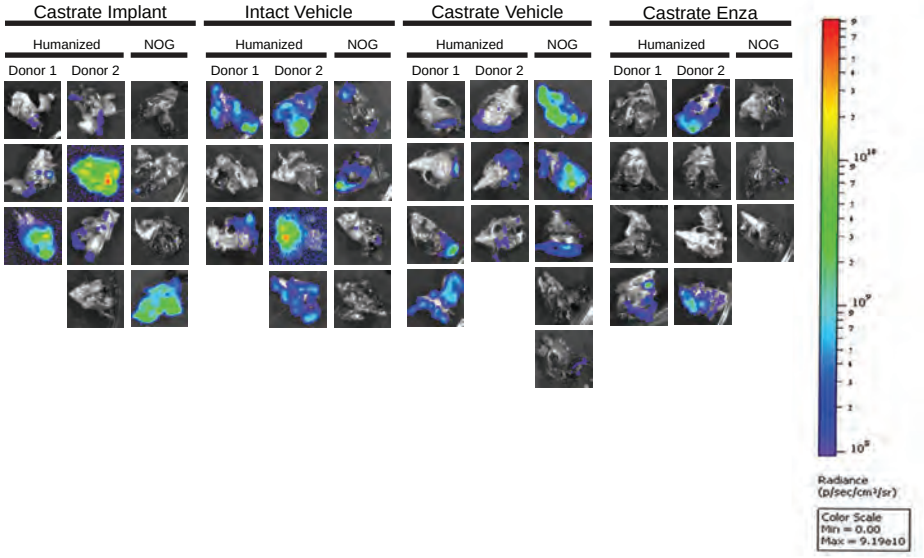
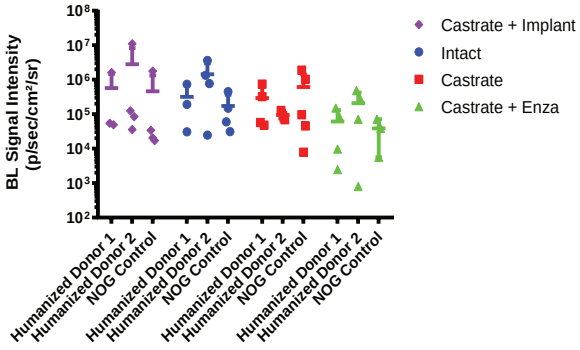
Skull huNOG-EXL





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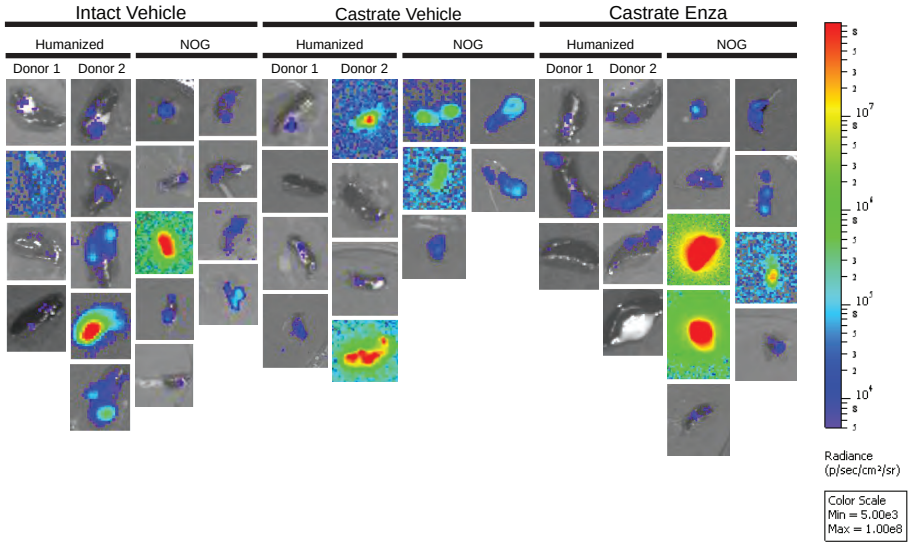
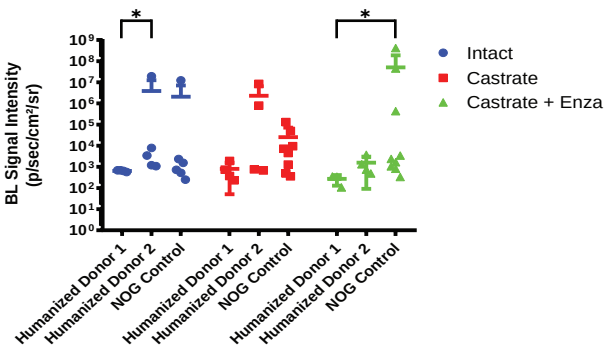
A

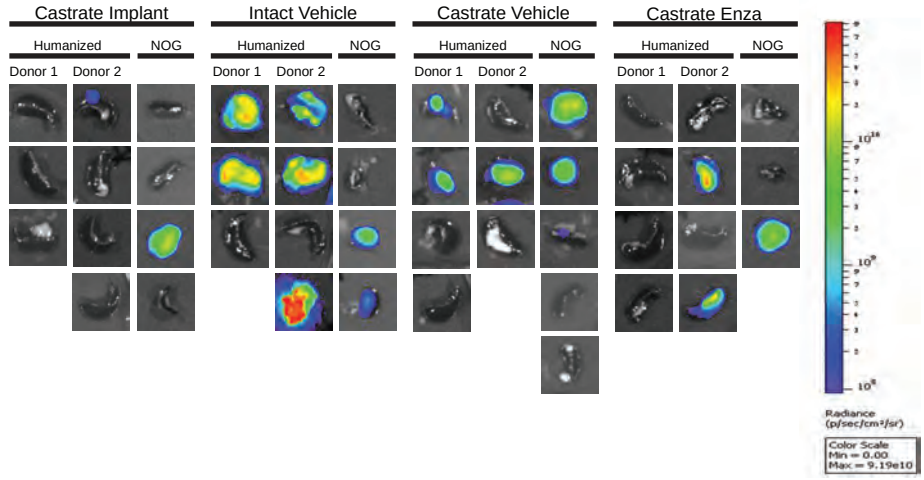
Spleen huNOG

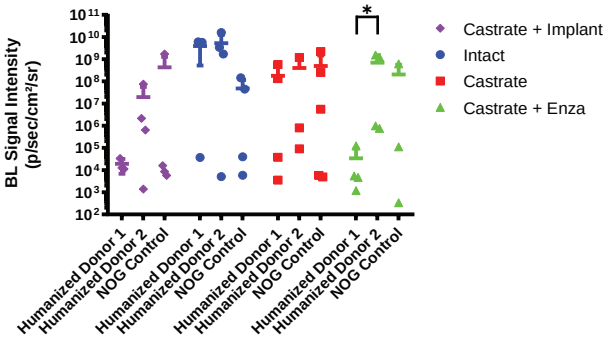




B

Spleen huNOG-EXL





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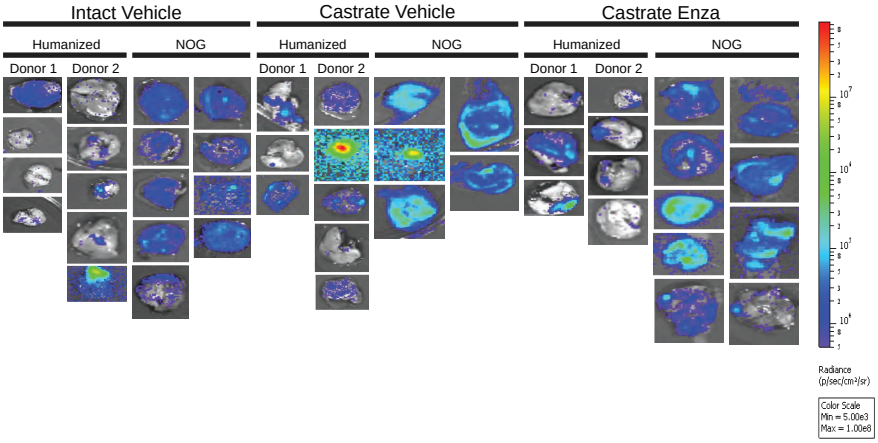
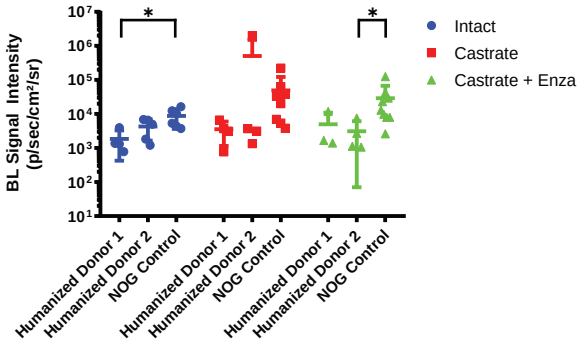
A

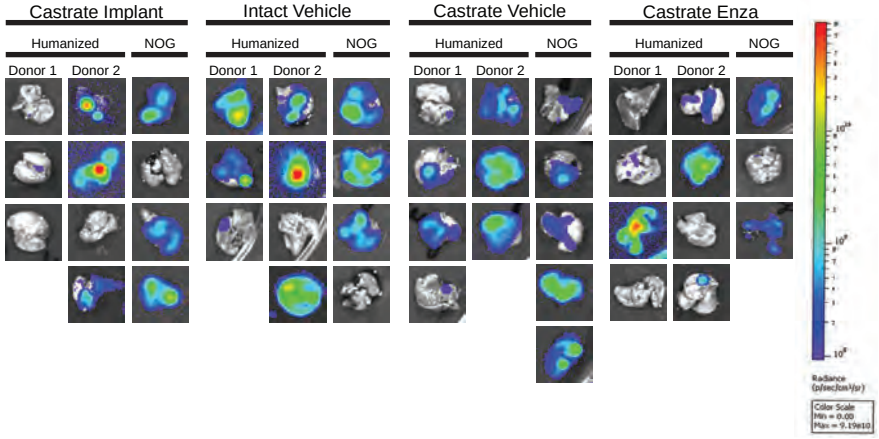
Lung huNOG

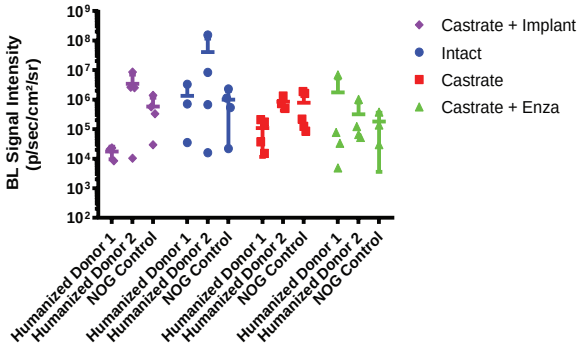




B

Lung huNOG-EXL





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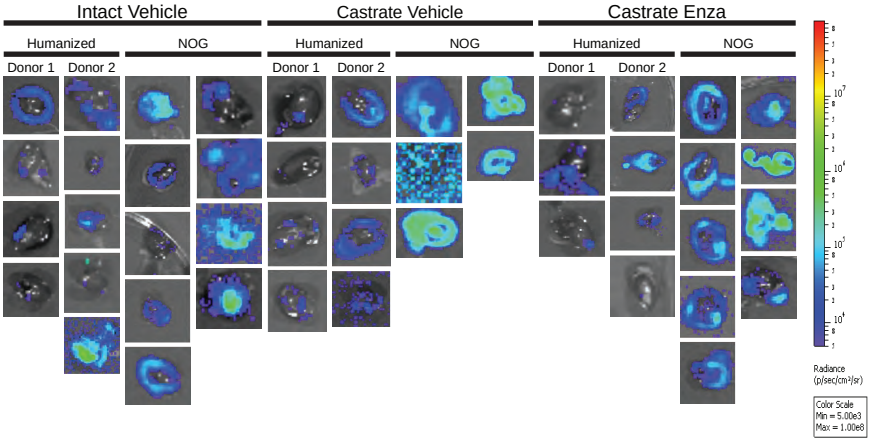
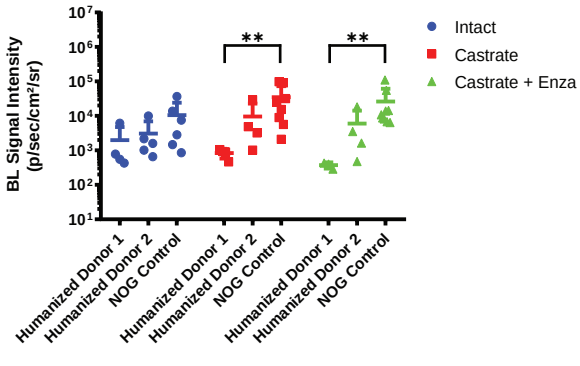
A

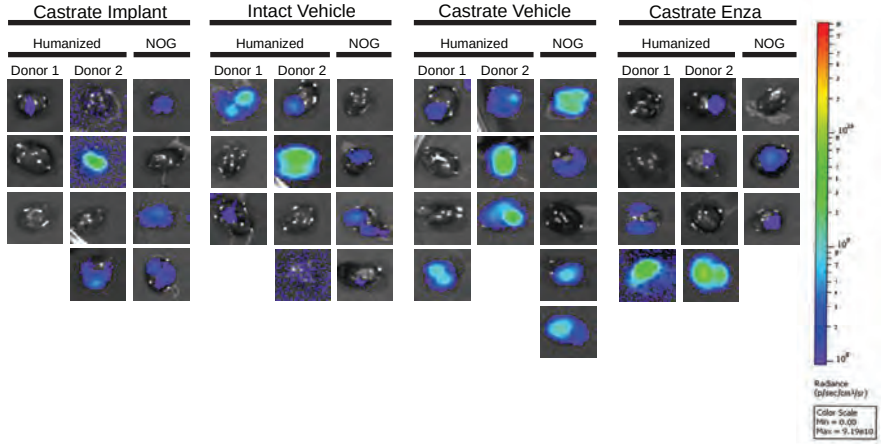
Heart huNOG

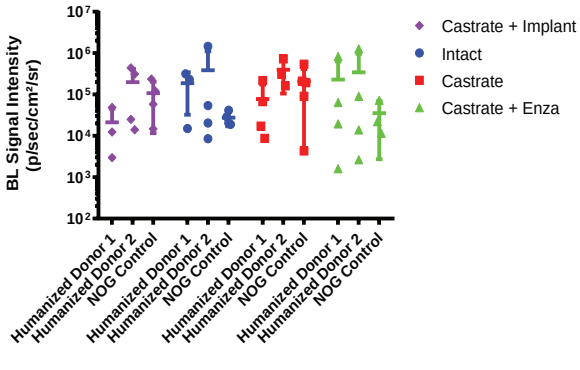




B

Heart huNOG-EXL





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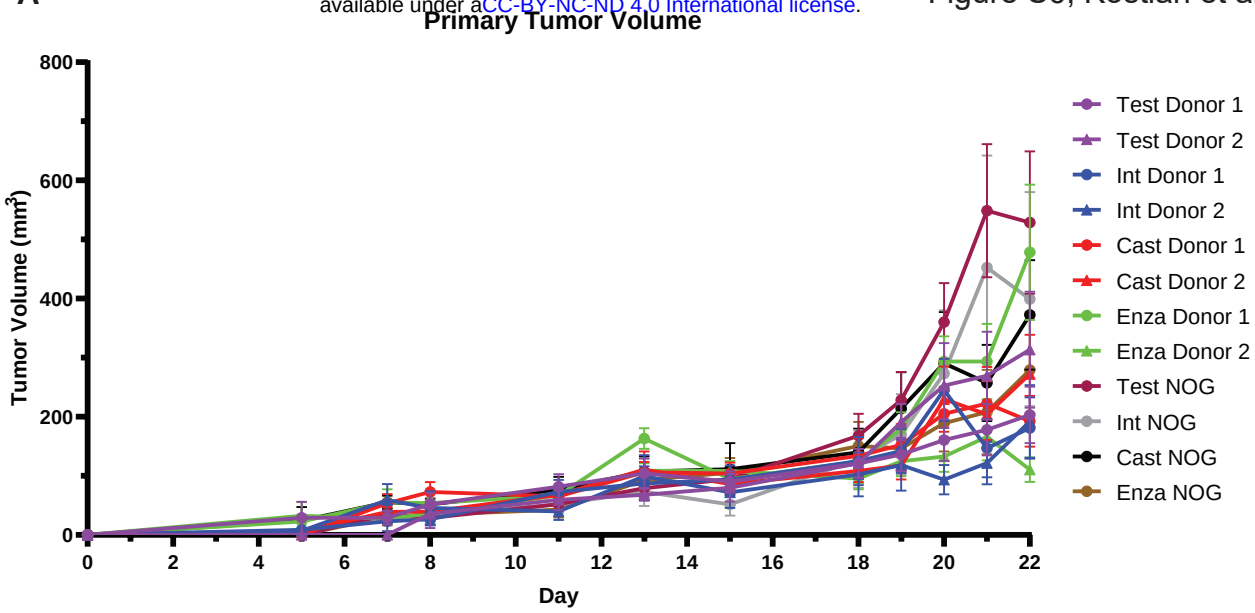

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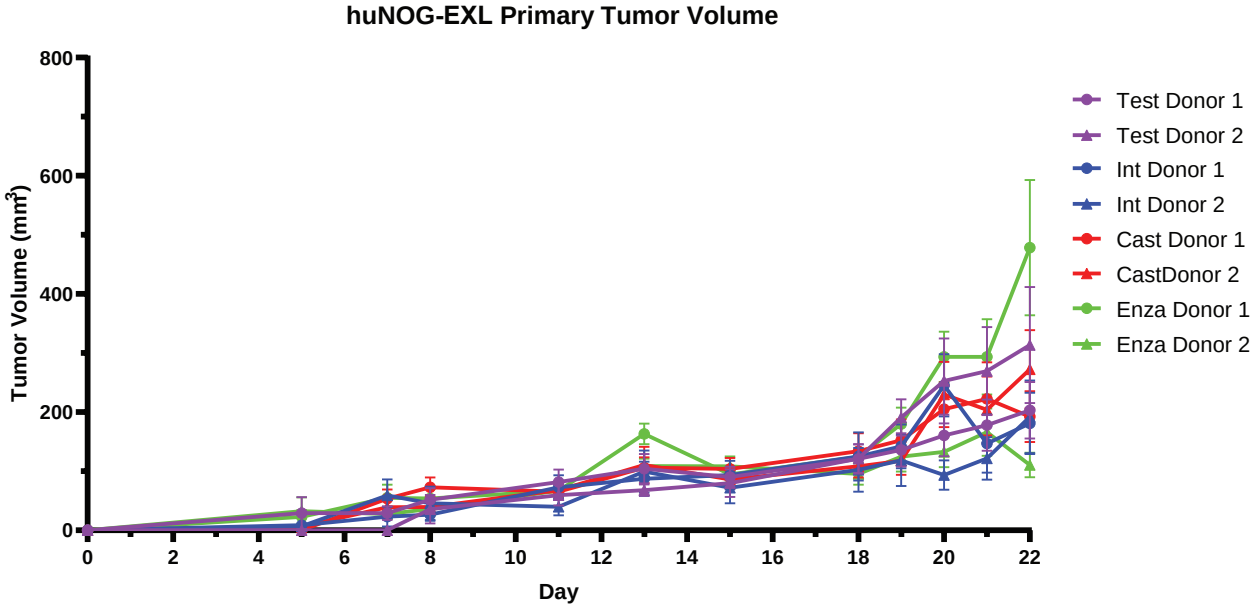

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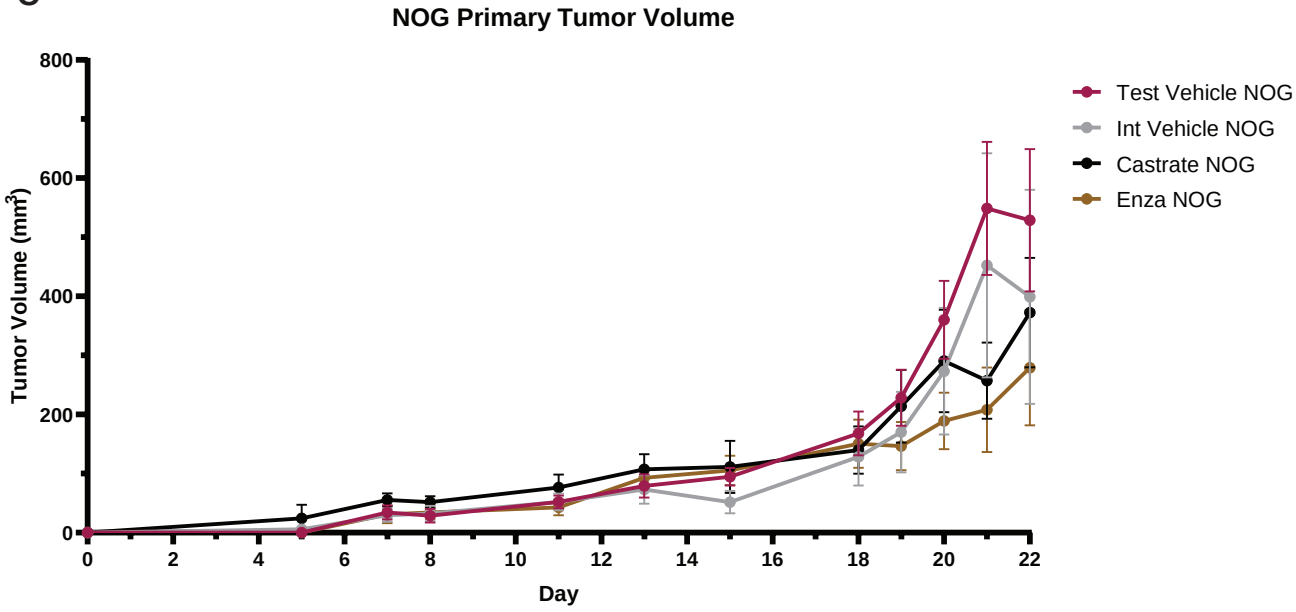

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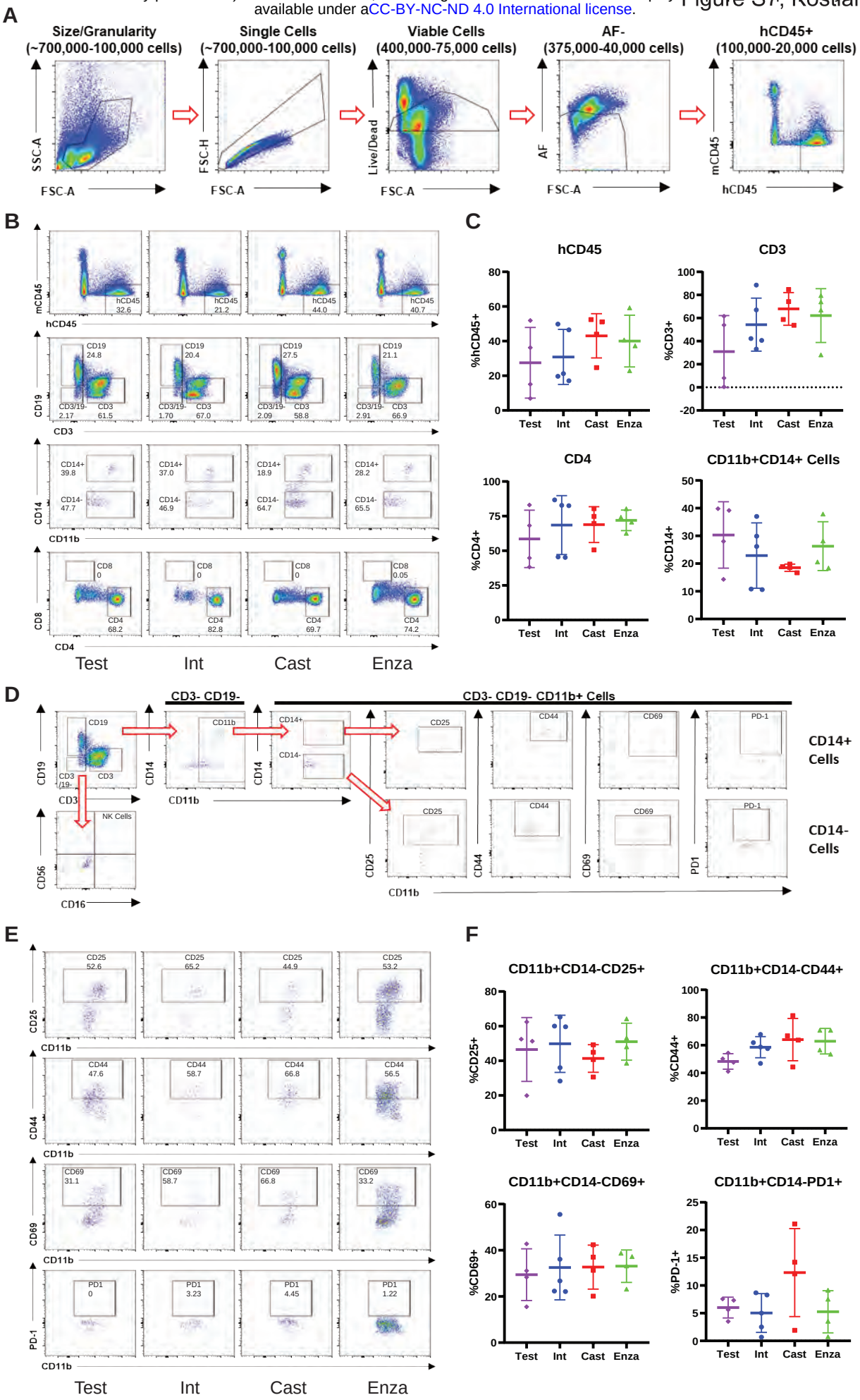

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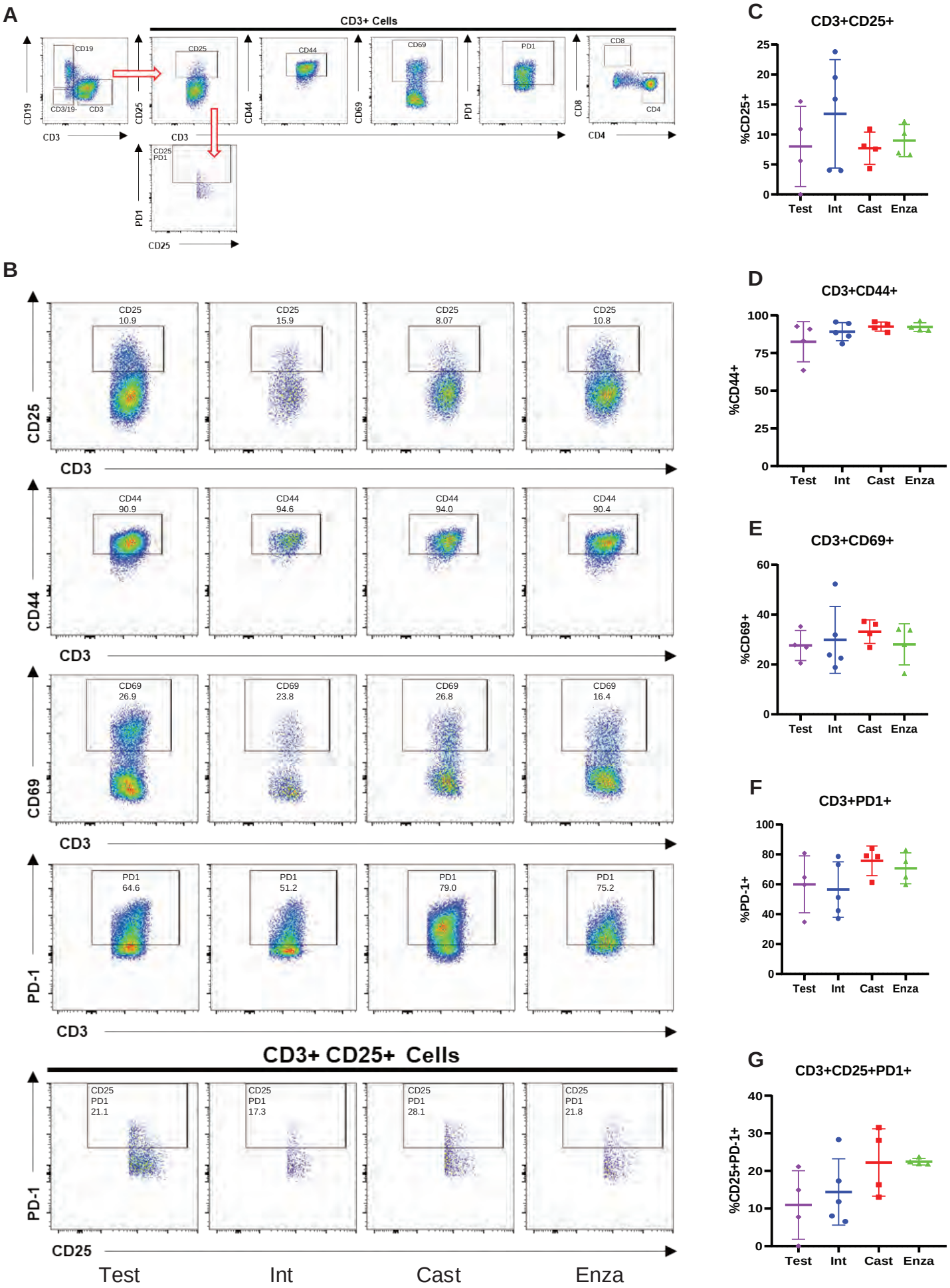
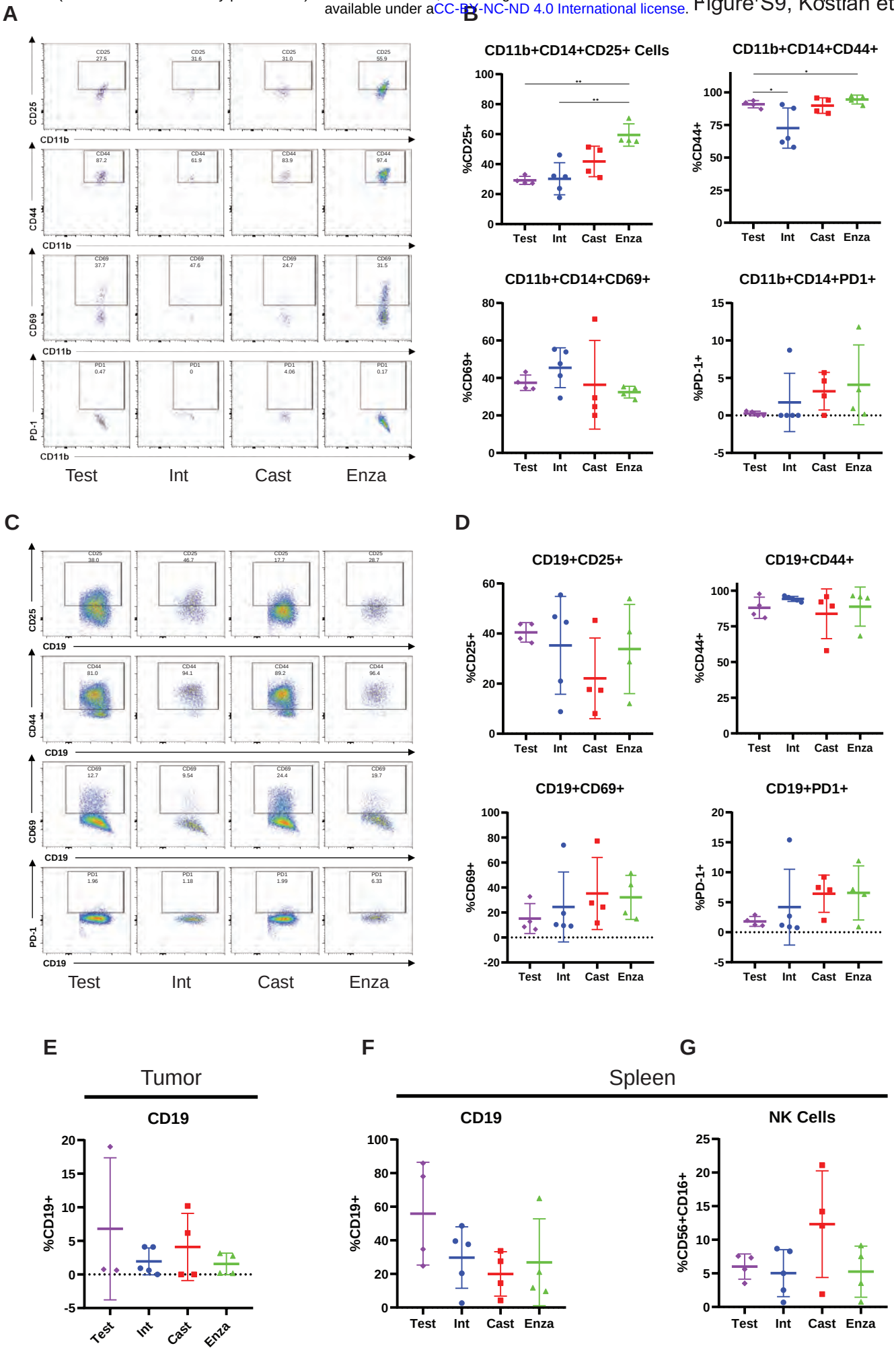
Figure S8. Kostian et al 2023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