



武汉大学
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Immune Checkpoint

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A Brand New Approach for Cancer Therapy,



**the 2018 Nobel Prize in Physiology or Medicine :
discovery of cancer therapy by inhibition of negative immune regulation**



James Allison

CTL-4



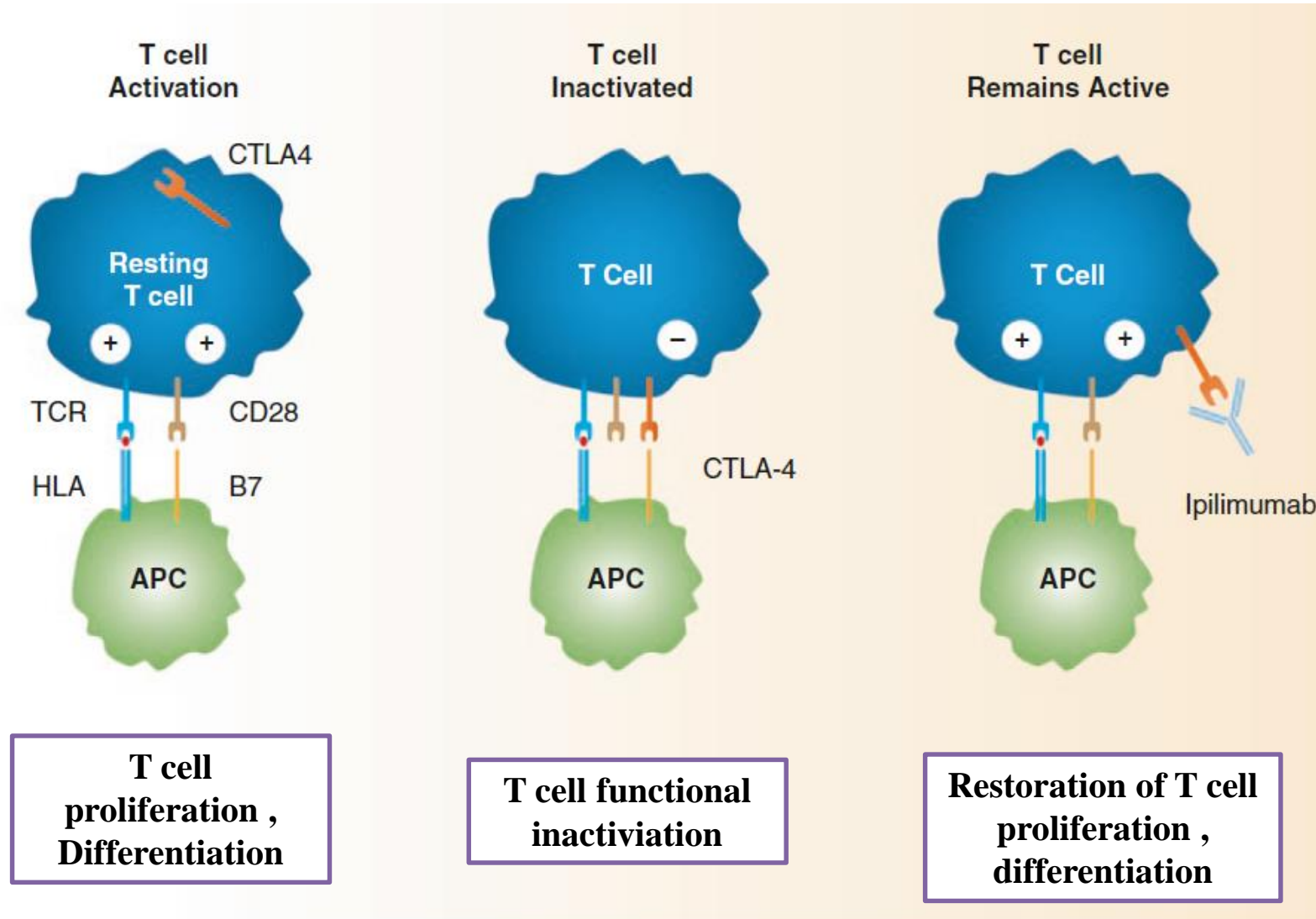
Tasuku Honjo

PD-1

“ It is all about interference with the brakes of our immune system as a means to unleash this defence. ”

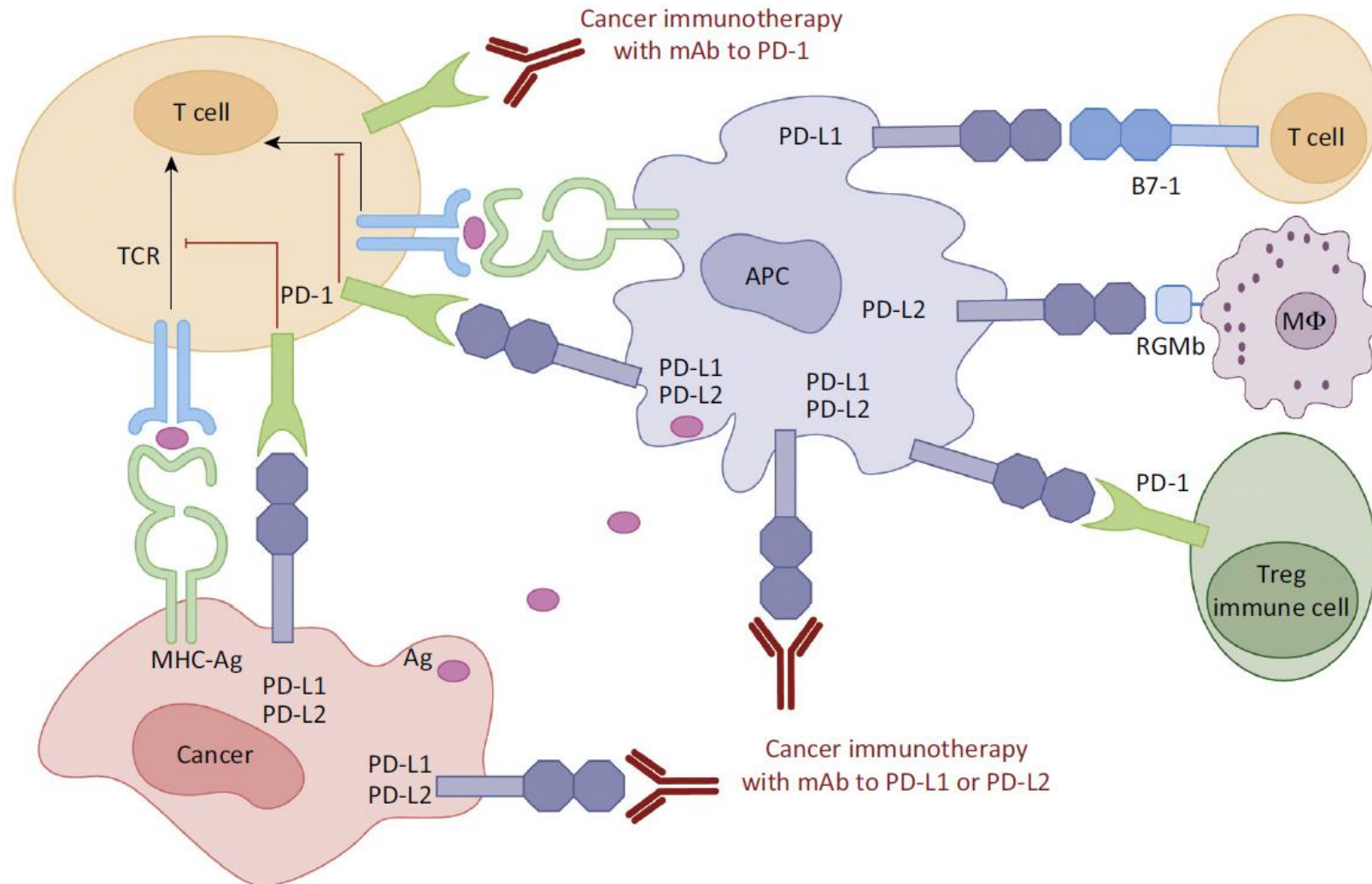
Function of CTLA-4

Cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4, CD152) was the first recognized inhibitory immune checkpoint molecule



Function of PD-1 and Its Ligands

Programmed death 1 (PD-1) is a more recently discovered immune checkpoint receptor that has generated considerable excitement based on favorable preclinical profiling and initial clinical results.



FDA-approved Immune Checkpoint Inhibitors

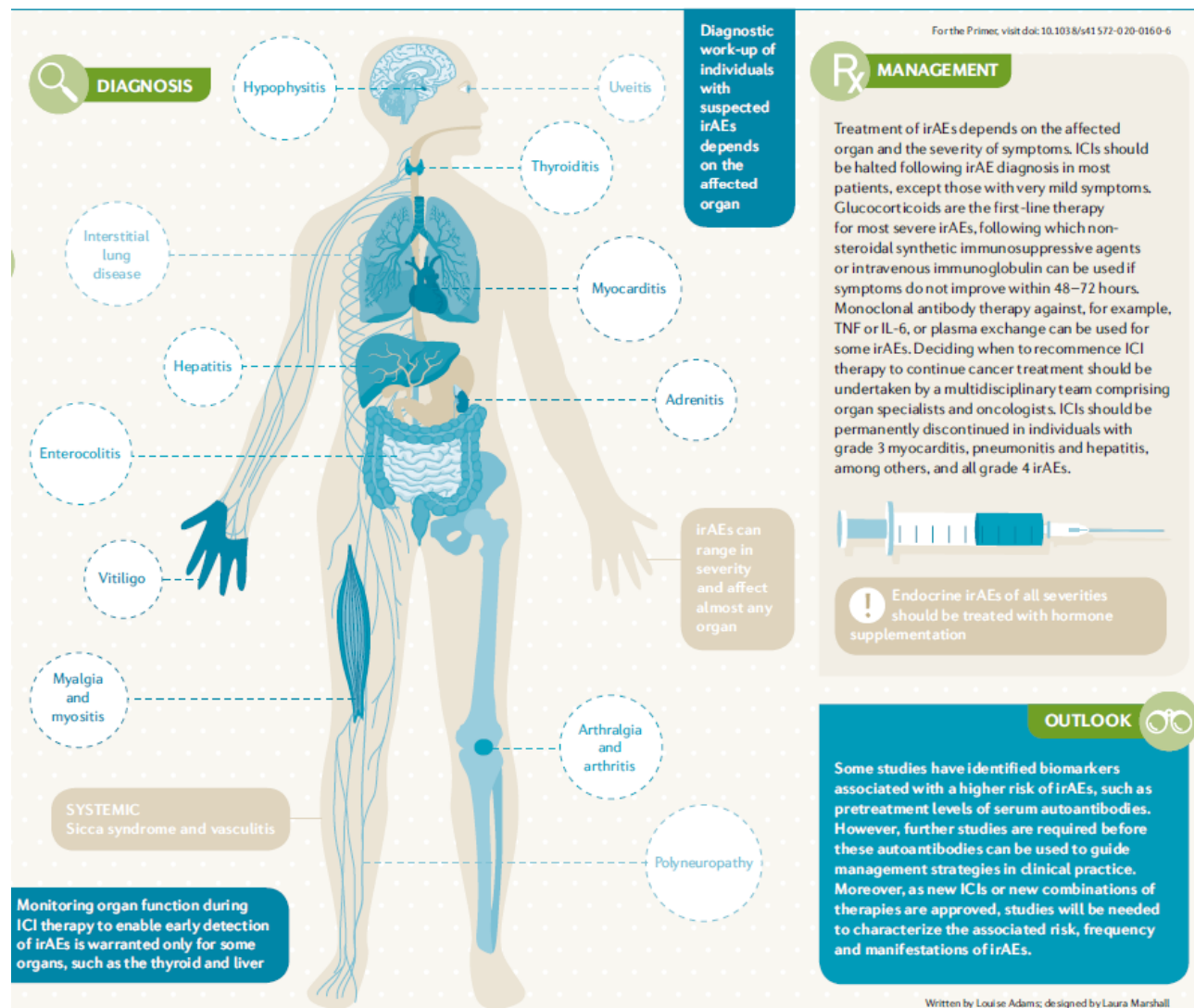


Drug (Trade name)	Company	Date of approval	Indication
CTLA-4 inhibitors			
Ipilimumab (Yervoy®)	Bristol-Myers Squibb	2011	Melanoma colorectal cancer Renal cell carcinoma
PD-1 inhibitors			
Nivolumab (Opdivo®)	Bristol-Myers Squibb	2014	Melanoma Hodgkin's lymphoma Diffuse large B-cell lymphoma Urothelial cancer Colorectal cancer Hepatocellular carcinoma Non-small cell lung cancer Small cell lung cancer Renal cell carcinoma Squamous cell carcinoma
Pembrolizumab (Keytruda®)	Merck	2014	Melanoma Cervical cancer Hodgkin's lymphoma Diffuse large B-cell lymphoma Gastric cancer Urothelial cancer Colorectal cancer Hepatocellular carcinoma Non-small cell lung cancer Small cell lung cancer Renal cell carcinoma Squamous cell carcinoma Esophageal cancer Merkel cell carcinoma Cutaneous squamous cell carcinoma
Cemiplimab (Libtayo®)	Sanofi	2018	Cutaneous squamous cell carcinoma
PD-L1 inhibitors			
Atezolizumab (Tecentriq®)	Roche, Genentech	2016	Non-small cell lung cancer Triple negative breast cancer
Avelumab (Bavencio®)	Merck, Pfizer	2017	Merkel cell carcinoma Renal cell carcinoma Urothelial cancer
Durvalumab (Imfinzi®)	AstraZeneca	2017	Bladder cancer Non-small cell lung cancer

相较于靶向PD-1、PD-L1的药物，CTLA-4的抑制剂具有更高频率和严重性的免疫不良事件。

Immune-related Adverse Events (irAEs)

Immune-related adverse events are caused from non-specific activation of the immune system resulting in immune responses that target self-antigens.



人体内大部分器官都可能产生免疫不良反应，最严重的常发生在皮肤、胃肠道、肝脏和内分泌系统。

Next Generation Immune Checkpoint Inhibitors

Target	Binding partner	Drugs	Trial stage
LAG-3	MHC-II	Eftilagimod alpha (Immutep)	I/II
		Relatimab (Bristol Myers Squibb)	II/III
		Ieramilimab (Novartis)	II
		Favezelimab (Merck)	I/II
		Fianlimab (Regeneron)	I
		Encelimab (AnaptysBio/GlaxoSmithKline)	I
		Miptenalimab (Boehringer Ingelheim)	I
		Sym 022 (Symphogen)	I
		FS118 (F-star)	I
		Tebotelimab (MacroGenics)	I
TIM-3	Galactine-9, phosphatidyl serine, CEACAM	TSR-022 (GlaxoSmithKline)	I
		Sabatolimab (Novartis)	I/II
		Sym 023 (Symphogen)	I
		INCAGN 2390 (Incyte Corporation)	I
		LY3321367 (Eli Lilly and Company)	I/II
		BMS-986258 (Bristol Myers Squibb)	I/II
		SHR-1702 (Jiangsu HengRui)	I
		Vibostolimab (Merck)	III
TIGIT	CD155, CD112	Etigilimab (OncoMed Pharmaceuticals)	I
		Tiragolumab (Genentech)	II
		BMS-986207 (Bristol Myers Squibb)	I/II
		Domvanalimab (Arcus Biosciences)	I
		JNJ-61610588 (Johnson & Johnson)	I
VISTA	VSIG-3	CI-8993 (Curis Inc)	
B7-H3	Unknown	Enoblituzumab (MacroGenics)	II
		¹³¹ I-omburtamab (Y-mAbs Therapeutics)	II/III
		¹²⁴ I-omburtamab (Y-mAbs Therapeutics)	I