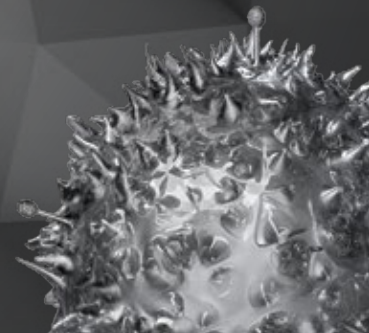
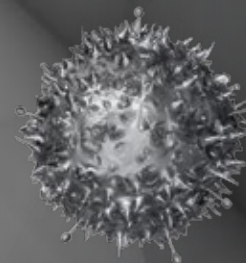


INVESTIGATING ENGAGEMENT OF ADAPTIVE AND INNATE IMMUNE SYSTEMS

No conclusions about safety and efficacy can be drawn from this presentation.



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CHAPTER 5

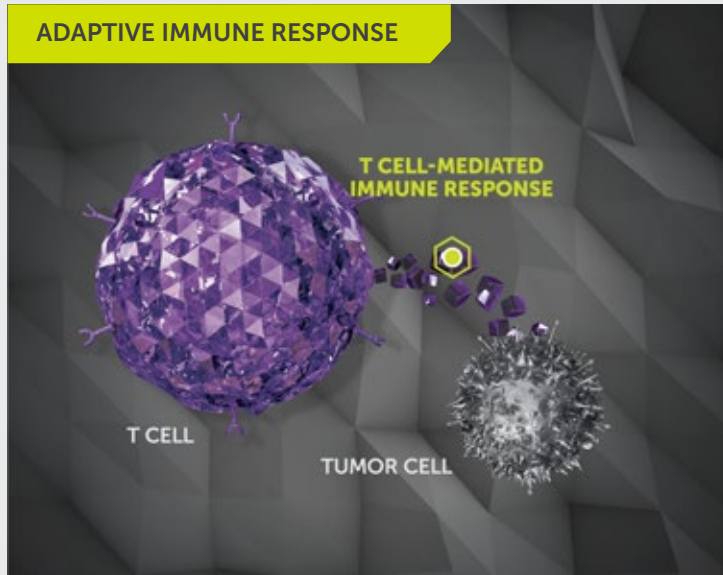
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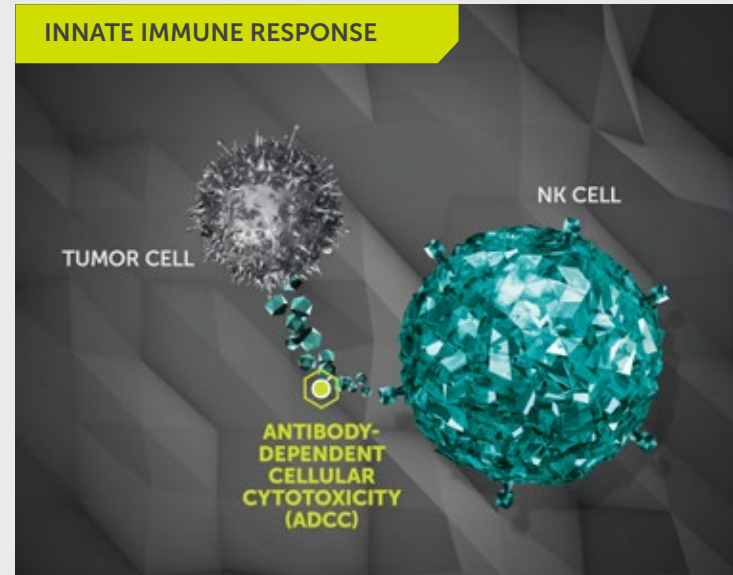
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PD-L1 PERSPECTIVES

The adaptive and innate immune systems have the ability to detect and destroy tumor cells



The adaptive immune system can destroy tumor cells via a T cell-mediated immune response.



The innate immune system can also destroy tumor cells via NK cell-mediated antibody-dependent cellular cytotoxicity, or ADCC.

Investigating engagement of adaptive and innate immune systems may lead to new ideas about fighting cancer.

No conclusions about safety and efficacy can be drawn from this presentation.

References: Chen DS, Mellman I. *Immunity*. 2013;39:1-10. Furness AJS, Vargas FA, Peggs KS, Quezada SA. *Trends Immunol*. 2014;35:290-298. Kohrt HE, Houot R, Marabelle A, et al. *Immunotherapy*. 2012;4:511-527.

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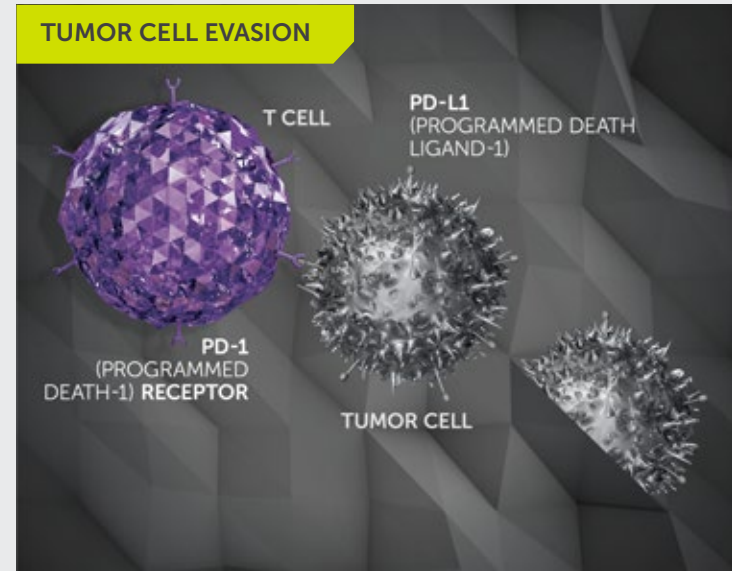


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PD-L1 PERSPECTIVES

Tumor cells can use signaling pathways to evade detection and destruction

- Tumor cells may often express programmed death ligand-1, or PD-L1. The binding of programmed death-1 receptors, or PD-1 receptors, and PD-L1 has the potential to inactivate T cells, which may silence the adaptive immune response

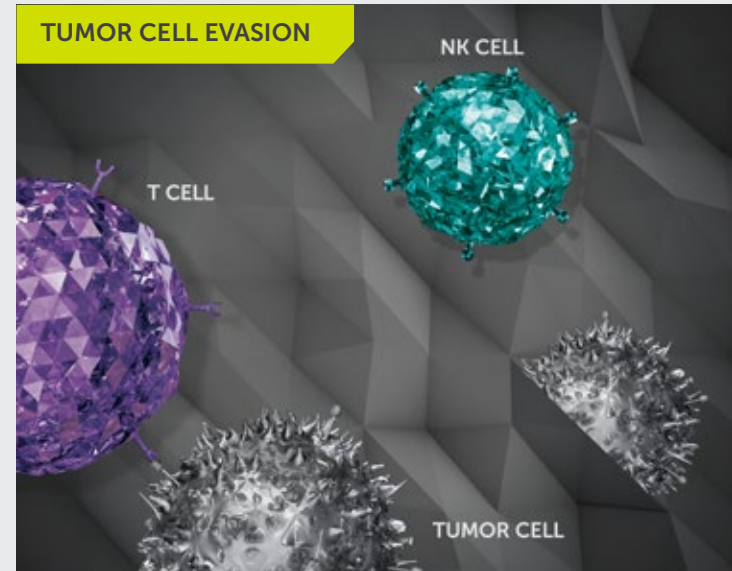


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References: Colombo MP, Piconese S. *Nat Rev Cancer*. 2007;7:880-887. Dolan DE, Gupta S. *Cancer Control*. 2014;21:231-237. Freeman-Keller M, Weber JS. *Ther Adv Med Oncol*. 2015;7:12-21. Momtaz P, Postow MA. *Pharmgenomics Pers Med*. 2014;7:357-365. Pardoll DM. *Nat Rev Cancer*. 2012;12:252-264. Philips GK, Atkins M. *Int Immunol*. 2015;27:39-46.

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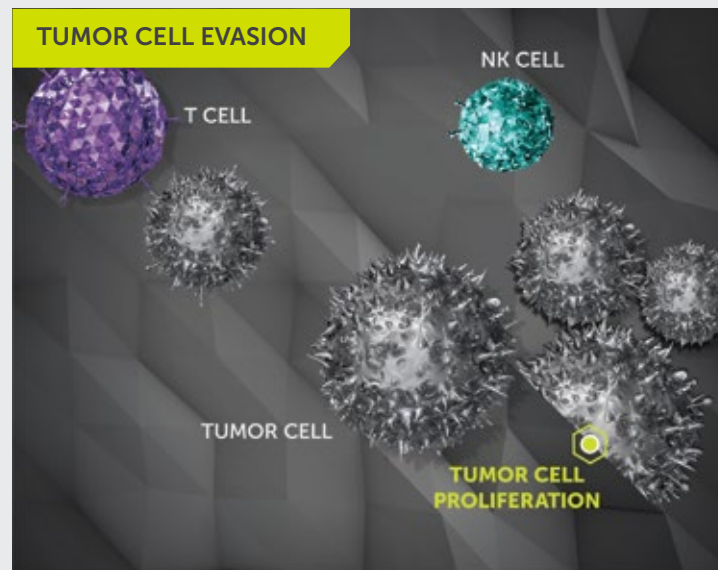


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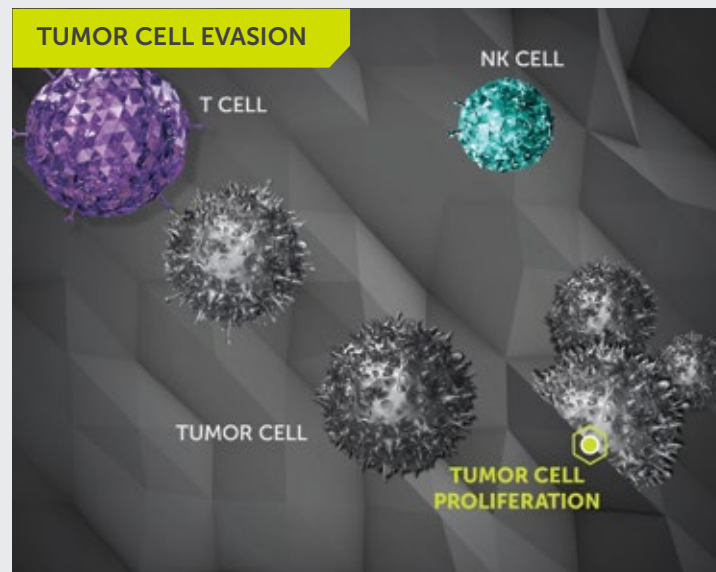


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What if interfering with tumor cell evasion of adaptive immunity and inducing innate immunity were possible?

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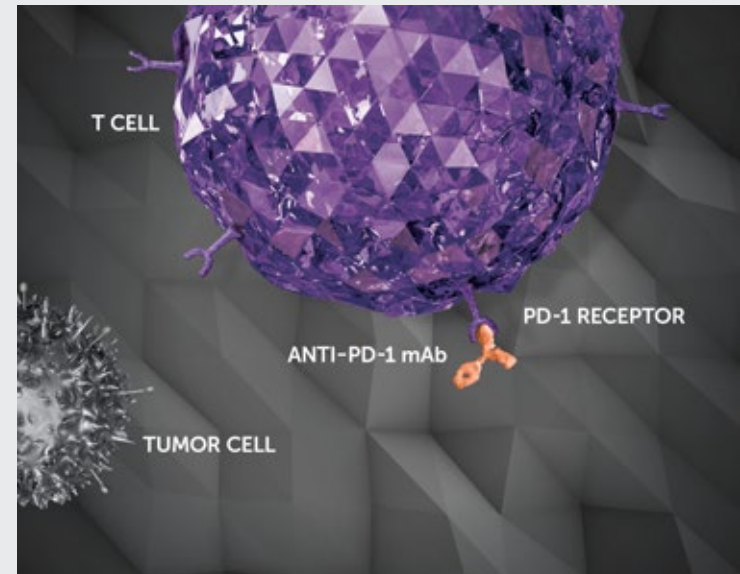


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PD-L1 PERSPECTIVES

Interrupting PD-1/PD-L1 pathway signaling offers a possible approach to reengaging an adaptive immune response

- Anti-PD-1 antibodies binding to PD-1 receptors on T cells may disrupt the tumor cell's ability to evade T cell-mediated adaptive immune response

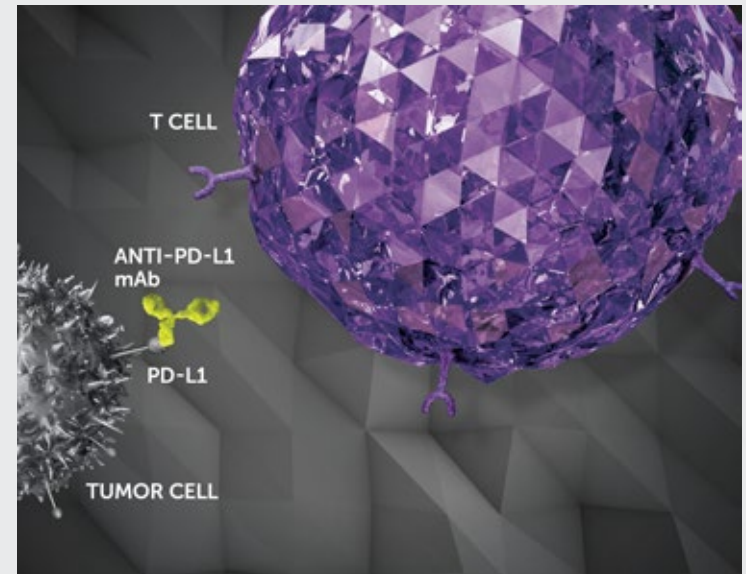


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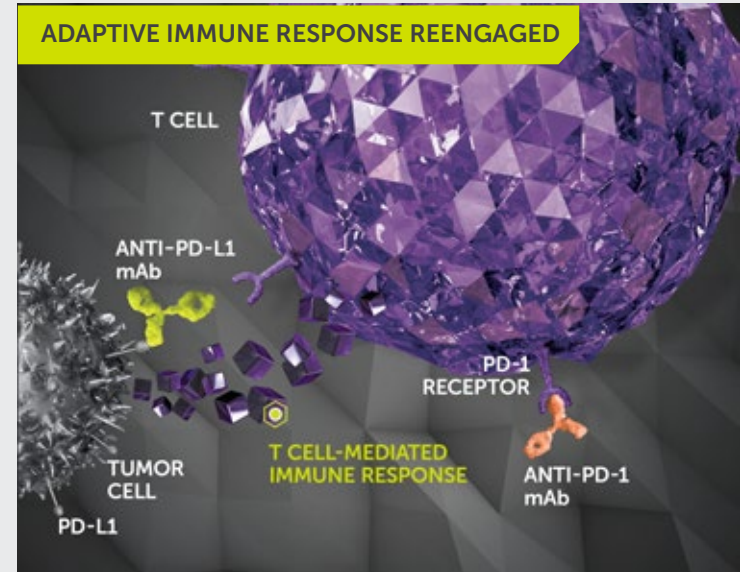


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- When PD-1/PD-L1 signaling is disrupted by either anti-PD-1 antibodies or anti-PD-L1 antibodies, T cells may be able to reinitiate an adaptive immune response

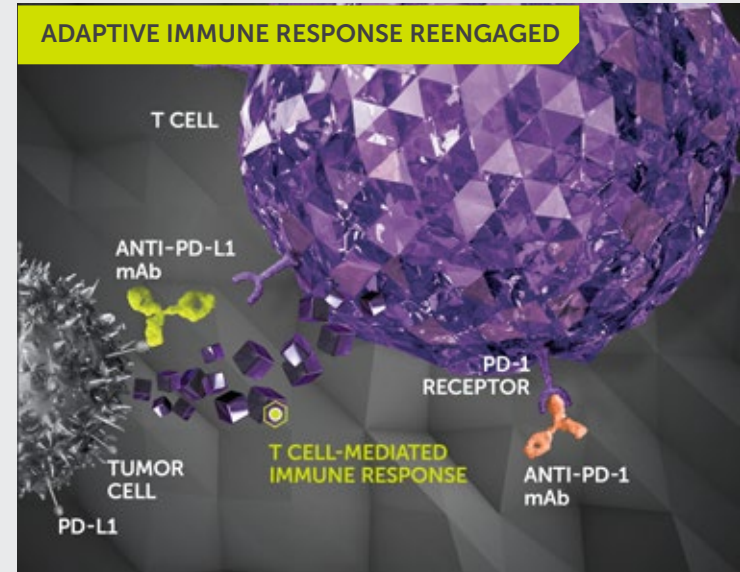


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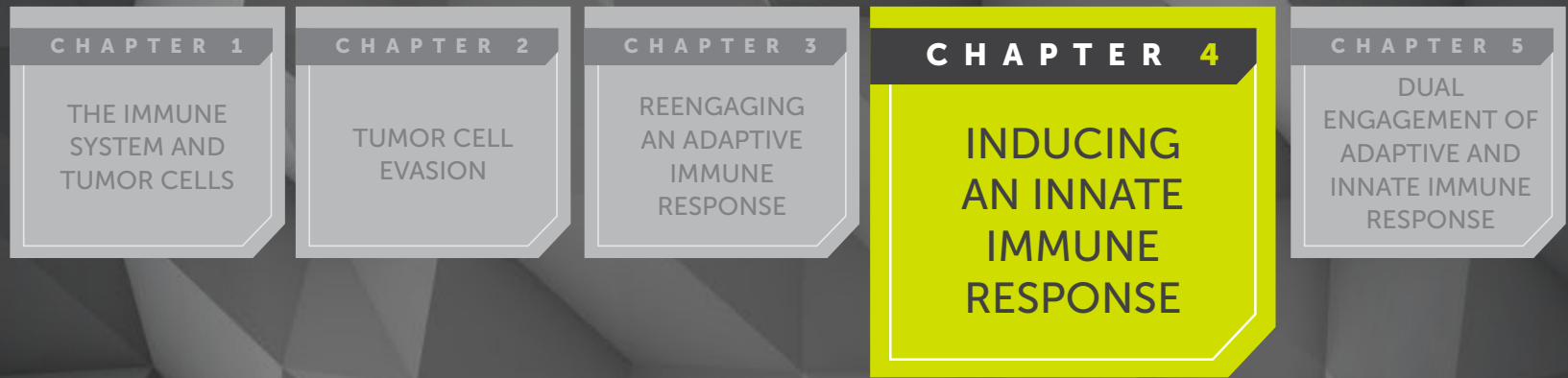


Anti-PD-1 antibodies binding to PD-1 receptors on T cells or anti-PD-L1 antibodies attaching to PD-L1 on tumor cells may interrupt signaling, which may allow reinitiation of an adaptive immune response.

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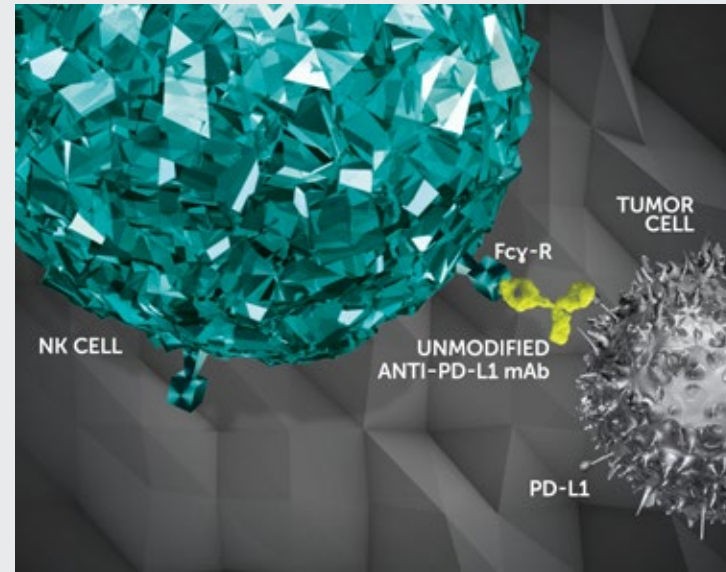
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Binding of unmodified anti-PD-L1 antibodies to Fc γ receptors on NK cells may induce an innate immune response

- Anti-PD-L1 antibodies with an unmodified Fc region may attach to PD-L1 on tumor cells and Fc γ receptors on NK cells

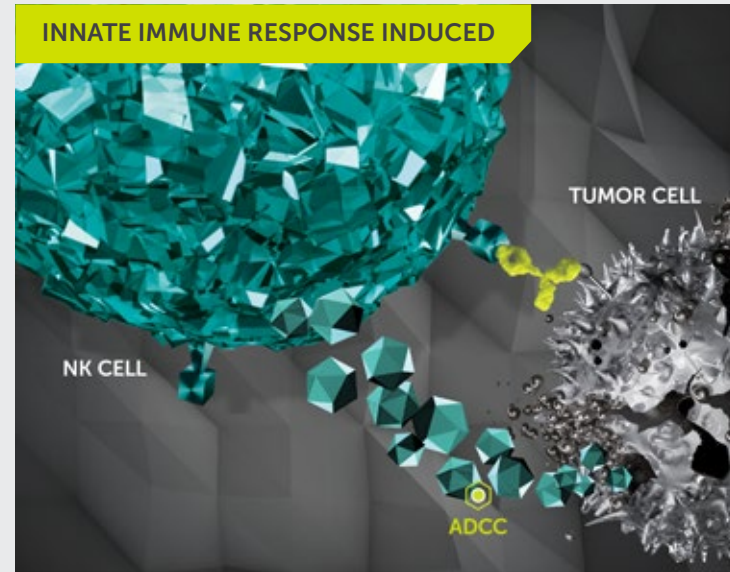


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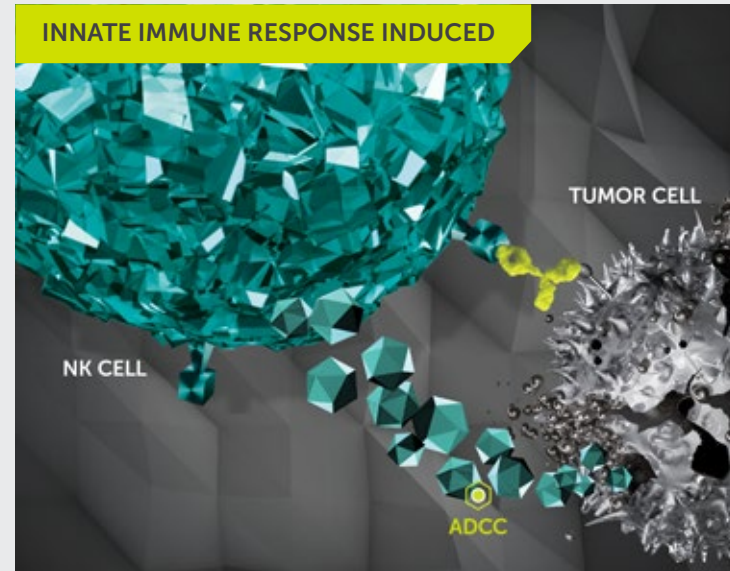


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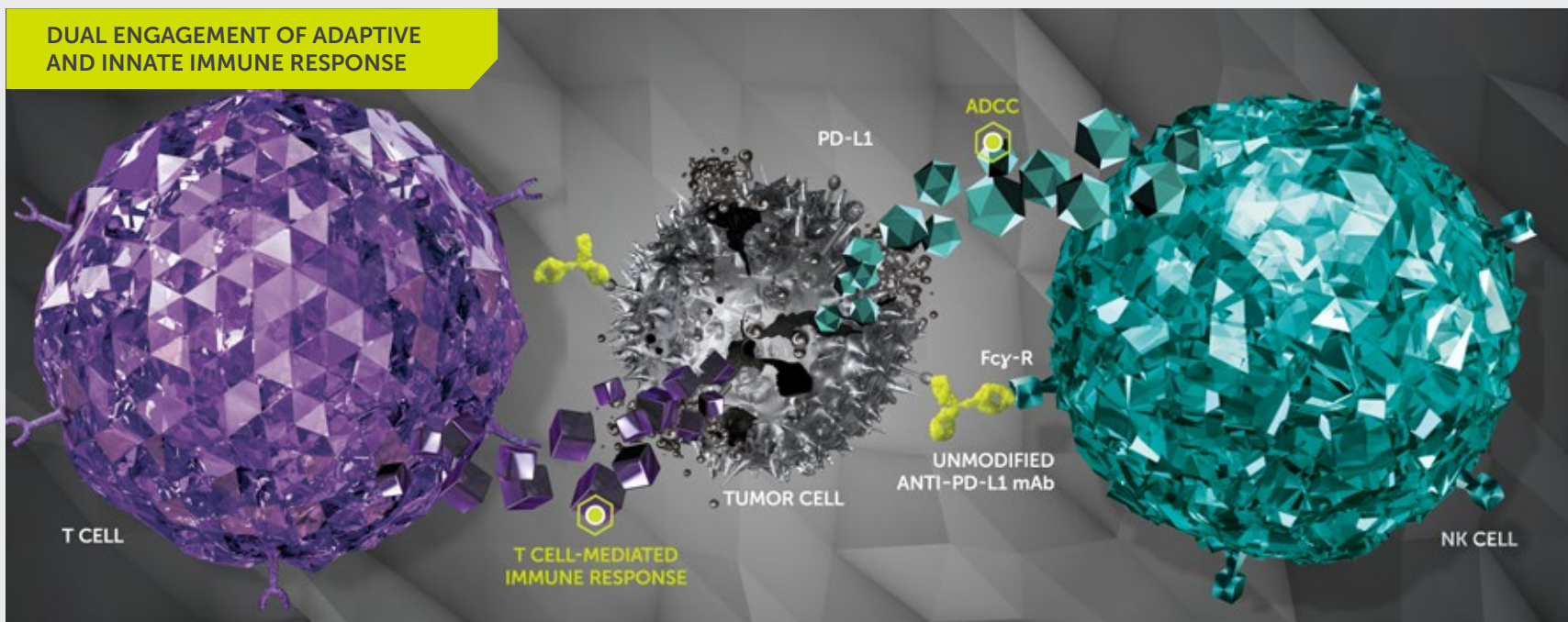
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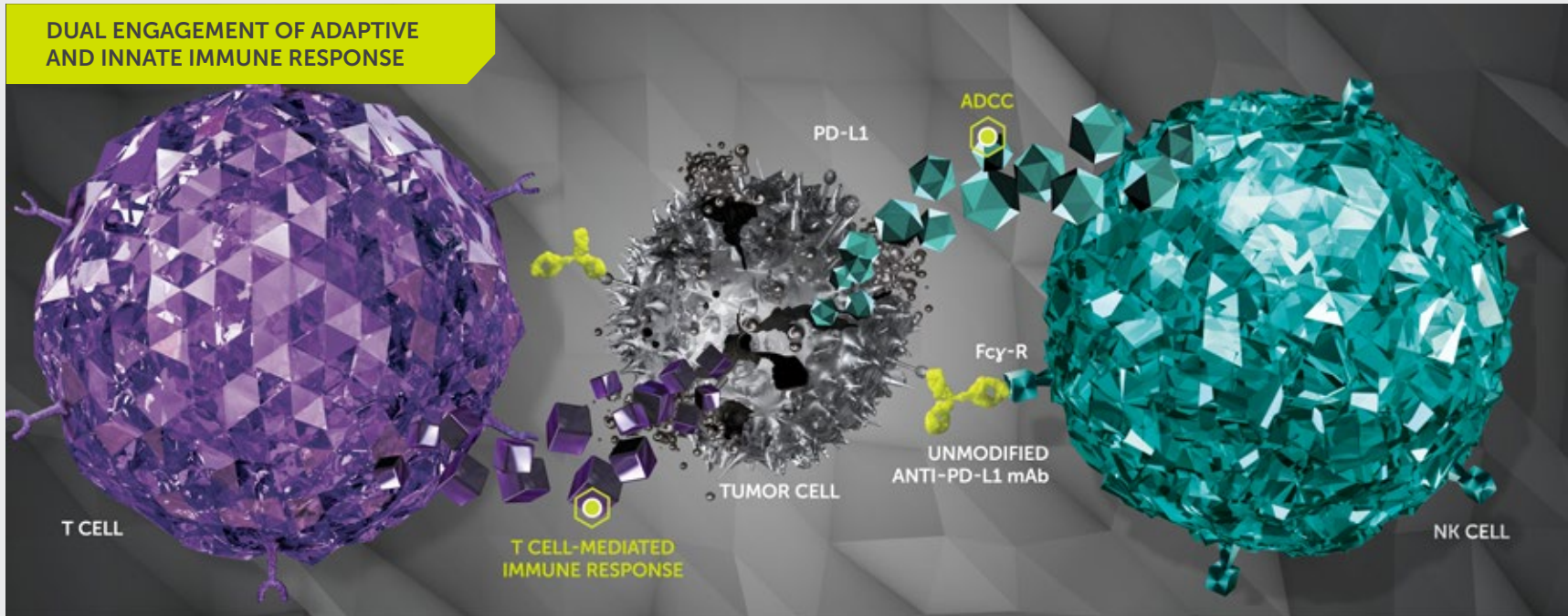
Dual engagement of adaptive and innate immune response may be possible with the introduction of unmodified anti-PD-L1 antibodies



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Reengaging the adaptive immune system and activating the innate immune system in a dual immune attack may offer a new approach in immuno-oncology.

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