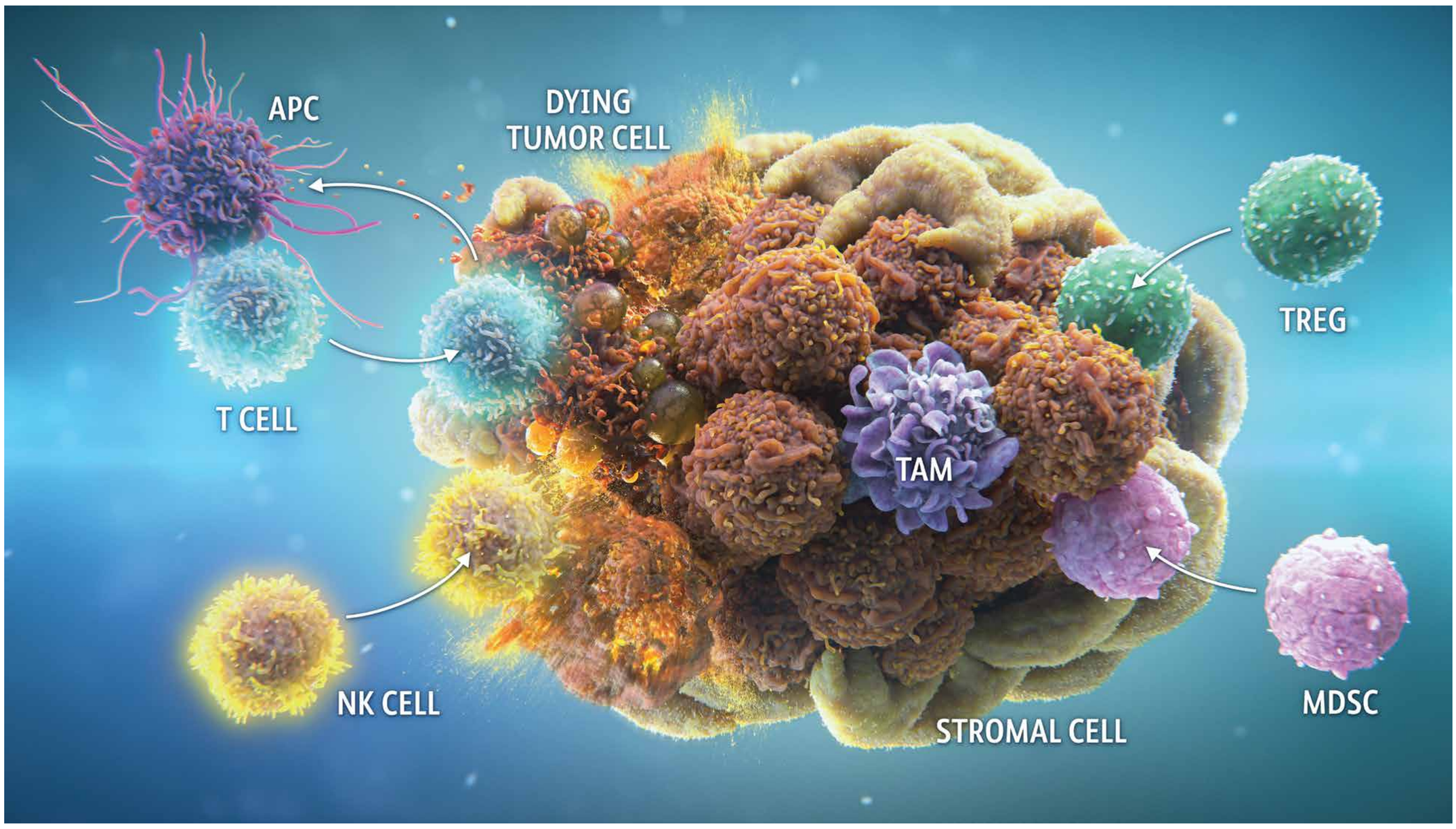
Bristol Myers Squibb™

Immuno-Oncology

Oncology research seeks to restore the body's ability to fight cancer and inhibit tumor-intrinsic drivers of oncogenesis



Tumor cell recognition*			Immunosuppression*	Effector cell function*			Tumor-intrinsic pathways*
Antigen presentation			Immunosuppressive effect of Tregs	Inhibitory immune checkpoints		Effector cell activation, proliferation, and cytotoxicity	Protein degradation pathways
NLRP3	STING	TLR8	CTLA-4	TIM-3	TIGIT†	IL-2	OX40	Ubiquitin proteasome pathway
Phagocytosis of tumor cells			Immunosuppressive myeloid cells	CTLA-4	PD-1	IL-12		Androgen receptor degradation
SIRPα			CCR2/5	IL-8	LAG-3	NKG2A		
Antibody-dependent tumor-cell death			Immune exclusion	Immunosuppressive metabolic pathways		Tumor antigen to direct T-cell activity	Epigenetic drivers of oncogenesis	
FucGM1			TGFβ1 & 3	IDO1	AHR	PSCA	BET	LSD1

*Select pathways investigating solid tumors. †Targets are listed by primary mechanism. Secondary mechanisms may exist.

The immune system uses a network of signaling pathways to detect and eliminate tumor cells.[1,2] Tumors use various mechanisms to escape detection and enable growth within the complex network.[3,4]

Ongoing Immuno-Oncology research at Bristol Myers Squibb focuses on these pathways, either alone or in combination, to understand how they may be modulated to restore the body's natural ability to fight cancer.

To find out more about Immuno-Oncology and our research, visit IOHCP.com.
For information on investigational studies, including study sites, visit BMSStudyConnect.com.

AHR=aryl hydrocarbon receptor; APC=antigen-presenting cell; BET=bromodomain and extra-terminal domain; CCR=chemokine (C-C motif) receptor; CTLA-4=cytotoxic T-lymphocyte antigen 4; FucGM1=fucosyl GM1; IDO1=indoleamine 2,3-dioxygenase-1; IL=interleukin; LAG-3=lymphocyte-activation gene 3; LDD=ligand-directed degrader; LSD1=lysine-specific demethylase 1; MDSC=myeloid-derived suppressor cell; NK=natural killer; NKG2A=NK group 2 member A; NLRP3=nucleotide-binding oligomerization domain-like receptor family, pyrin domain containing 3; PD-1=programmed death receptor-1; PSCA=prostate stem cell antigen; SIRPa=signal-regulatory protein alpha; STING=stimulator of interferon genes; TAM=tumor-associated macrophage; TGF=transforming growth factor; TIGIT=T-cell immunoreceptor with Ig and ITIM domains; TIM-3=T-cell immunoglobulin mucin-3; TLR8=toll-like receptor 8; Treg=regulatory T cell.

References: 1. Leung J, Suh WK. The CD28-B7 family in anti-tumor immunity: emerging concepts in cancer immunotherapy. *Immune Netw*. 2014;14(6):265-276. **2.** Long EO, Kim HS, Liu D, Peterson ME, Rajagopalan S. Controlling natural killer cell responses: integration of signals for activation and inhibition. *Annu Rev Immunol*. 2013;31:227-258. **3.** Melero I, Berman DM, Aznar MA, Korman AJ, Pérez Gracia JL, Haanen J. Evolving synergistic combinations of targeted immunotherapies to combat cancer. *Nat Rev Cancer*. 2015;15(8):457-472. **4.** Smyth MJ, Ngiow SF, Ribas A, Teng MWL. Combination cancer immunotherapies tailored to the tumour microenvironment. *Nat Rev Clin Oncol*. 2016;13(3):143-158.

Bristol Myers Squibb: At the forefront of **Immuno-Oncology** research