

SITC 2019

Gaylord National Hotel
& Convention Center

Nov. 6-10

NATIONAL HARBOR, MARYLAND



Society for Immunotherapy of Cancer



Novel dsRNA-sensing dendritic cells enhance anti-tumor immunity

Ellen Duong | Spranger Lab at MIT

Concurrent Session 207

November 8, 2019



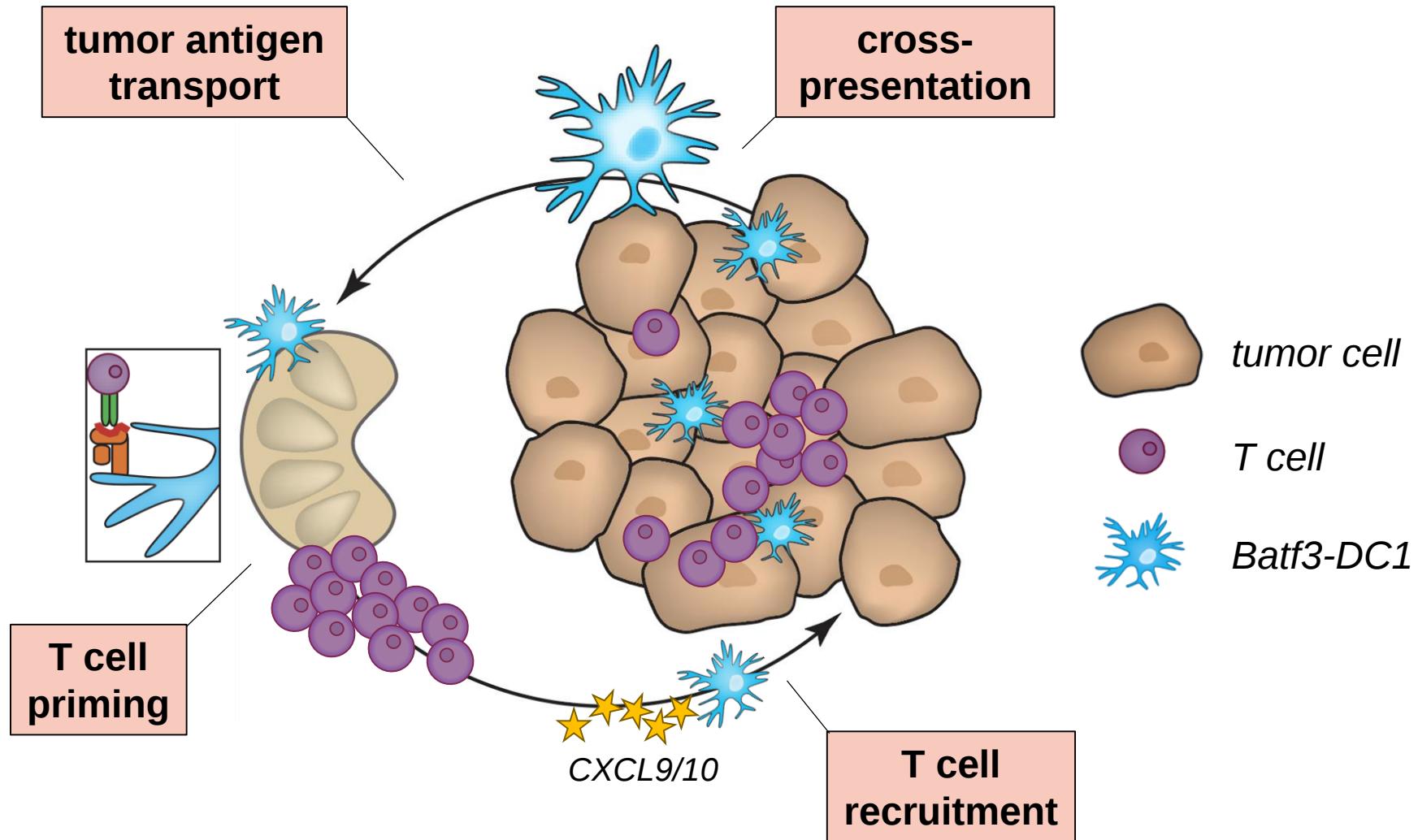
Society for Immunotherapy of Cancer

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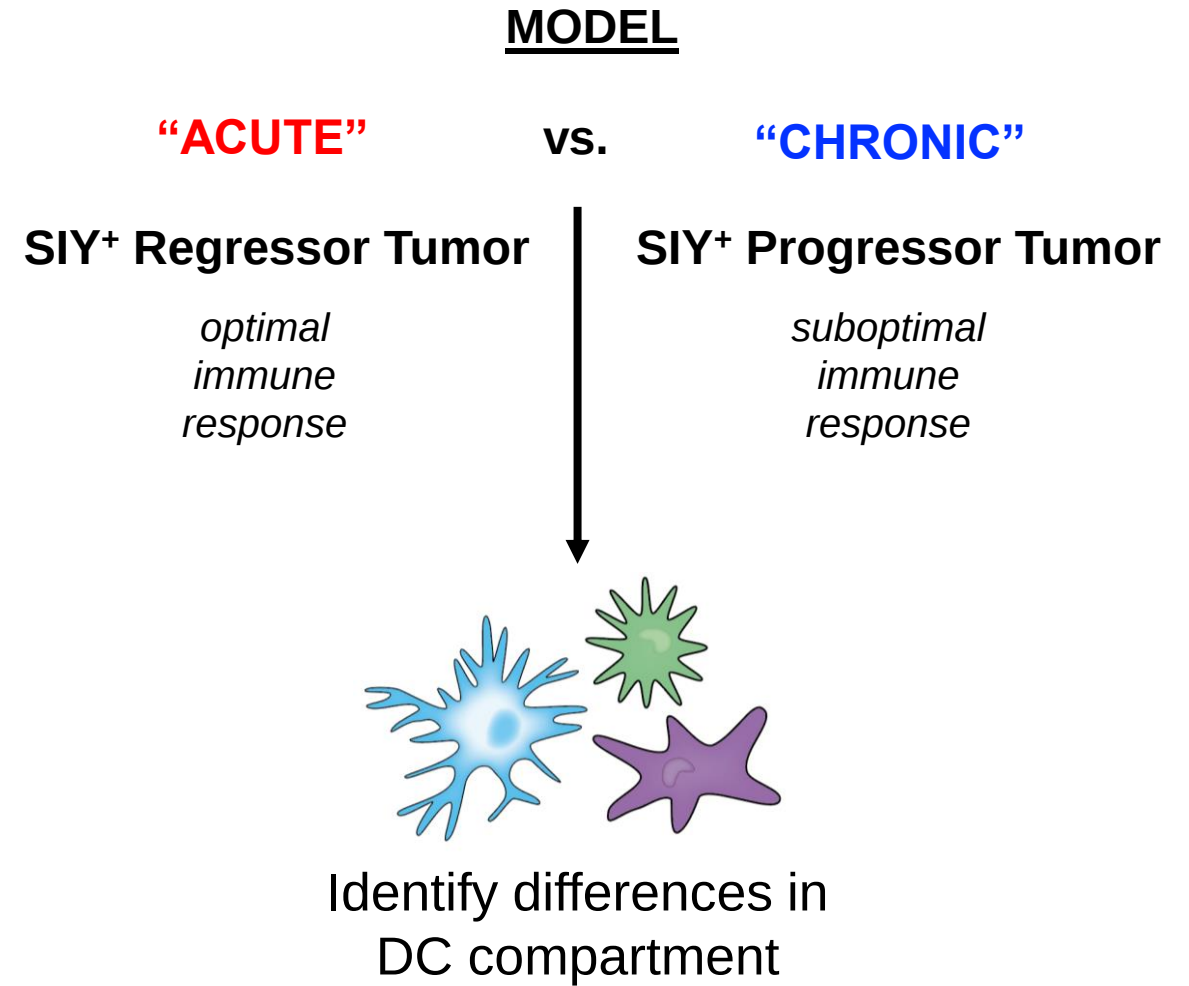
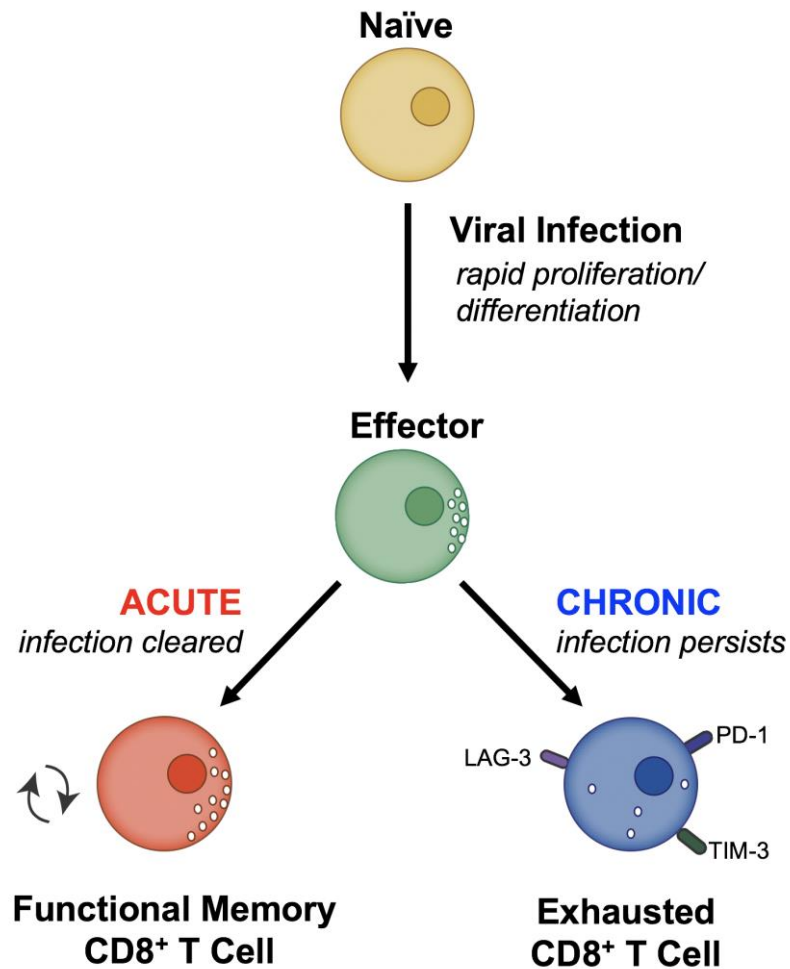
Disclosures

I have no disclosures.

Batf3-driven dendritic cells (DC1) are critical for anti-tumor T cell responses

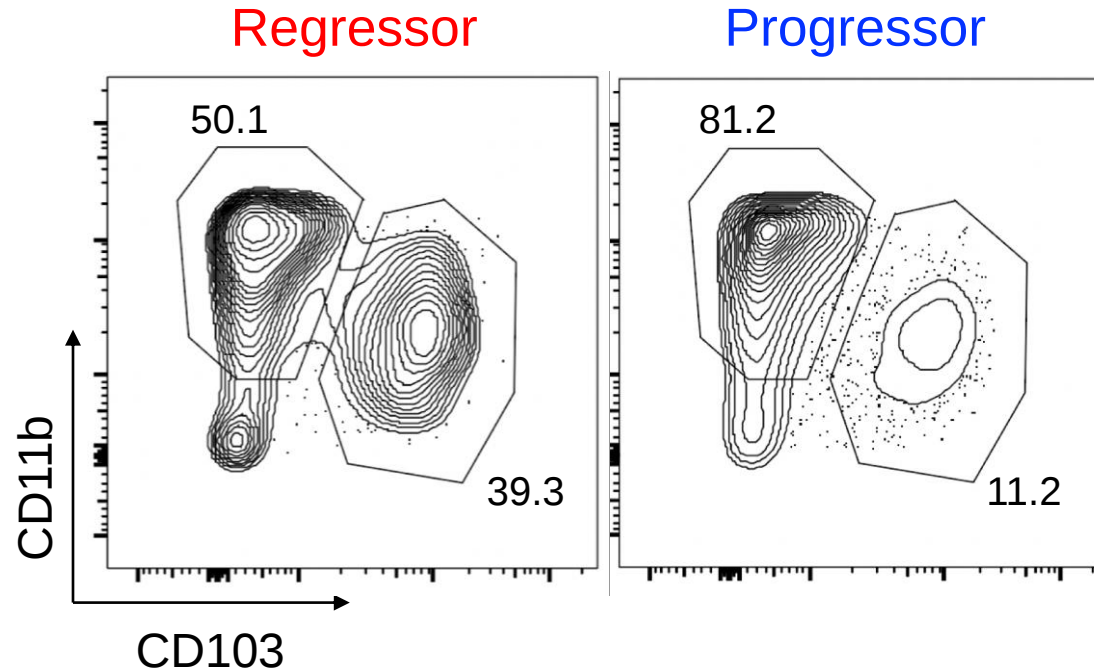
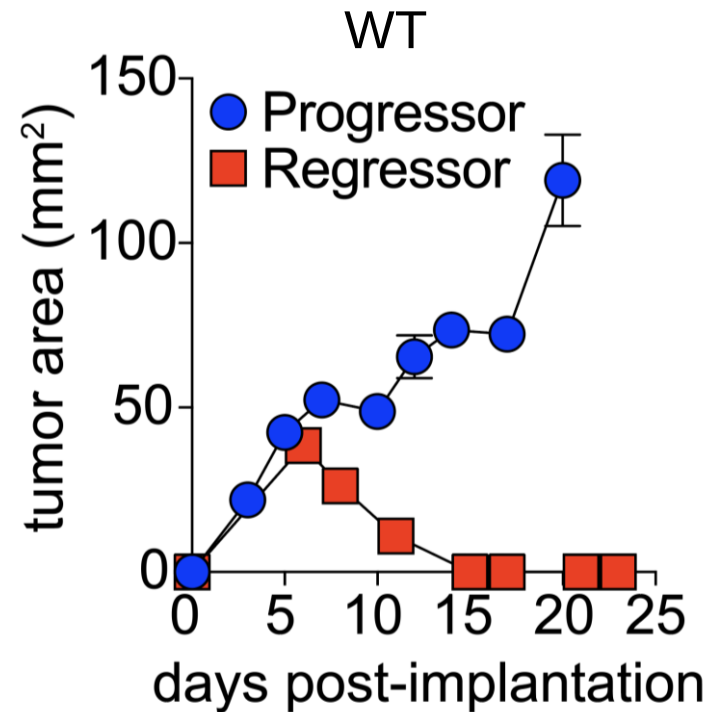


What other functions do tumor-residing DC have in the local tumor microenvironment?



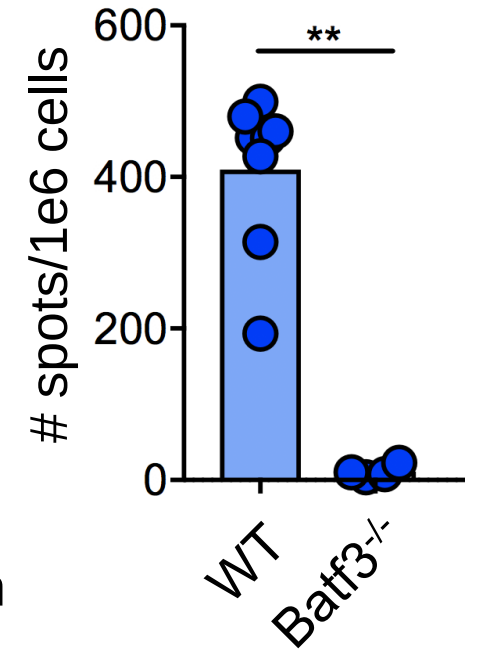
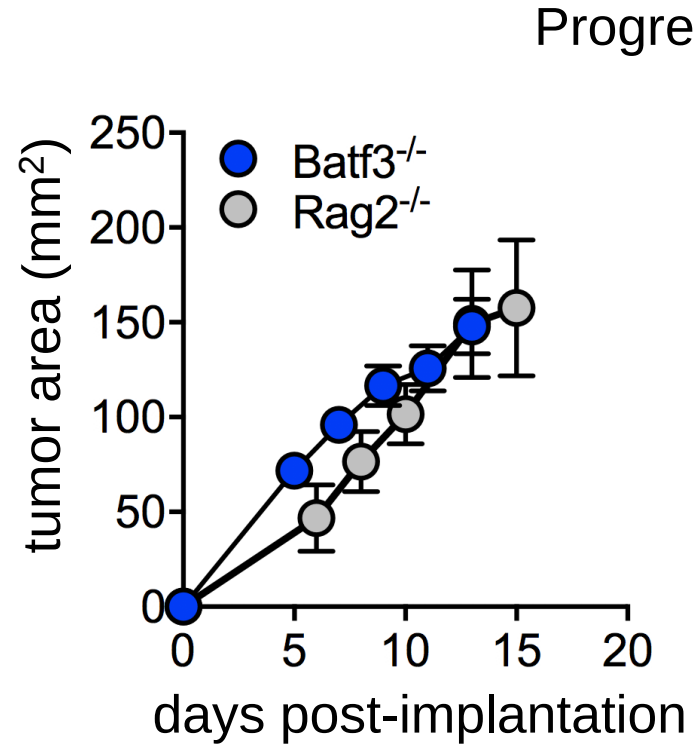
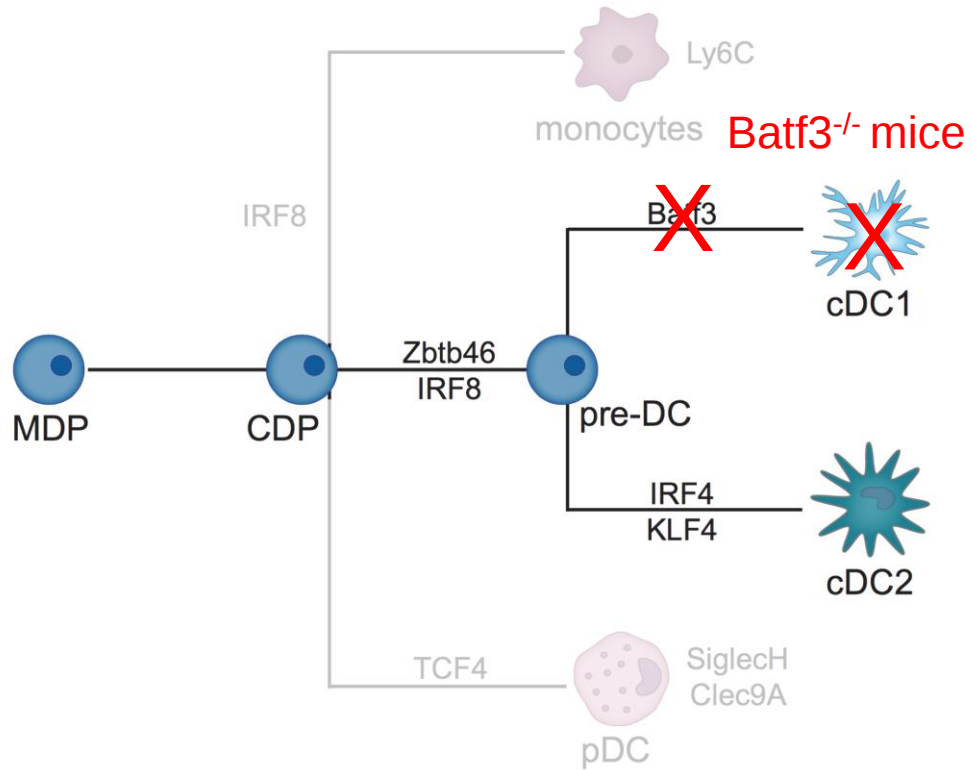
Adapted from Wherry et al, PNAS, 2004.

Regressor tumors are more enriched with DC1 compared to progressor tumors



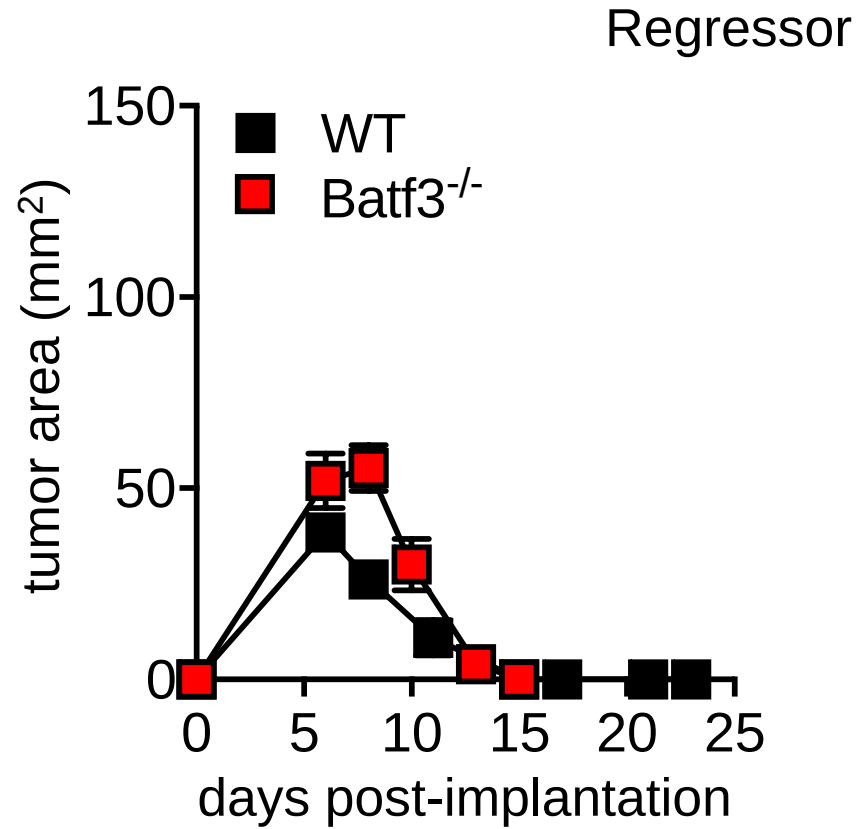
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Are DC1 necessary mediators of tumor regression?



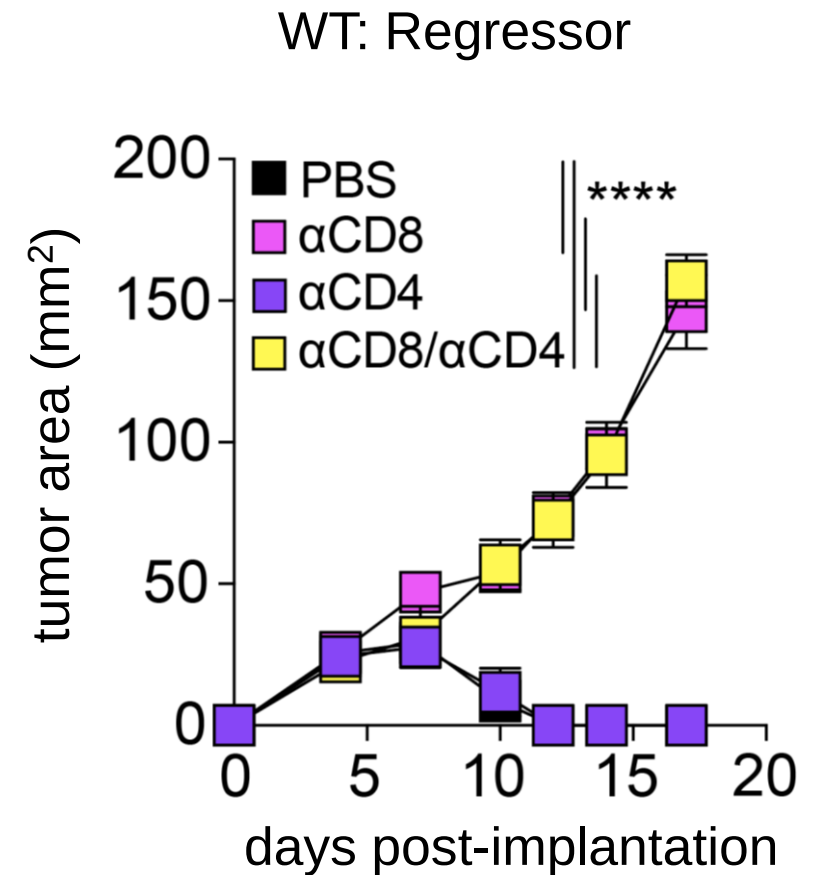
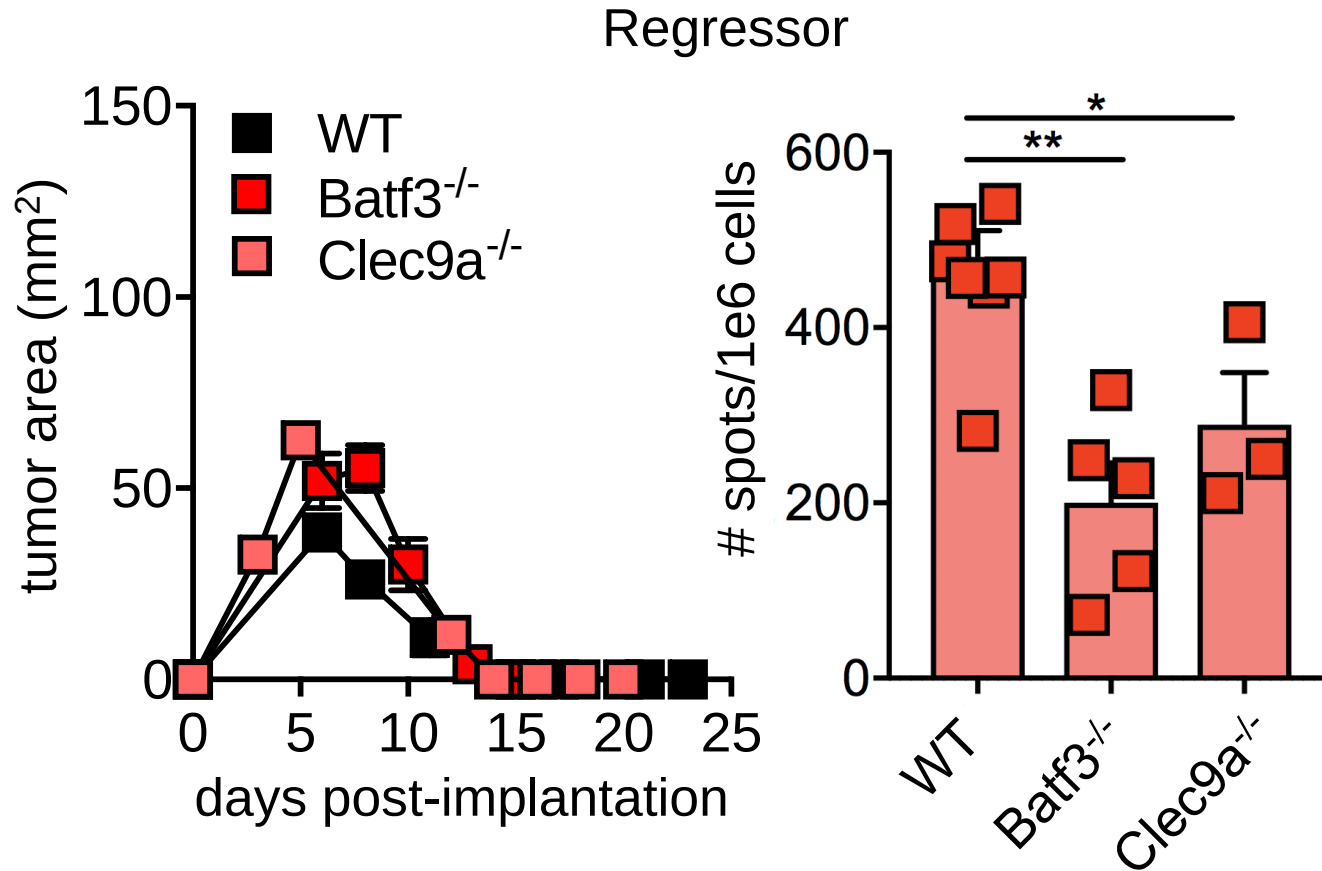
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The clearance of the regressor tumor is independent of DC1



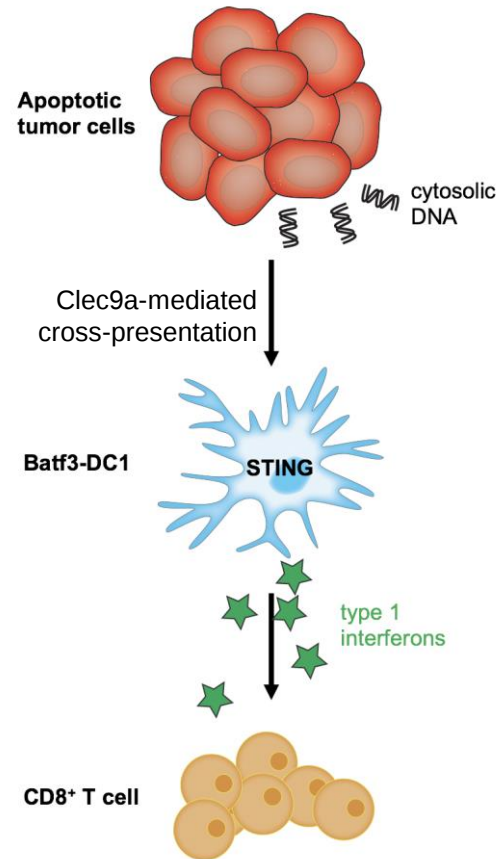
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The clearance of the regressor tumor is independent of DC1

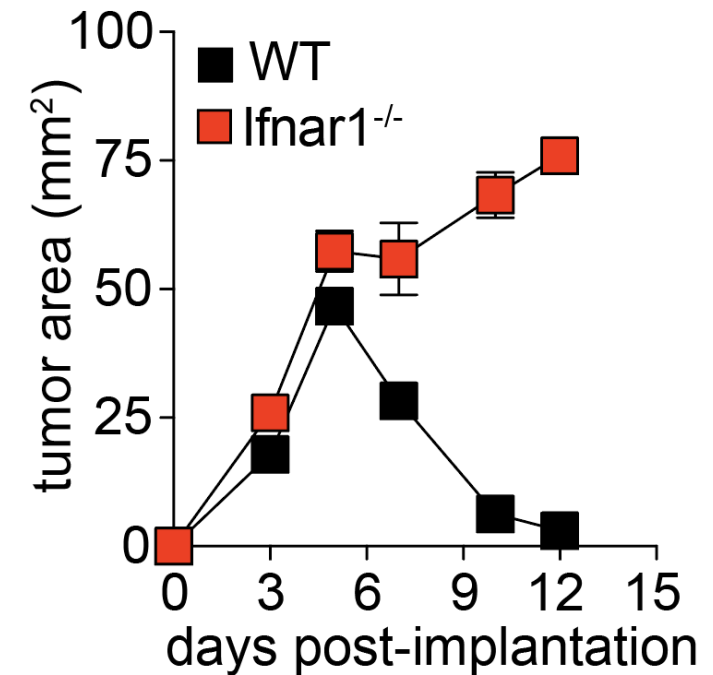
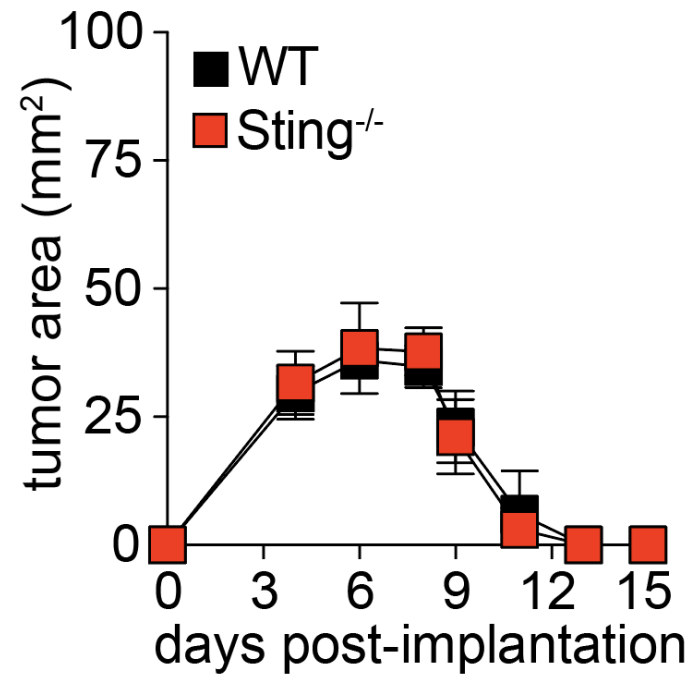


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Anti-tumor immunity against regressor tumors requires cGAS/STING-independent type-I-IFN sensing

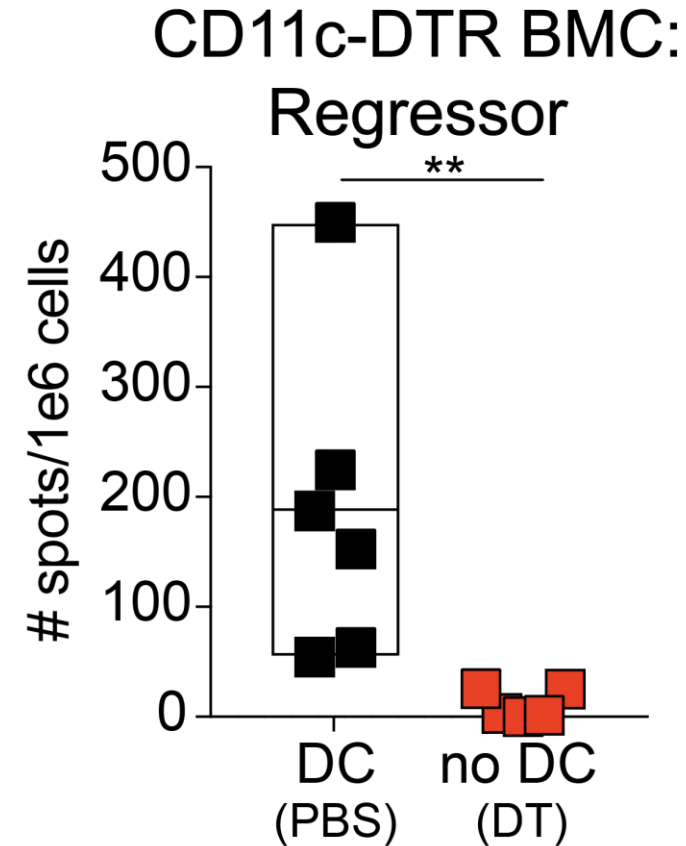
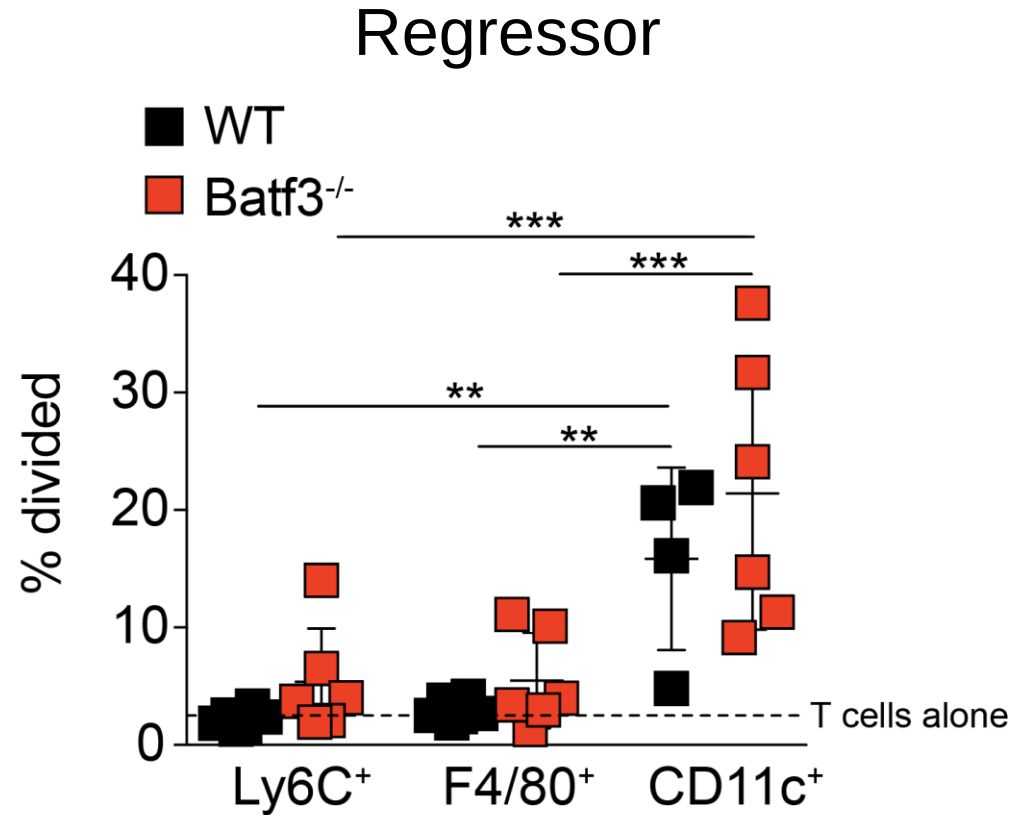


Regressor



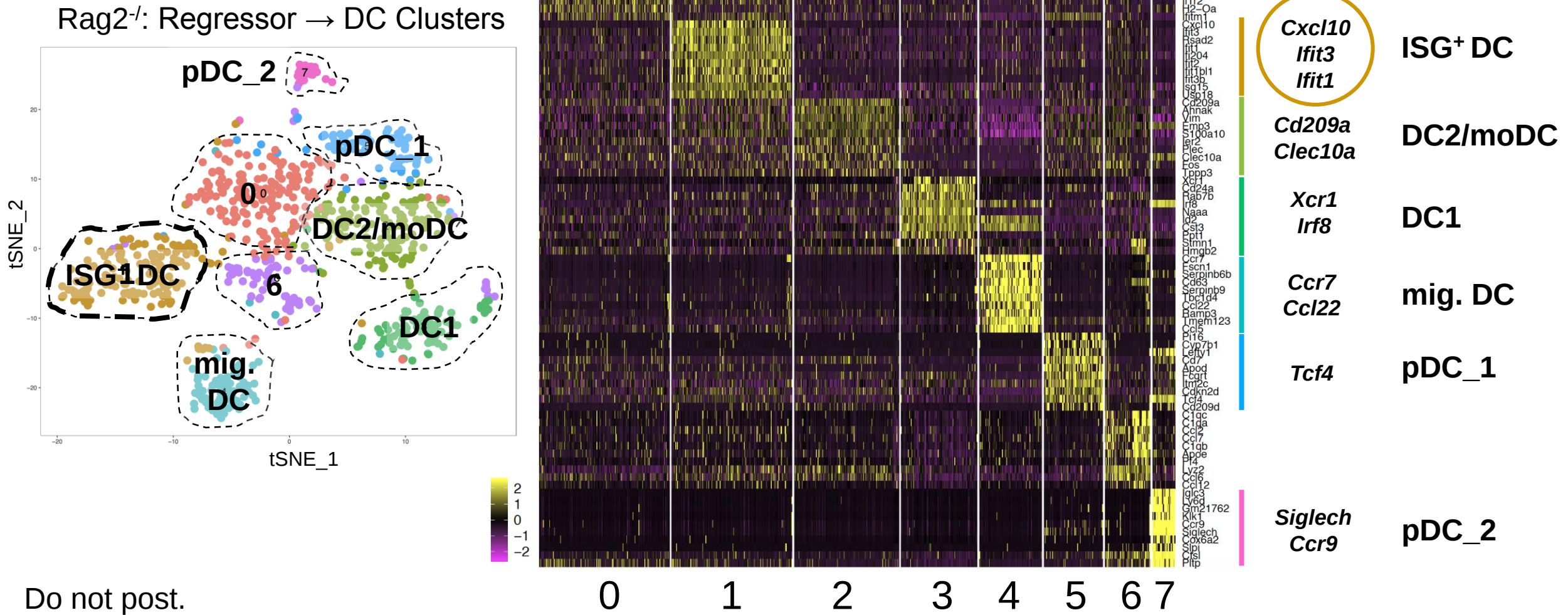
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The cell type capable of priming in $Batf3^{-/-}$ mice is likely in the $CD11c^{+}$ DC compartment

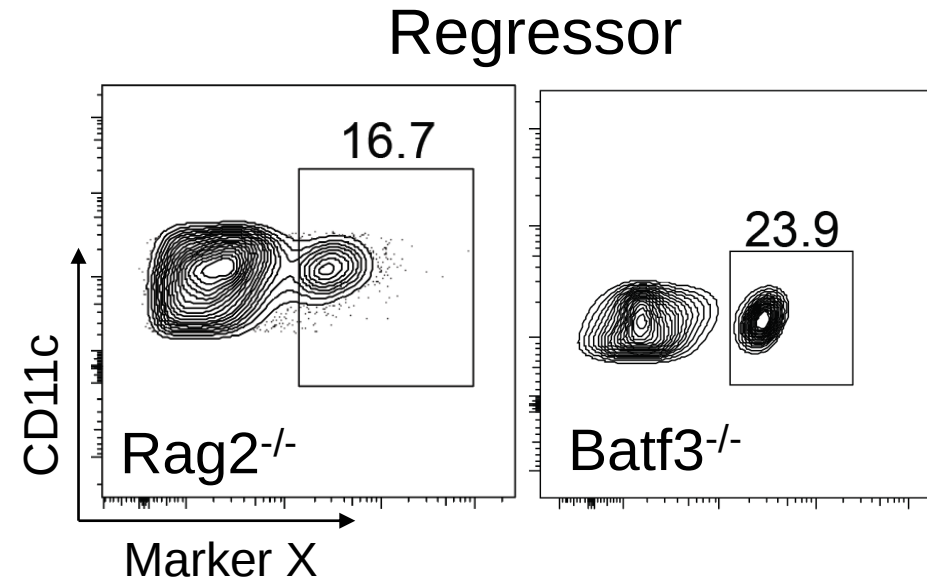
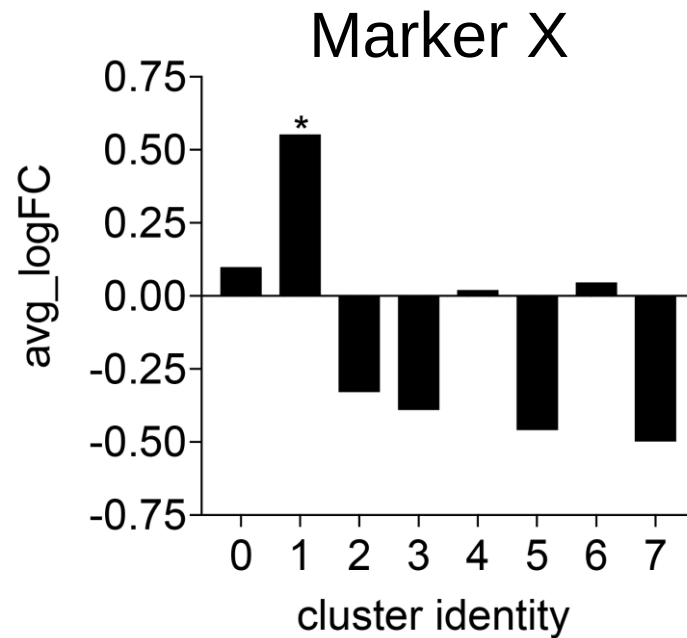


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DC Cluster 1 exhibits a strong type-I-IFN gene signature

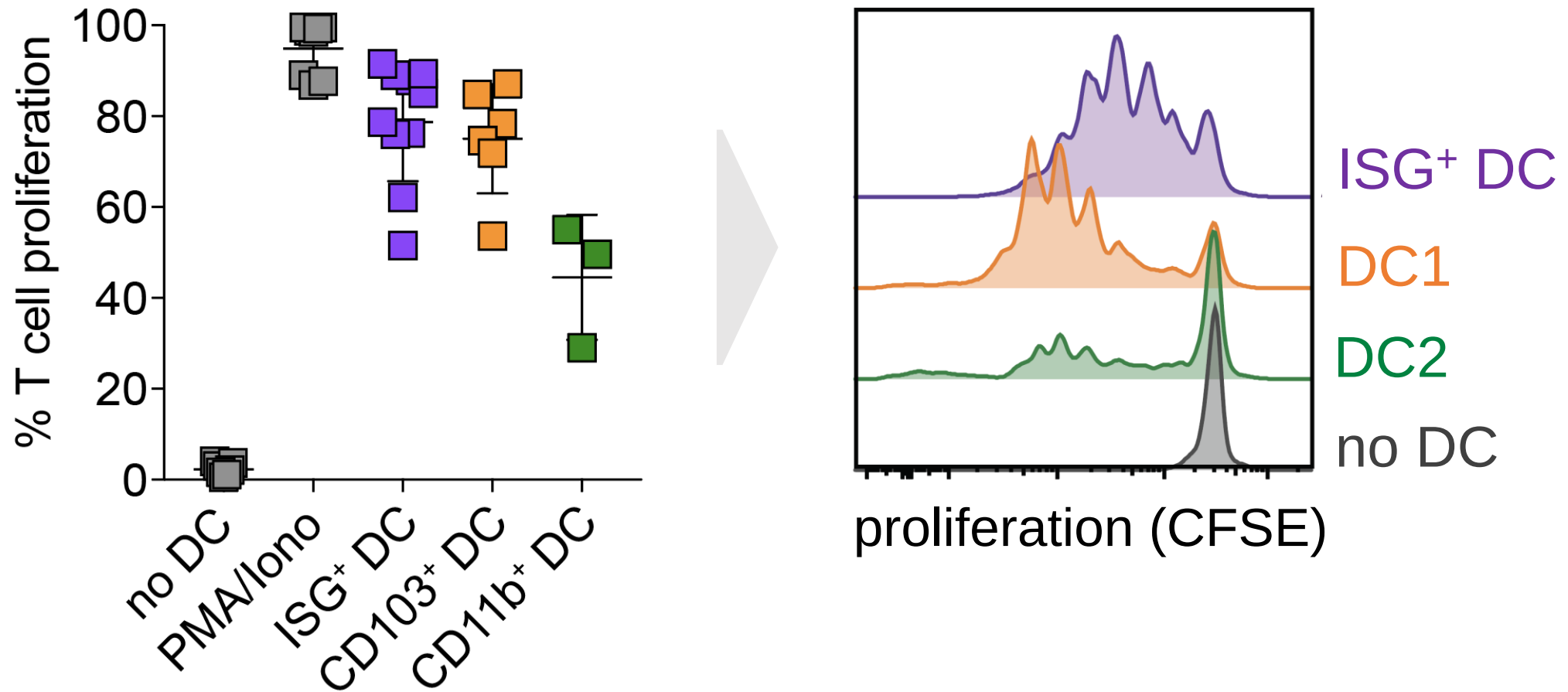


ISG⁺ DC are present in regressor tumor-bearing Rag2^{-/-} and Batf3^{-/-} mice



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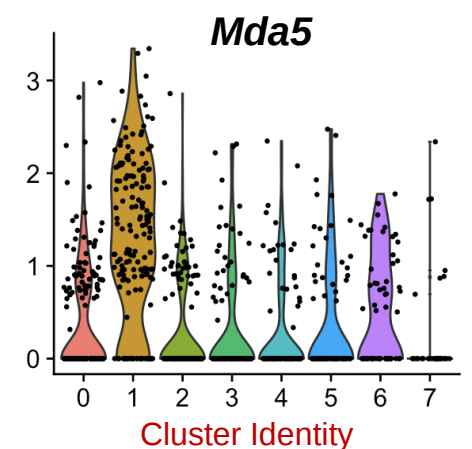
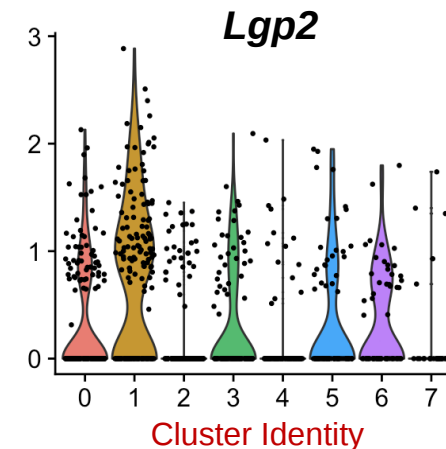
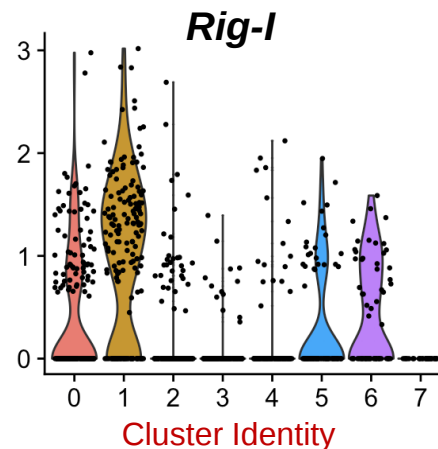
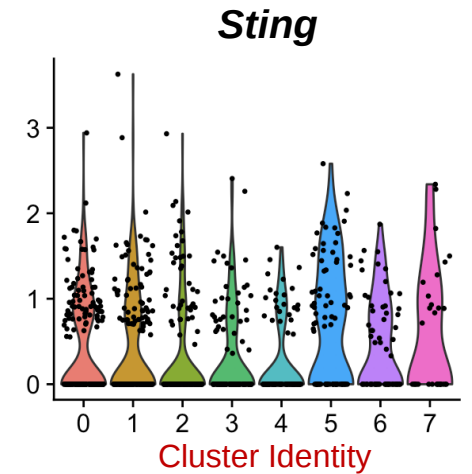
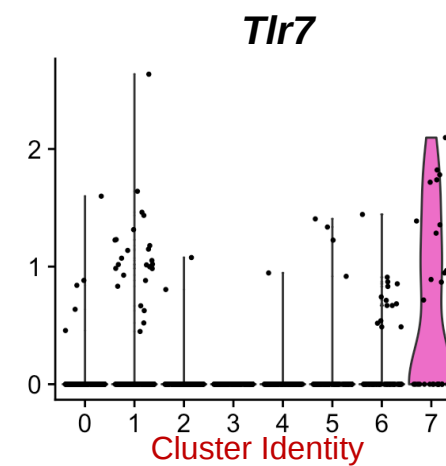
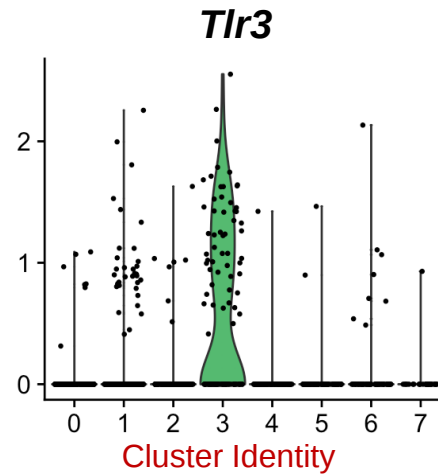
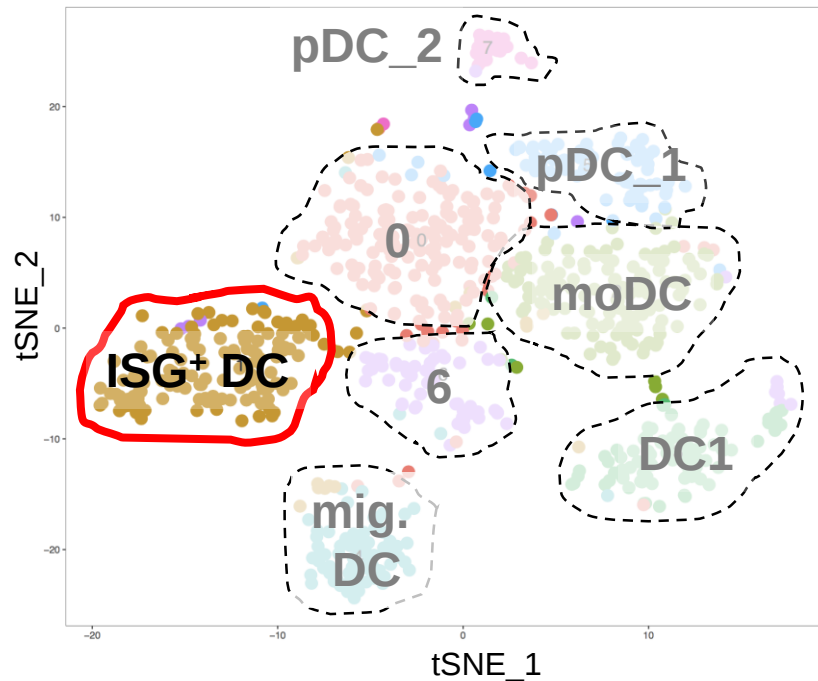
ISG⁺ DC are capable of priming cytotoxic T cells



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What are ISG⁺ DC sensing?

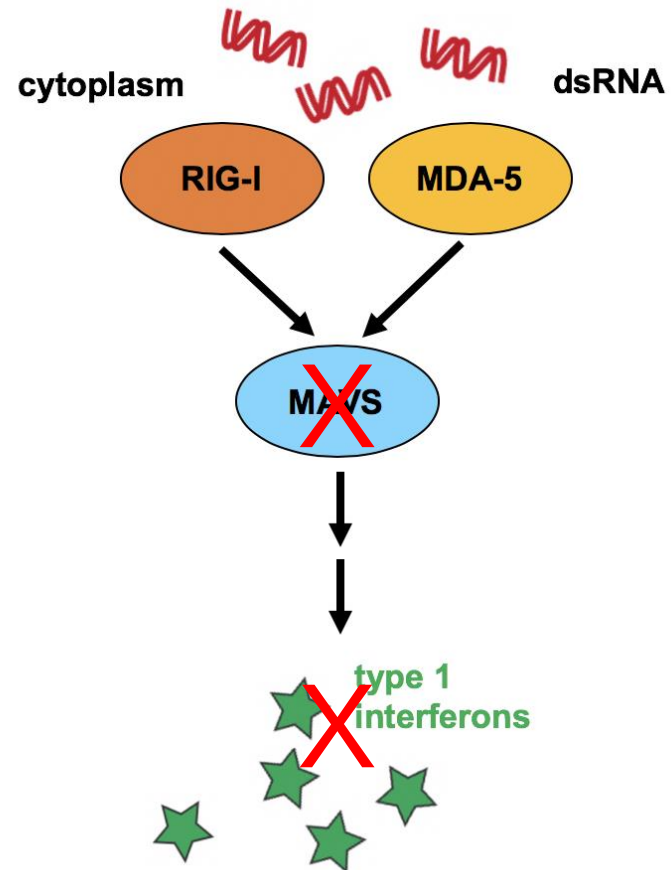
Rag2^{-/-}: Regressor → DC Clusters



Cytosolic dsRNA Sensors

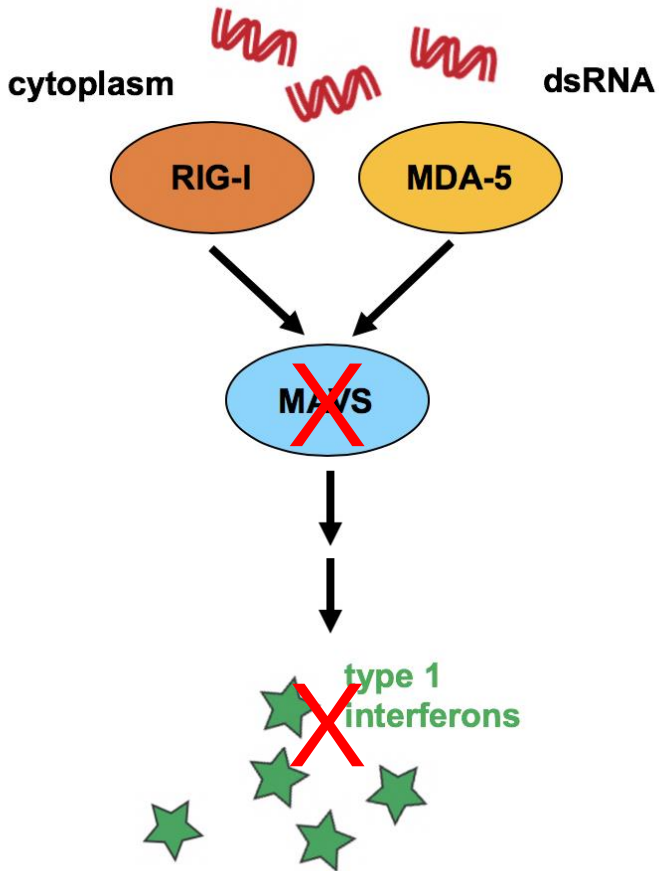
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Do regressor tumors produce dsRNA species?

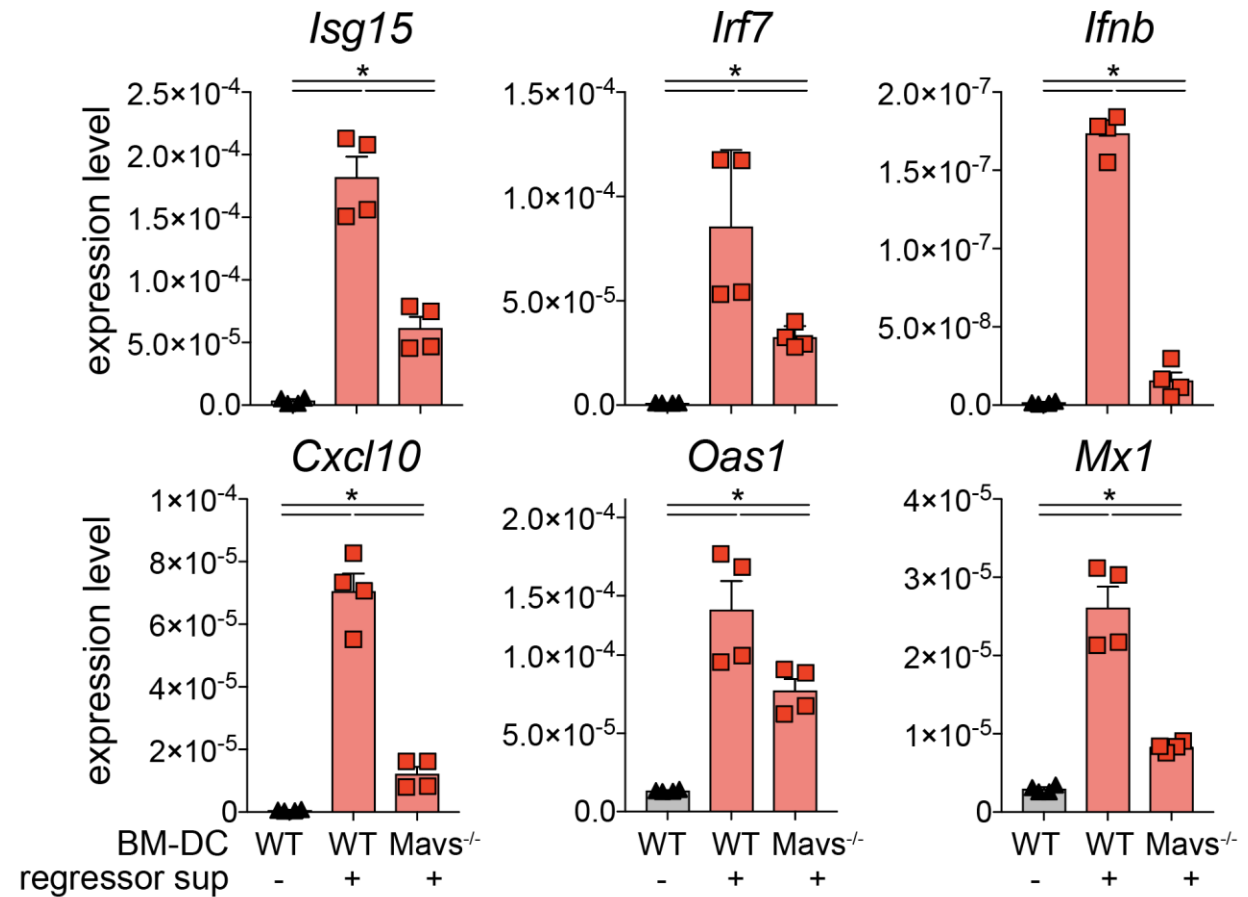


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Regressor tumor supernatant induces upregulation of MAVS-dependent type-I-IFN genes

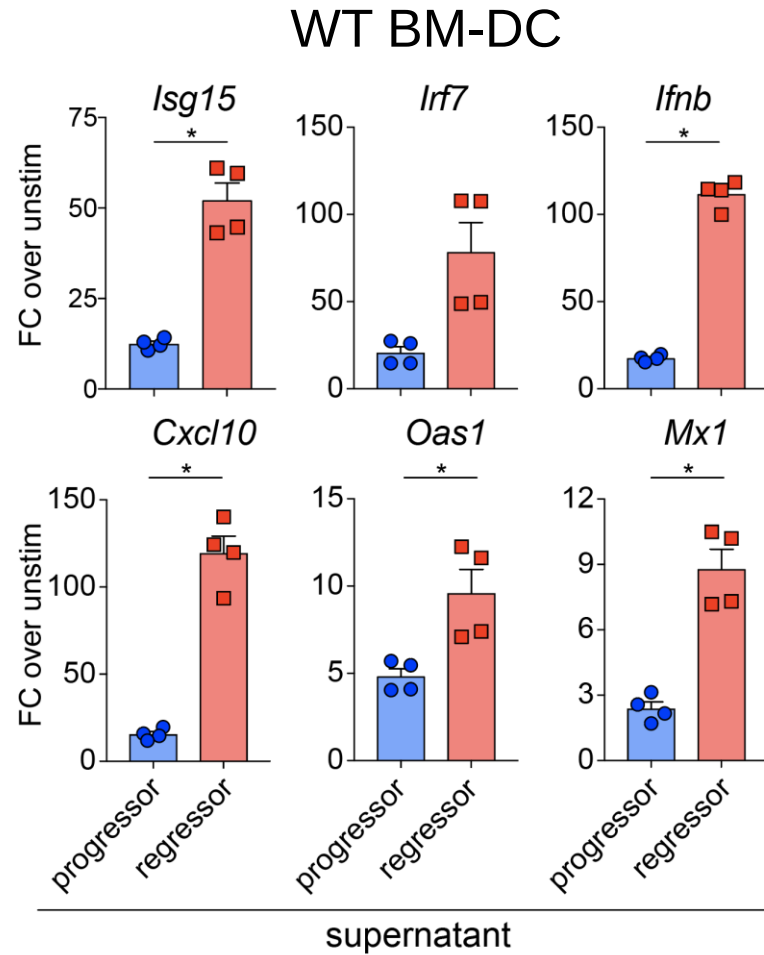


Type-I-IFN Genes

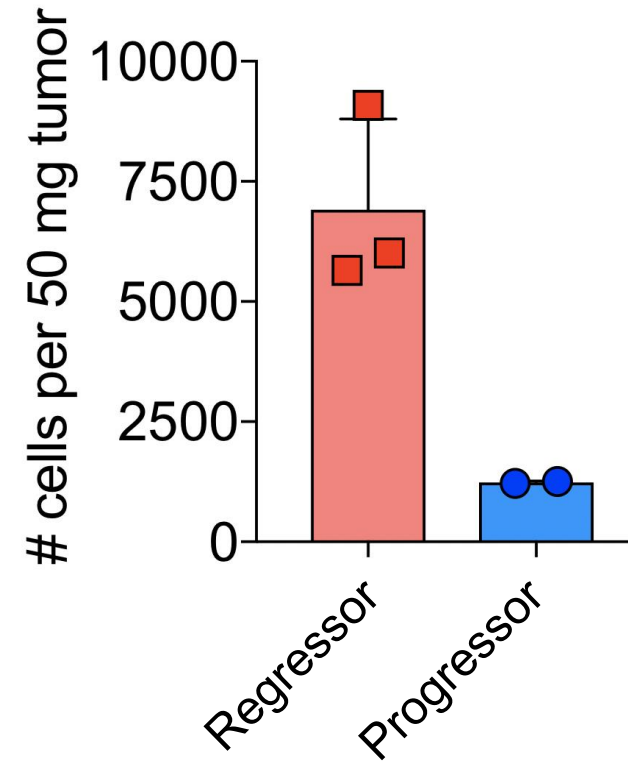


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Regressor tumors produce more nucleic acid species and are more infiltrated with ISG⁺ DC

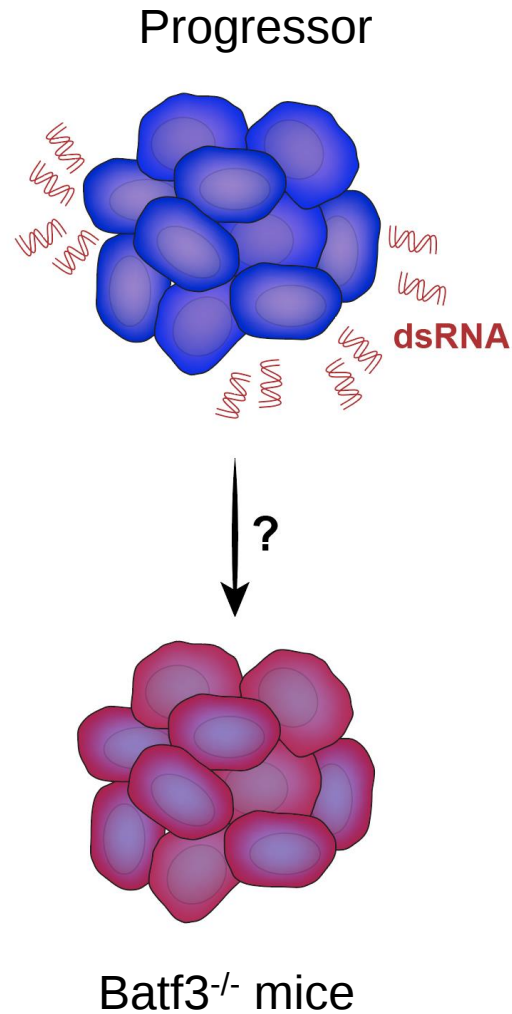


Rag2^{-/-}: ISG⁺ DC



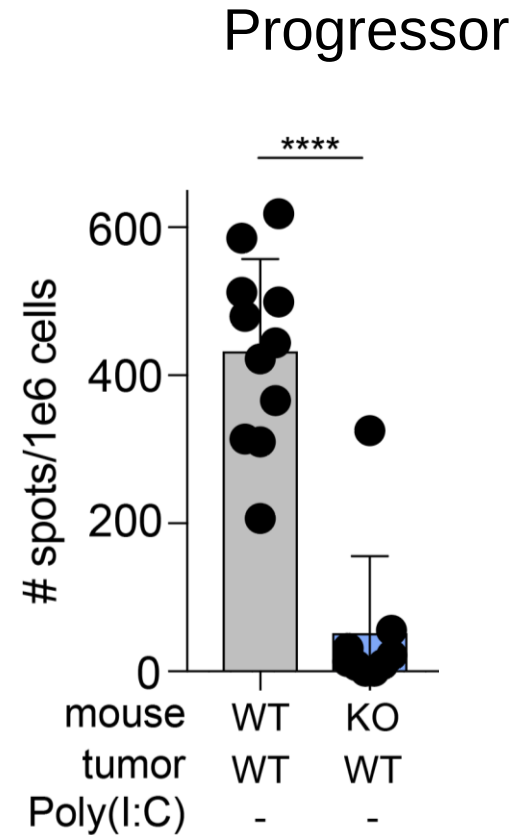
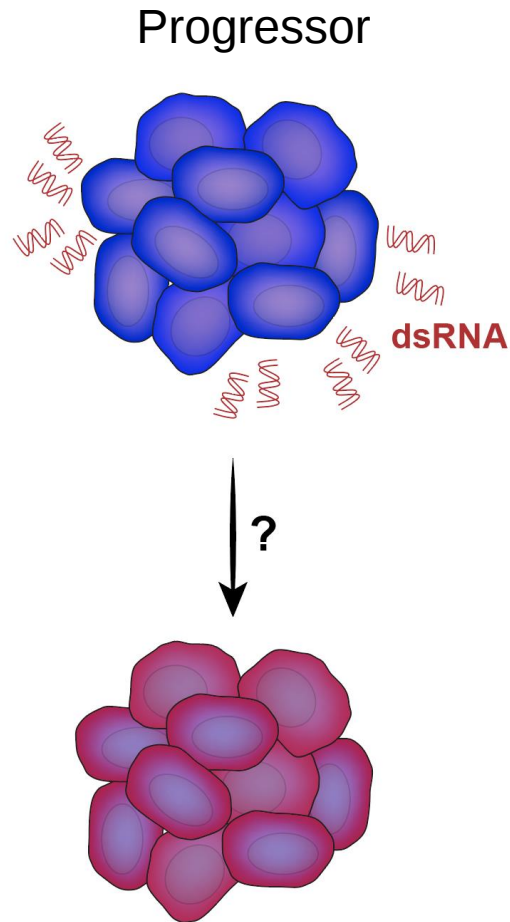
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Can we use a dsRNA analog to activate ISG⁺ DC and rescue T cell responses against progressor tumors in Batf3^{-/-} mice?



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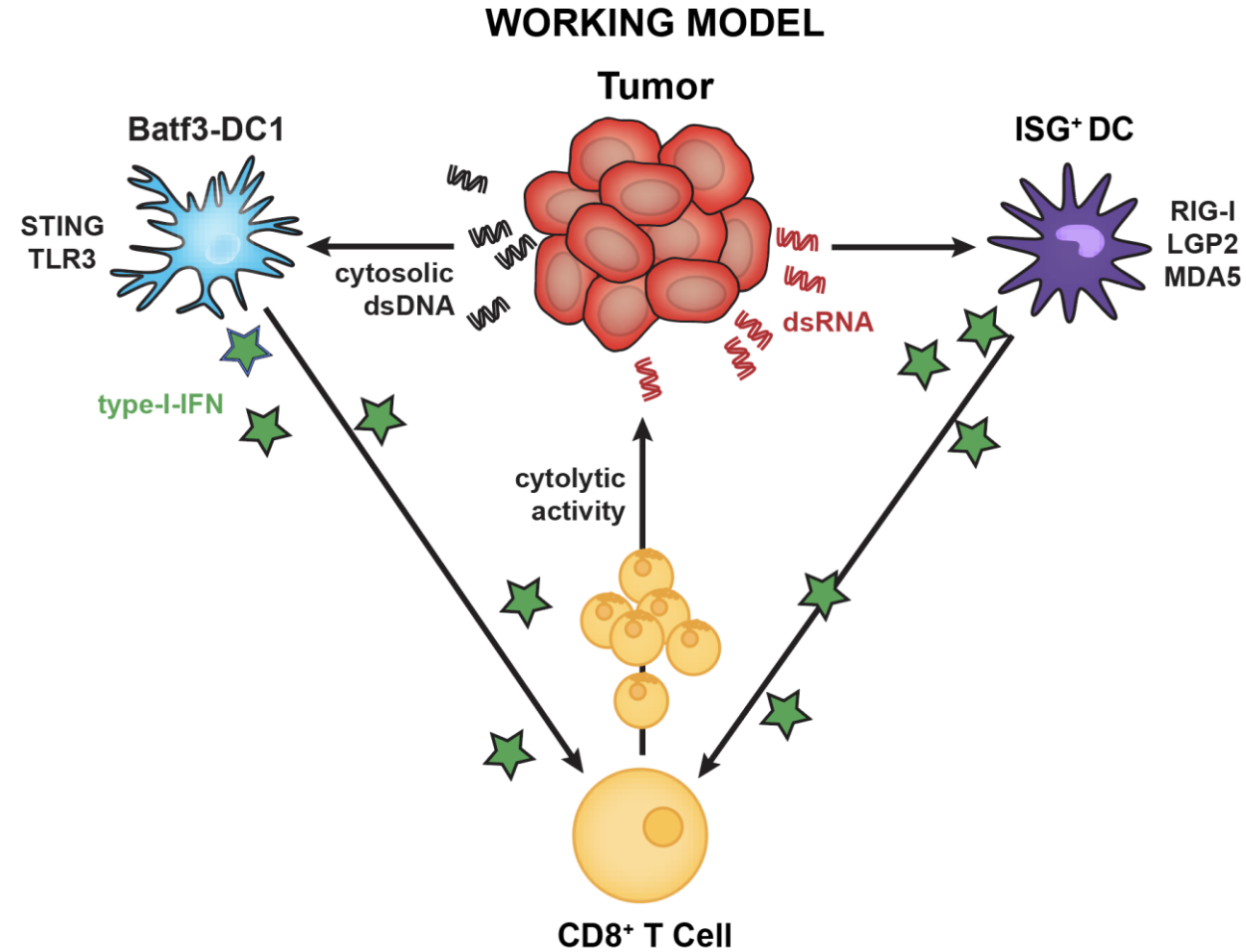
T cell responses in $Batf3^{-/-}$ mice are partially restored with Poly(I:C)-coated progressor tumor cells



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Batf3^{-/-} mice

The engagement of multiple stimulatory DC subsets boosts anti-tumor immunity



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Acknowledgments

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