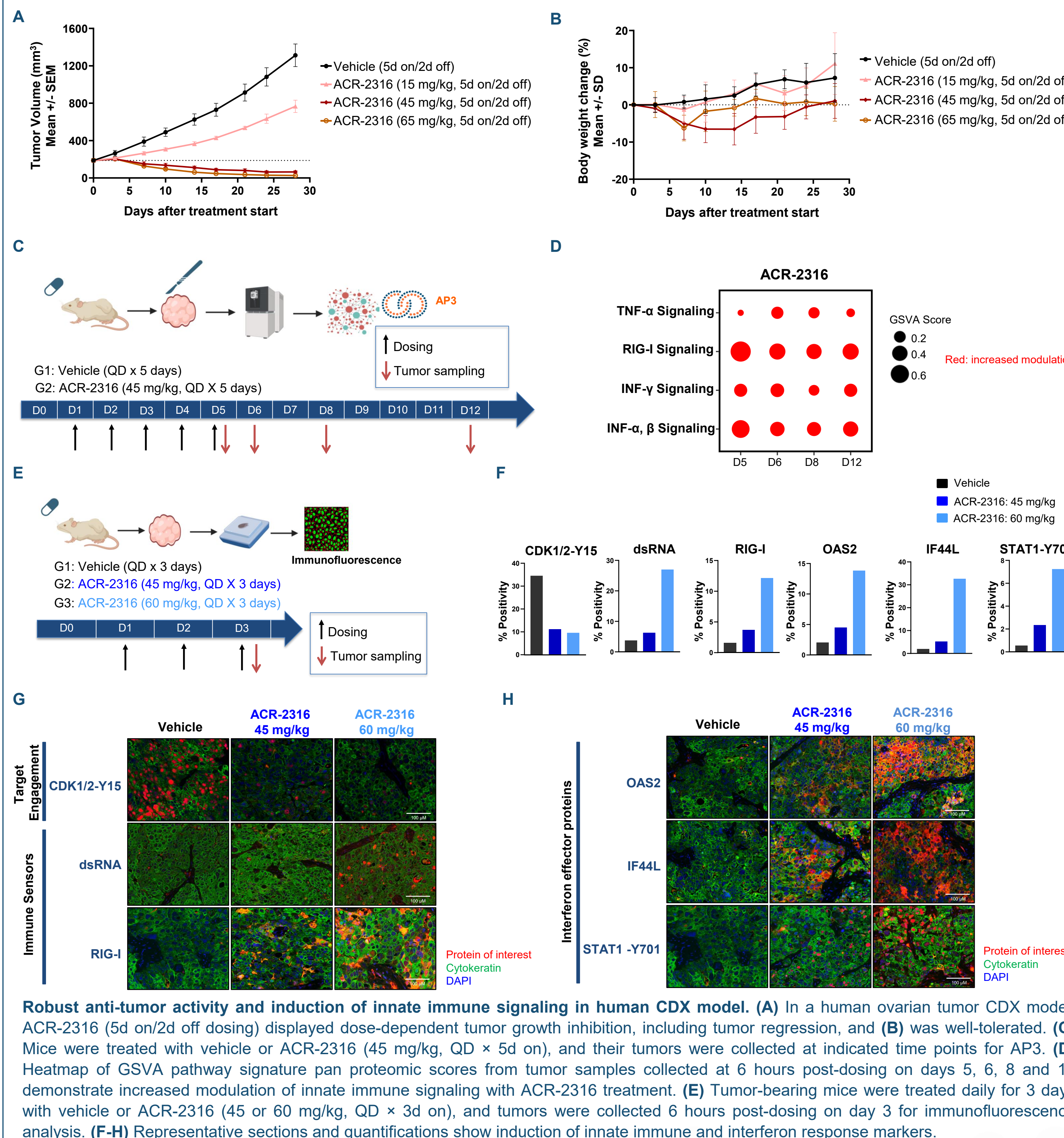


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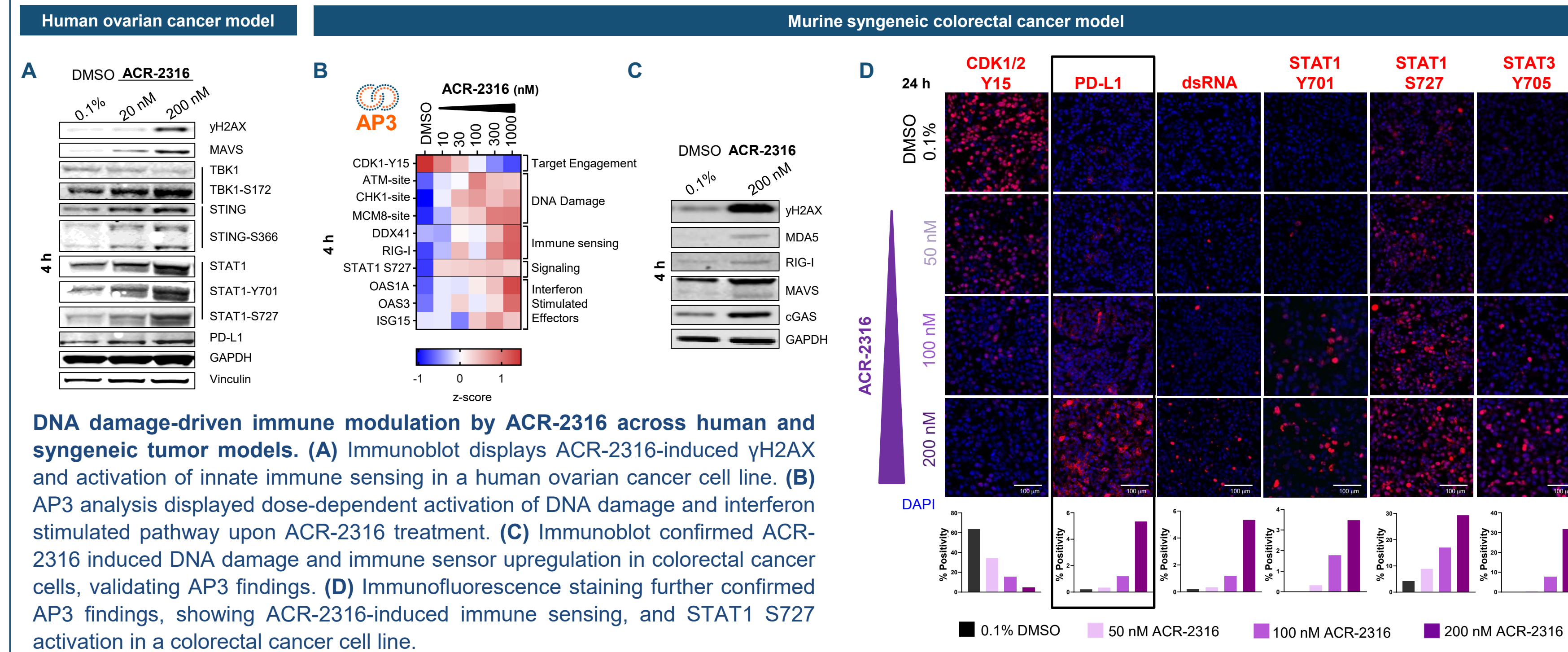
## Introduction

- WEE1 and PKMYT1 have critical roles in the S and G2/M checkpoint and replication stress response. ACR-2316 is a potent WEE1/PKMYT1 inhibitor designed by Acirvon's Predictive Precision Proteomics (AP3) for superior pro-apoptotic tumor cell killing through balanced inhibition of PKMYT1, uncovered by AP3 as a dominant resistance mechanism to WEE1 inhibition, resulting in potent activation of not only CDK1 and 2, but importantly also PLK-1.
- Based on this mechanism, ACR-2316 is expected to exacerbate tumor-intrinsic DNA damage and induce strong mitotic catastrophe in genetically unstable cancers, resulting in activation of innate immune sensing pathways, providing a mechanistic link between replication stress and adaptive anti-tumor immunity.
- Here, we evaluated ACR-2316 in human and murine syngeneic cancer models to characterize its effects on DNA damage response signaling and immune activation. We further assessed combination with anti-PD-L1 to determine whether DDR-driven tumor priming enhances tumor regression and induces durable immune memory, and profiled associated signaling using our AP3 platform.

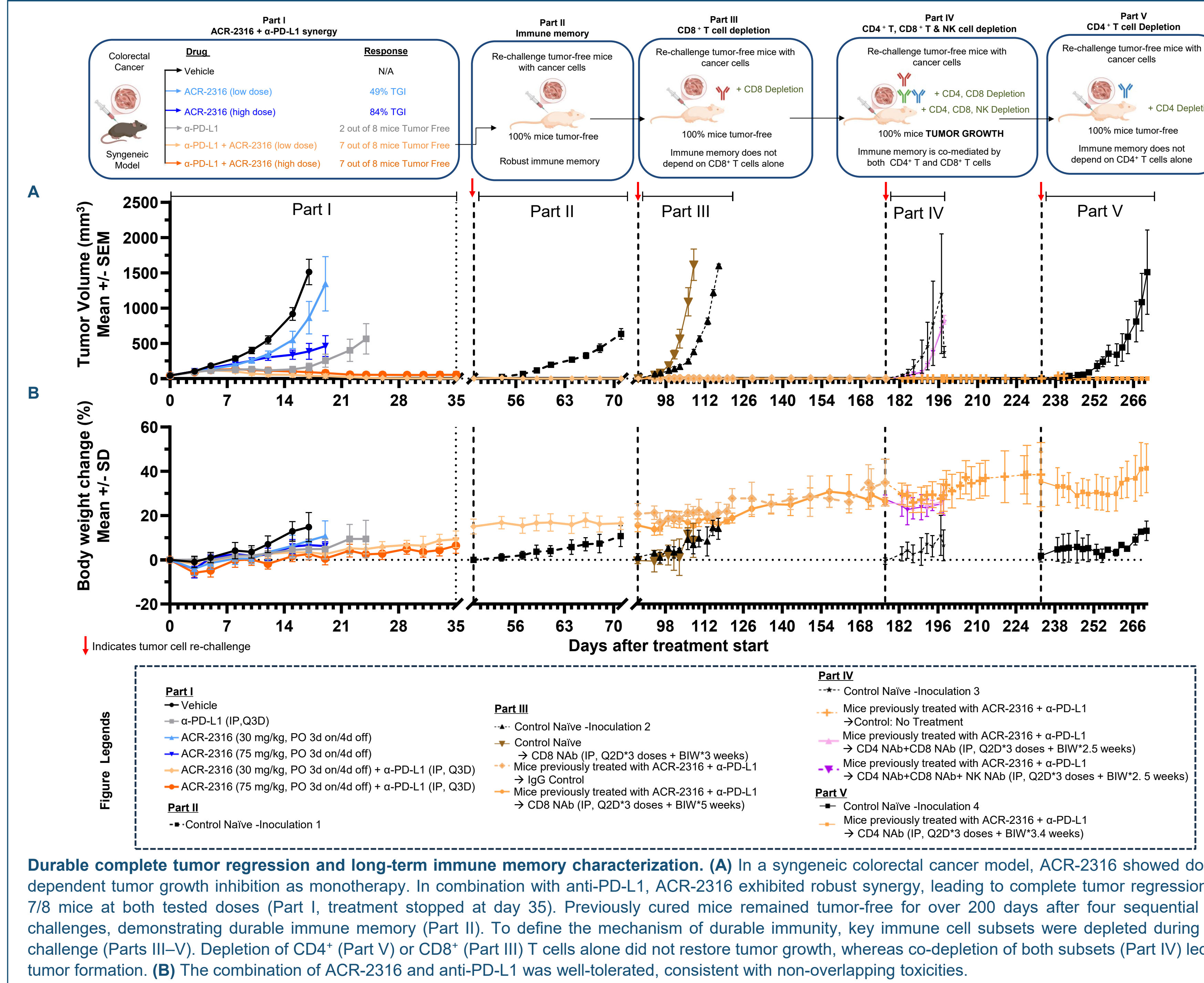
## AP3 profiling of ACR-2316-treated tumors reveals activation of innate immune signaling pathways



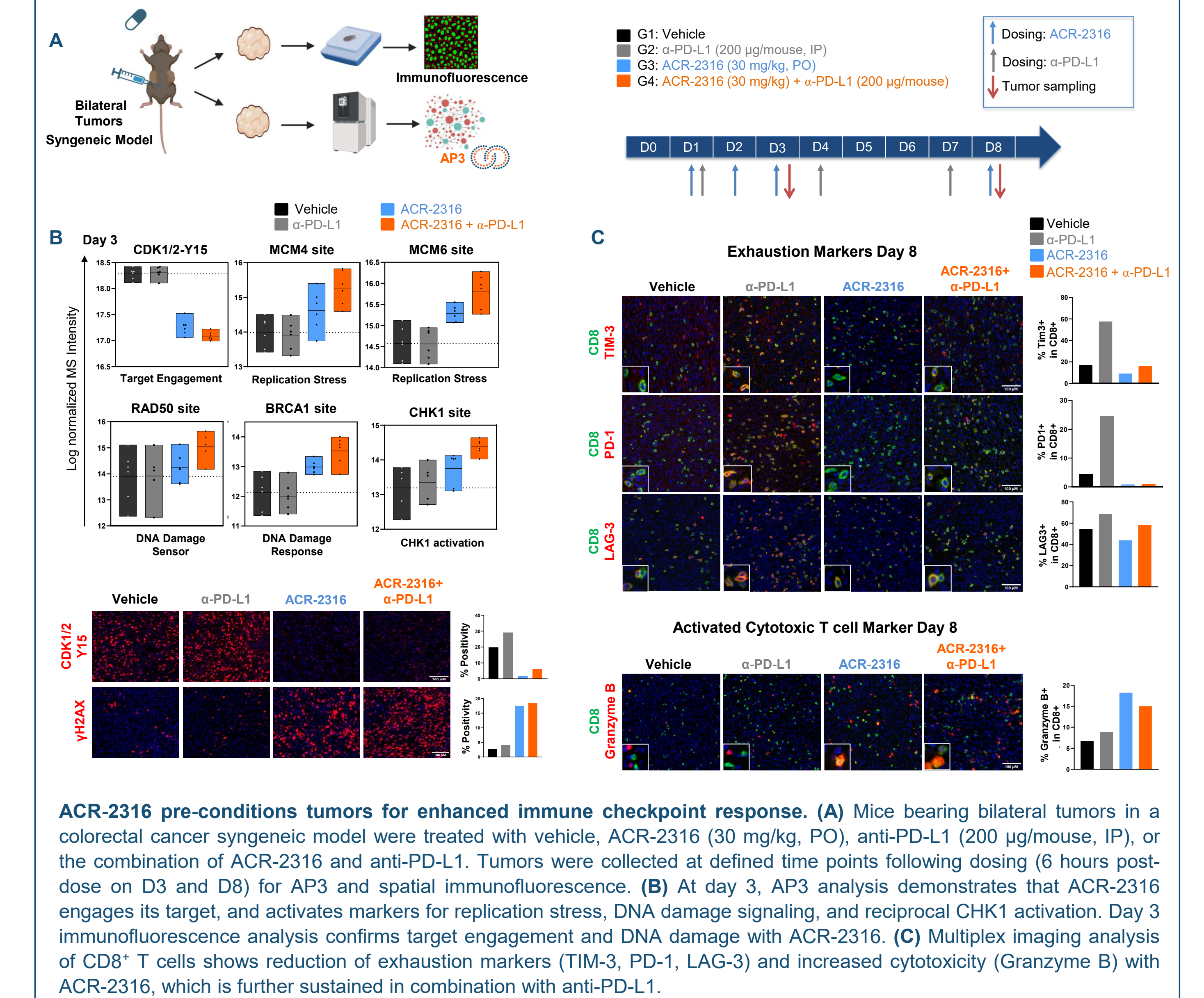
## ACR-2316 induces tumor-intrinsic DNA damage and activates multi-dimensional immune sensing in human and murine syngeneic cancer models



## ACR-2316 synergizes with anti-PD-L1 to induce complete response and durable immune memory in a syngeneic tumor model, co-mediated by CD4<sup>+</sup> and CD8<sup>+</sup> T cells



## ACR-2316 boosts immune-mediated tumor killing and overcomes anti-PD-L1 resistance by decreasing T-cell exhaustion



## Summary and Conclusions

