

Coordinated stimulation of APC and T cell functions by first-in-class, tri-specific AN8025 for next-generation cancer immunotherapy

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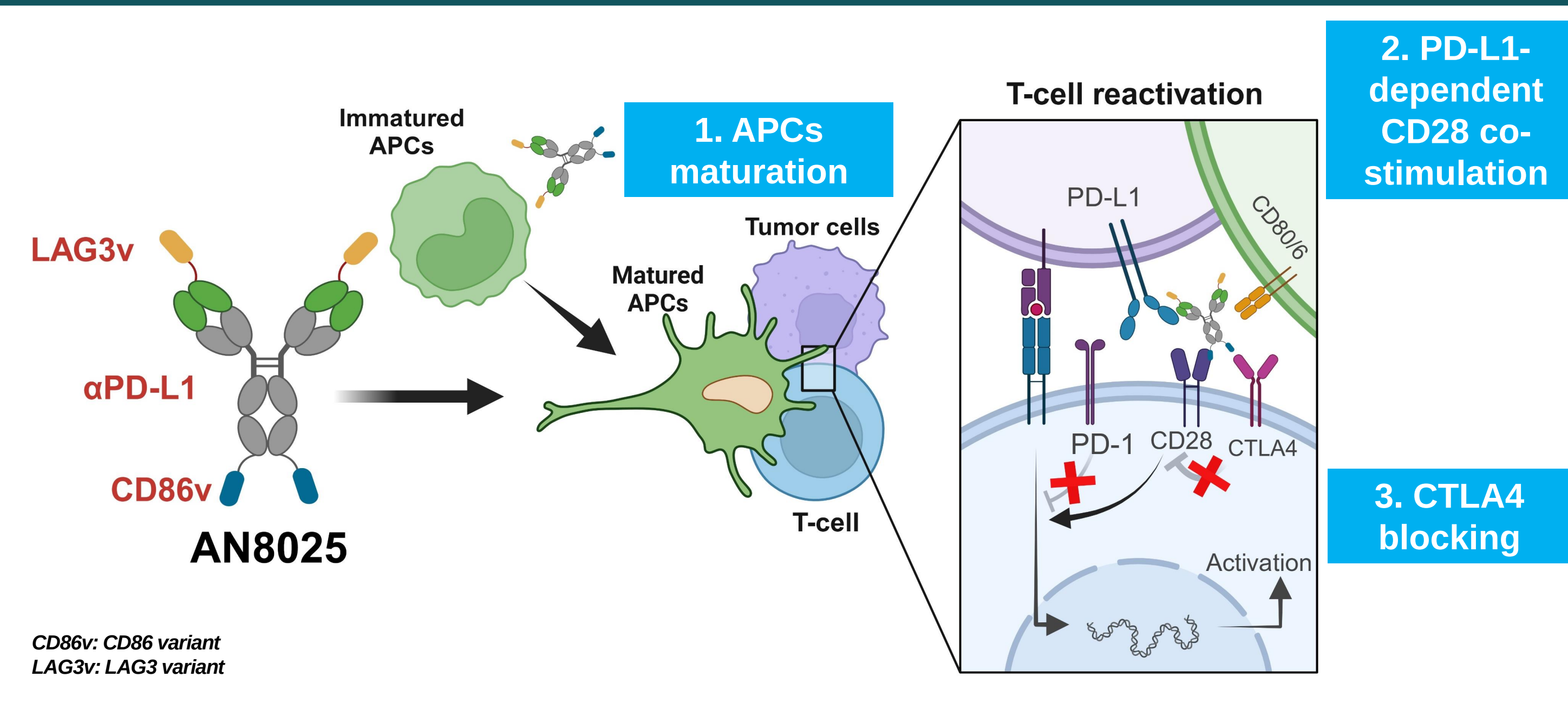
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Background

Immune checkpoint inhibitors, the cornerstone of current immunotherapies, primarily target T cells to reinvigorate the immune system against tumors. Recently, combinatory approaches, particularly in the form of bi-specific molecules have garnered significant interest for their potential to deliver superior clinical efficacy beyond the Immune checkpoint inhibitors(ICI) era. Building on this paradigm, AN8025 emerges as a tri-specific antibody fusion protein derived from a clinically validated and approved α PD-L1 antibody, fused with functionally optimized CD86 variant (CD86v) and LAG3 variant(LAG3v) on its C- and N-terminus of heavy chain, respectively. Here we report that AN8025 leverages the LAG3 component to stimulate the differentiation and maturation of antigen-presenting cells (APCs), while the CD86 and α PD-L1 components synergistically amplify tumor-specific T cell responses. Together, these actions orchestrate a multifaceted enhancement of immune function.

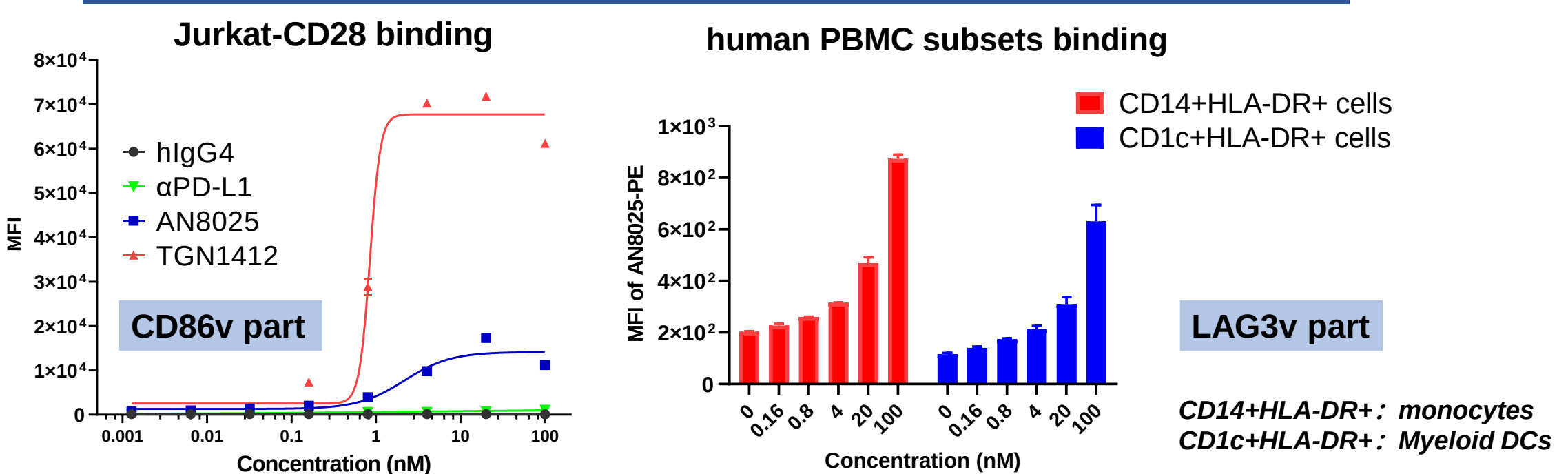
MOAs of AN8025



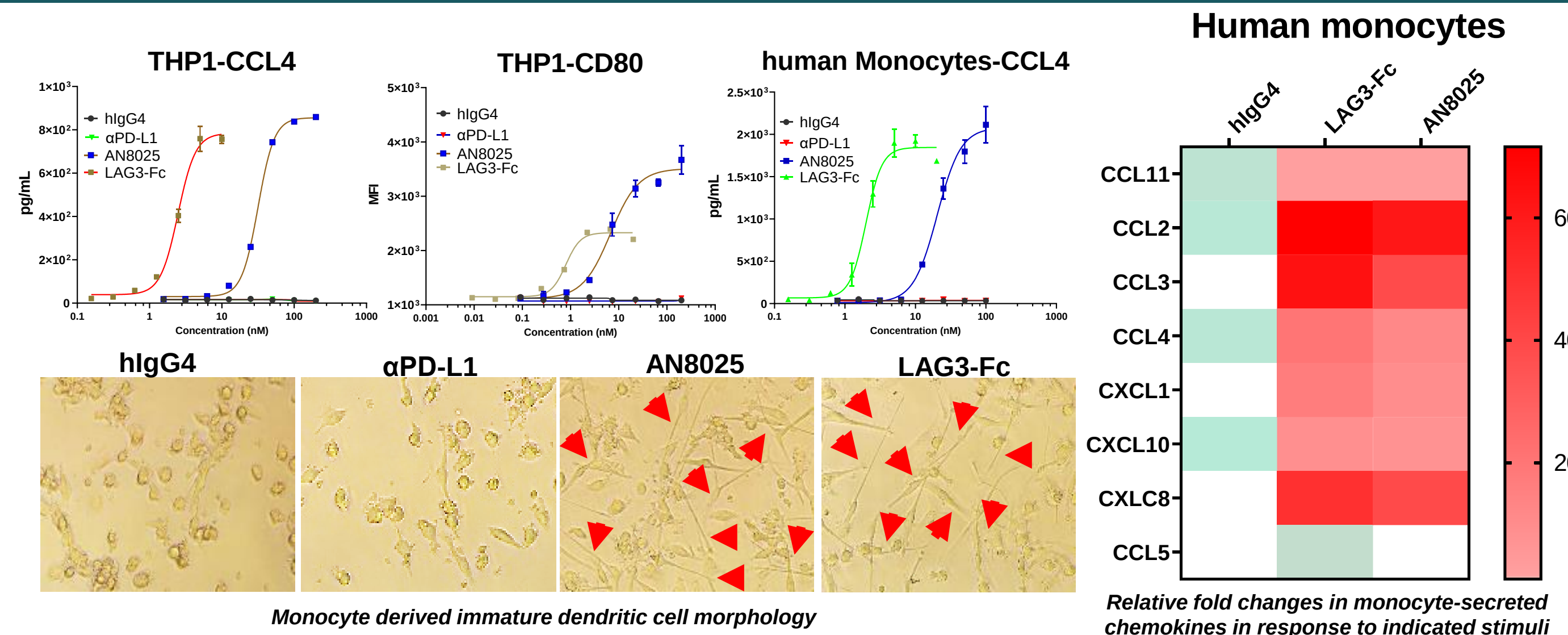
Target engagement of AN8025

hCTLA4		hCD28		hPD-L1	
Samples	KD (M)	Samples	KD (M)	Samples	KD (M)
IgG4 isotype	NA	IgG4 isotype	NA	IgG4 isotype	NA
AN8025	5.63E-09	AN8025	1.02E-08	AN8025	1.86E-09
α PD-L1	NA	α PD-L1	NA	α PD-L1	1.42E-09
Tremelimumab	7.32E-10	TGN1412	2.88E-12		
Ipilimumab	7.37E-09				

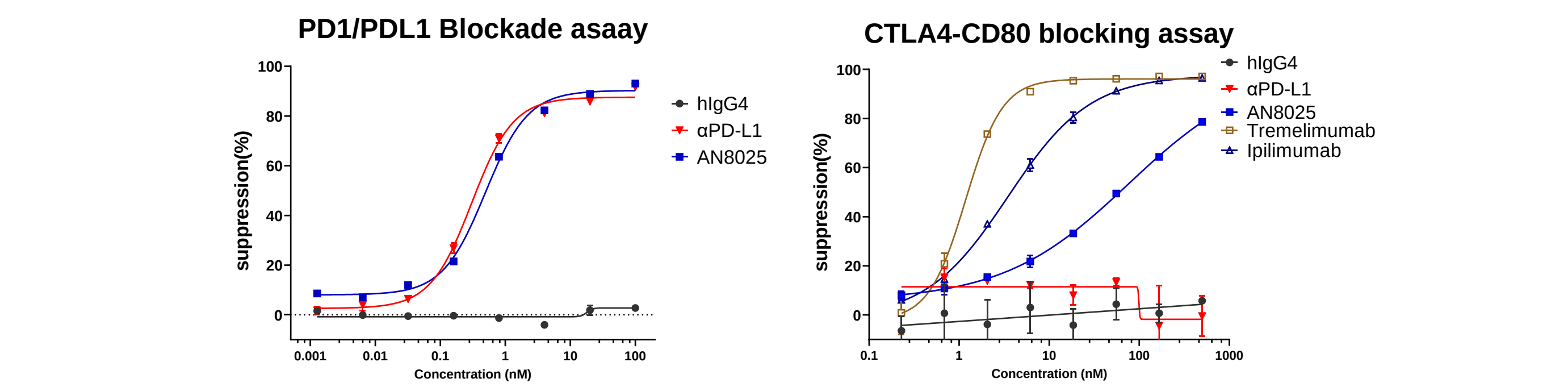
Cellular interaction of AN8025 to hCD28⁺ or HLA-DR⁺ cells



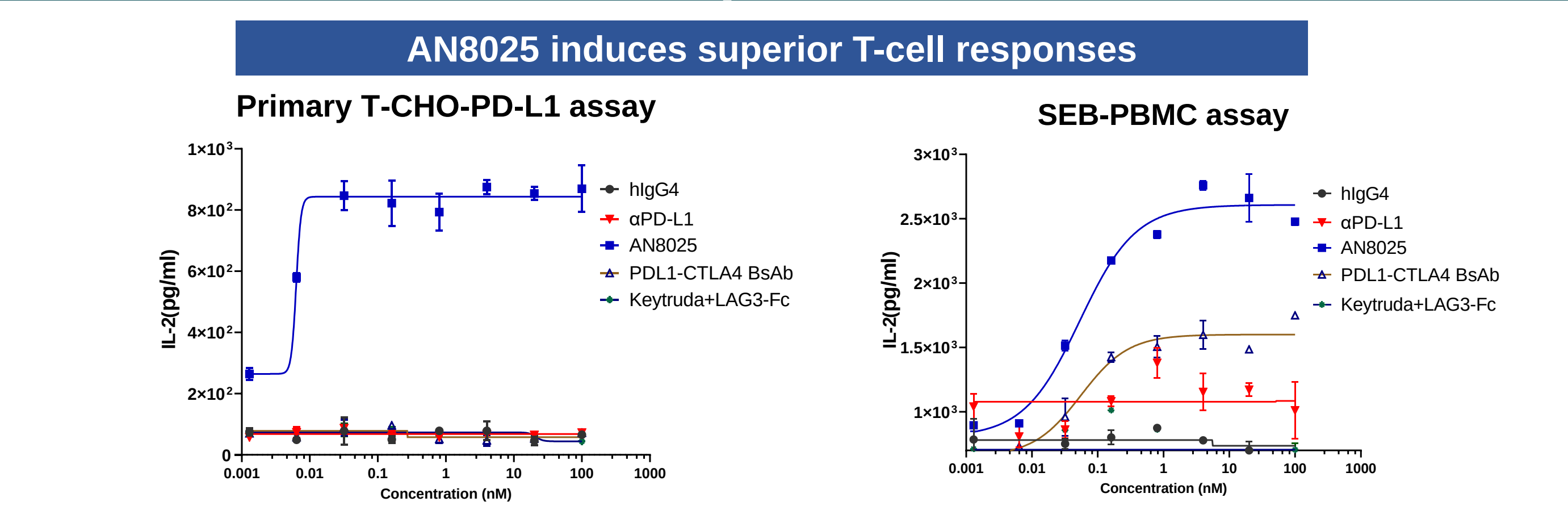
AN8025 enhances both the quantity and functionality of APCs



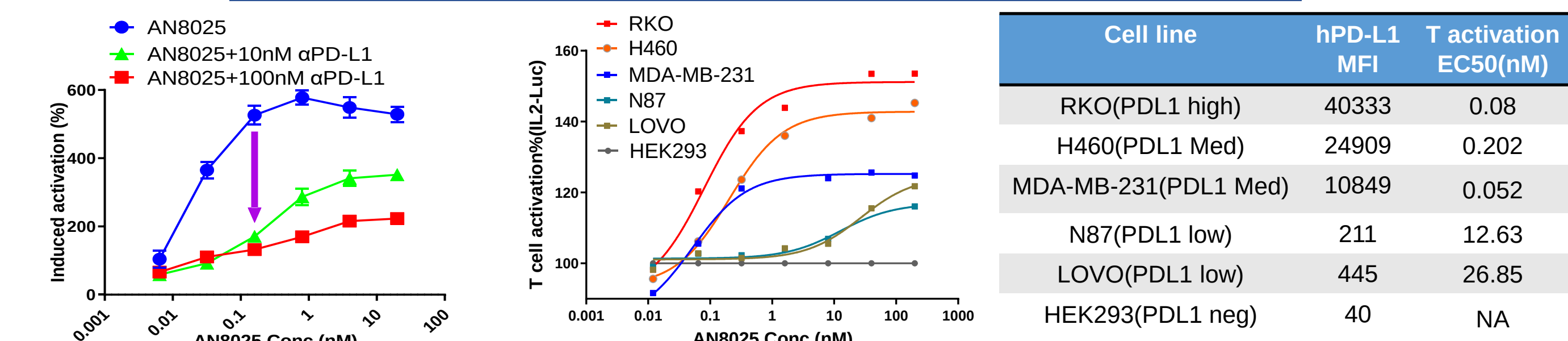
AN8025's blocking effect on PD-L1 and CTLA-4



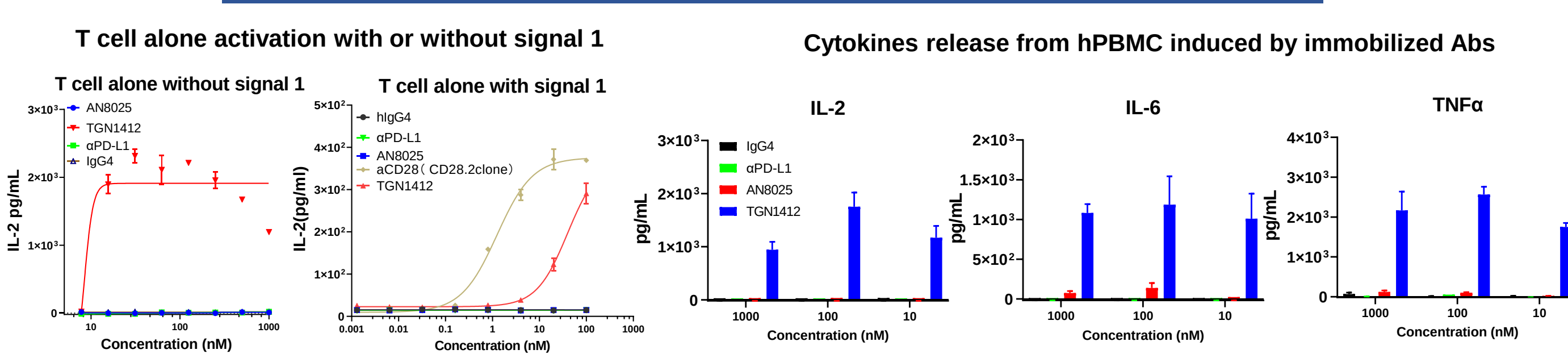
AN8025 promotes superior T cell activation in a PD-L1 dependent manner



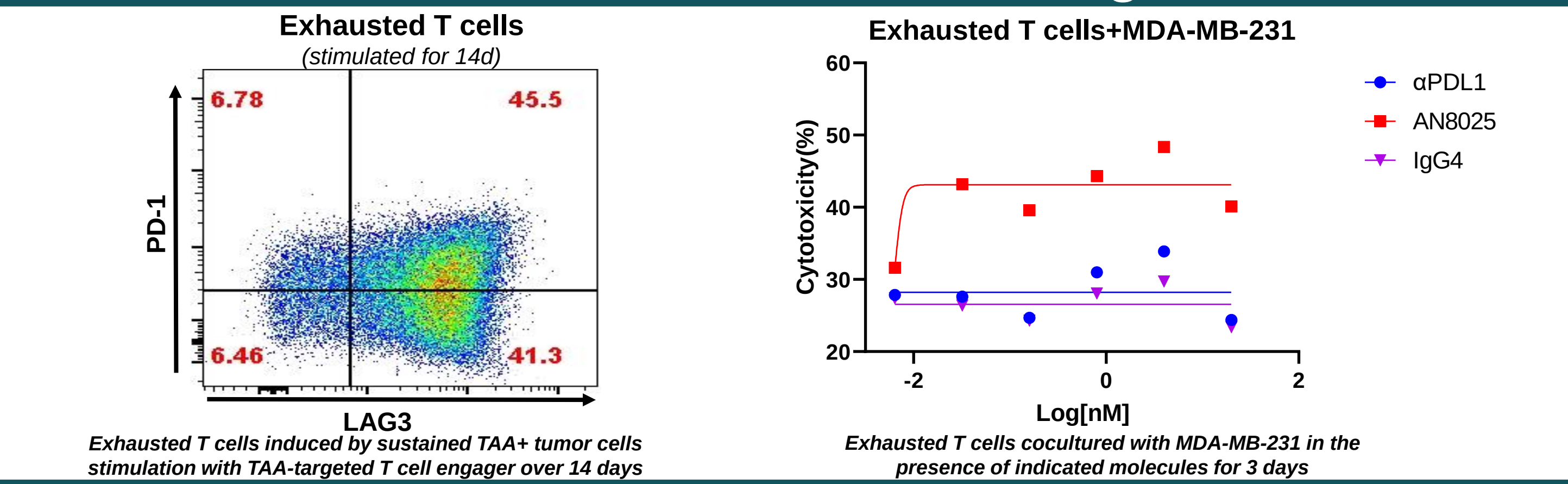
Enhanced T cell activation by AN8025 is PD-L1-dependent



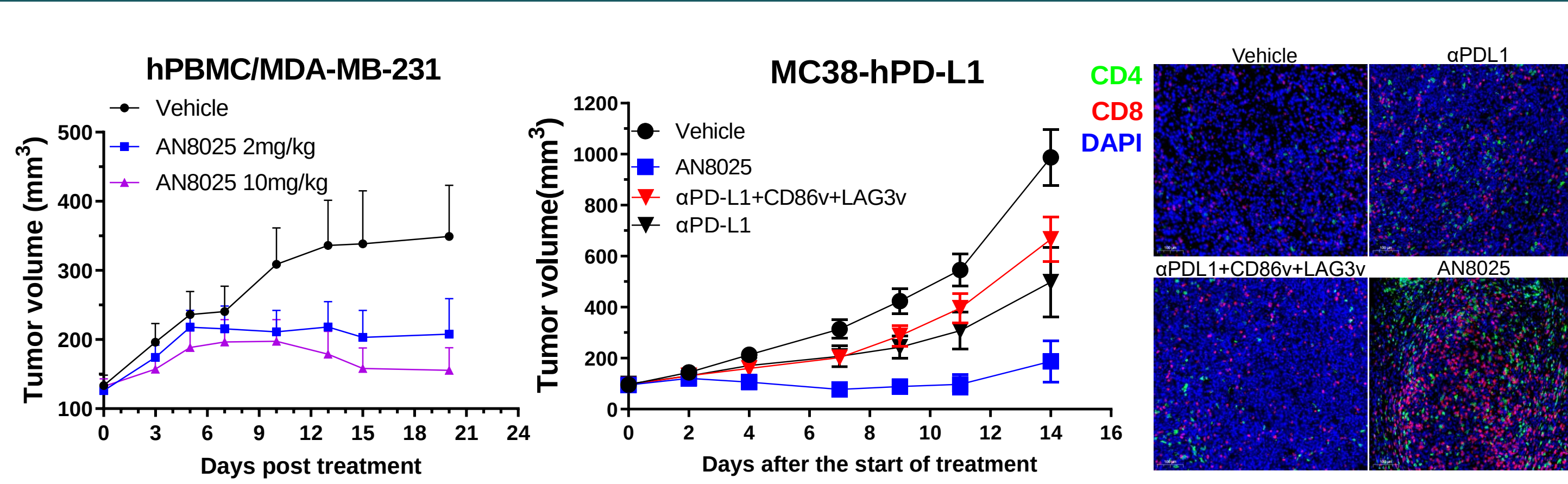
Unlike TGN1412, AN8025 does not act as a T cell superagonist



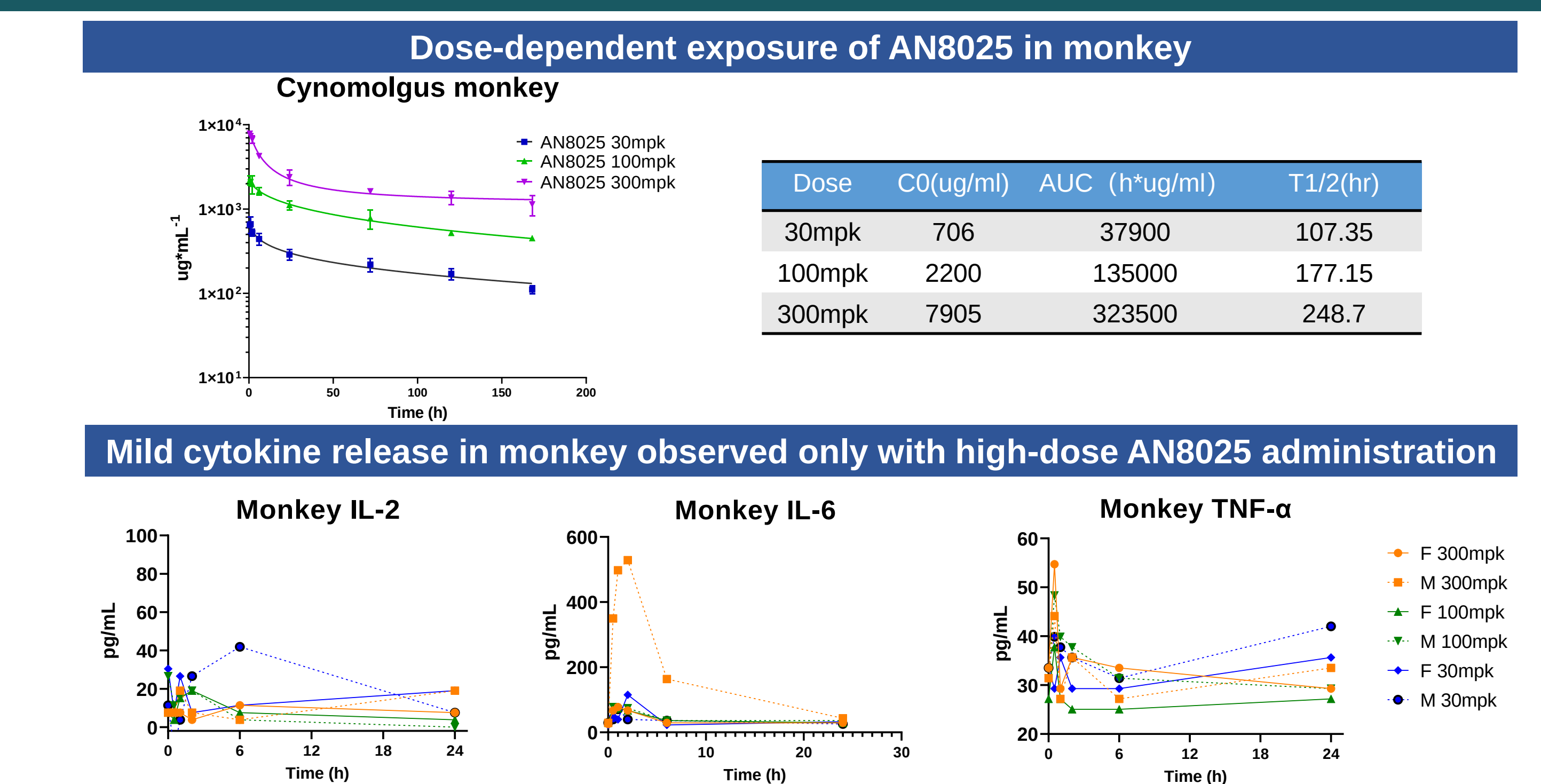
AN8025 reinvigorates exhausted T cells for efficient tumor cell killing



AN8025 exhibits potent anti-tumor activity in vivo



AN8025 demonstrates favorable PK and safety profiles in NHPs



Conclusions and Perspectives

- ✓ AN8025 is a first-in-class, tri-specific immunotherapy designed to provide coordinated stimulation of immune cells(APCs and T cells).
- ✓ AN8025 enhances both the quantity and quality of APCs.
- ✓ AN8025 promotes superior T cell activation in a PD-L1-dependent manner.
- ✓ AN8025 demonstrates a favorable PK and safety profile in NHPs.
- ✓ We plan to submit an IND for AN8025 in mid-2025.

