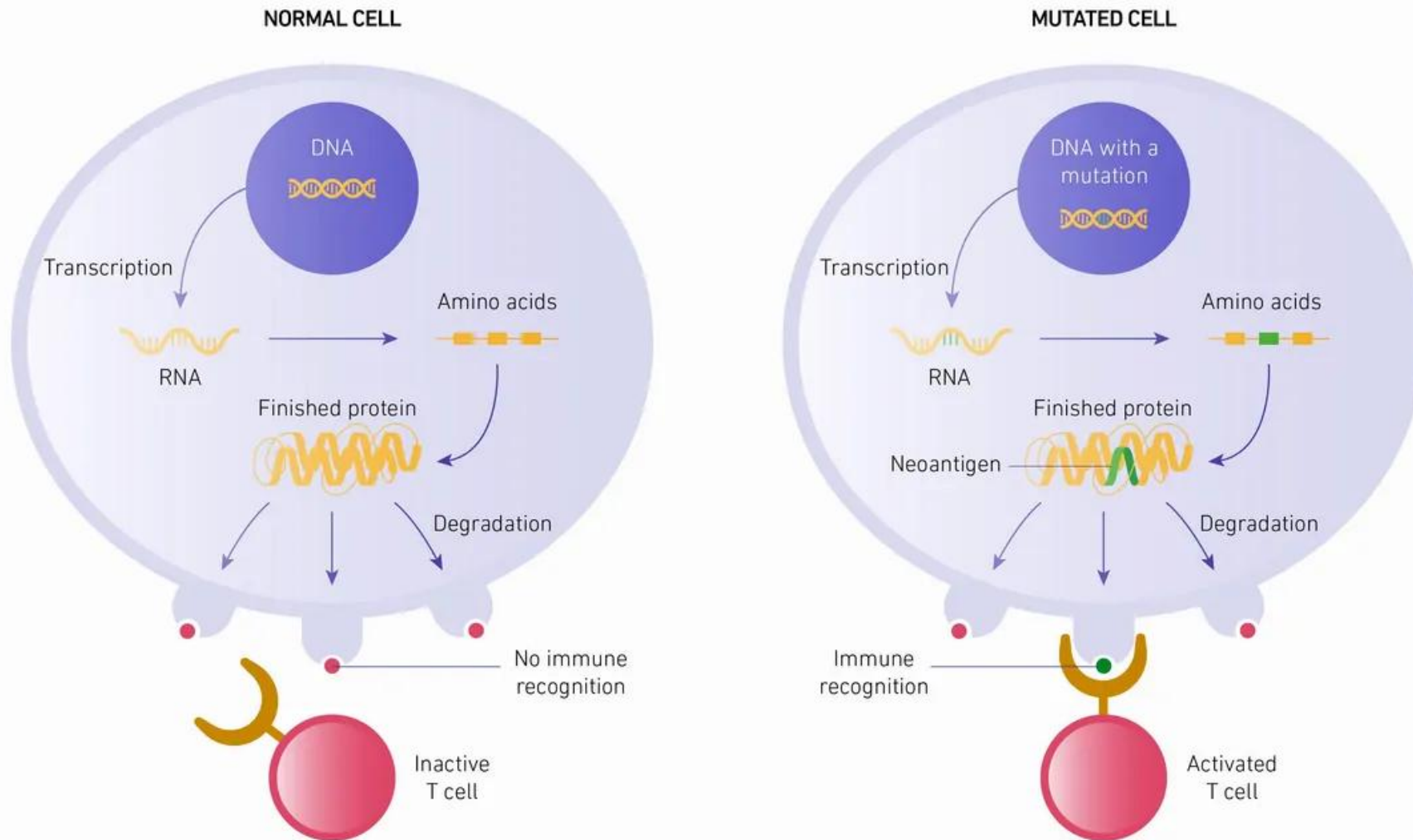


Immunological Basis of Cancer Immunotherapy

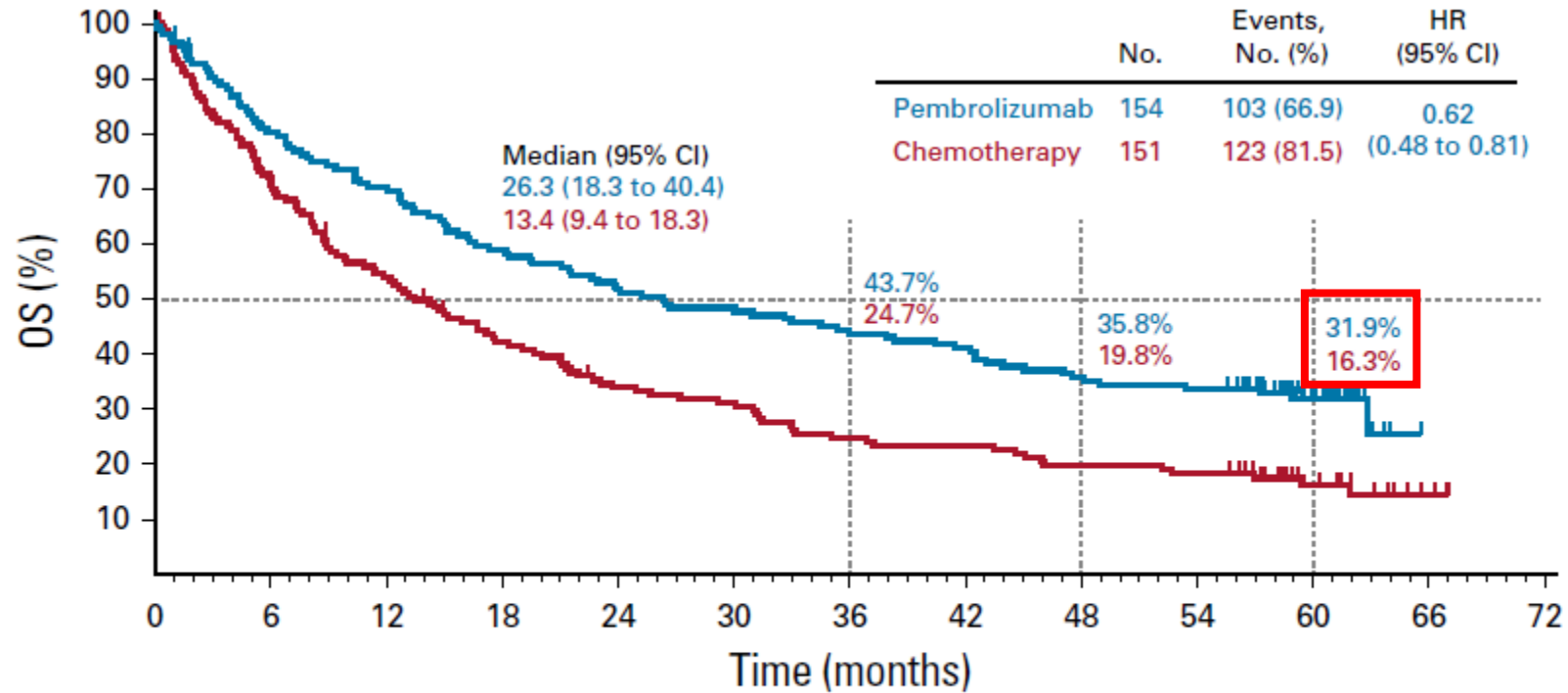
Jun Hyeok Lim
Division of Pulmonology
Department of Internal Medicine
Inha University Hospital

Why Immunology in Lung Cancer?



Why Immunology in Lung Cancer?

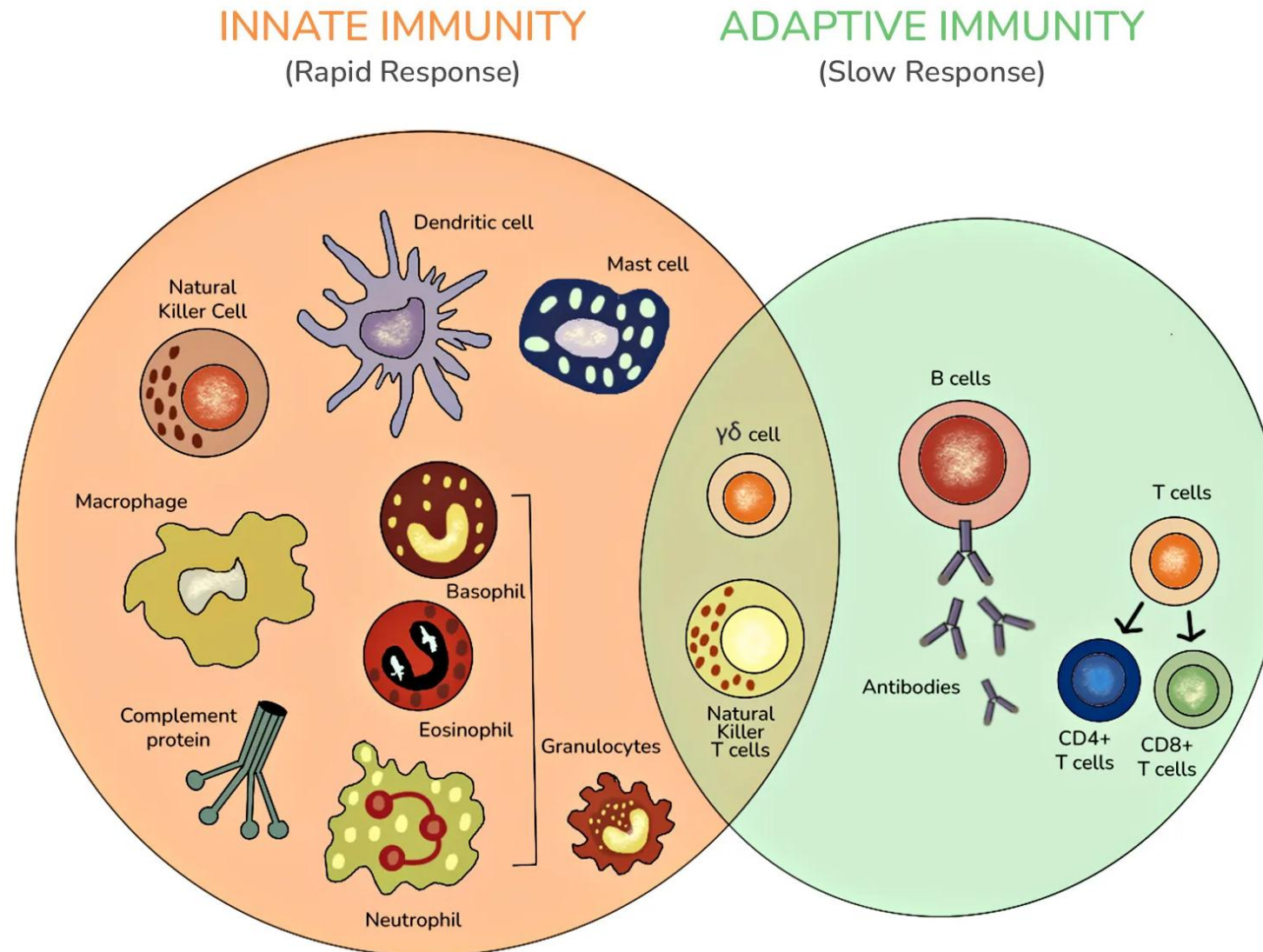
KEYNOTE-024: overall survival



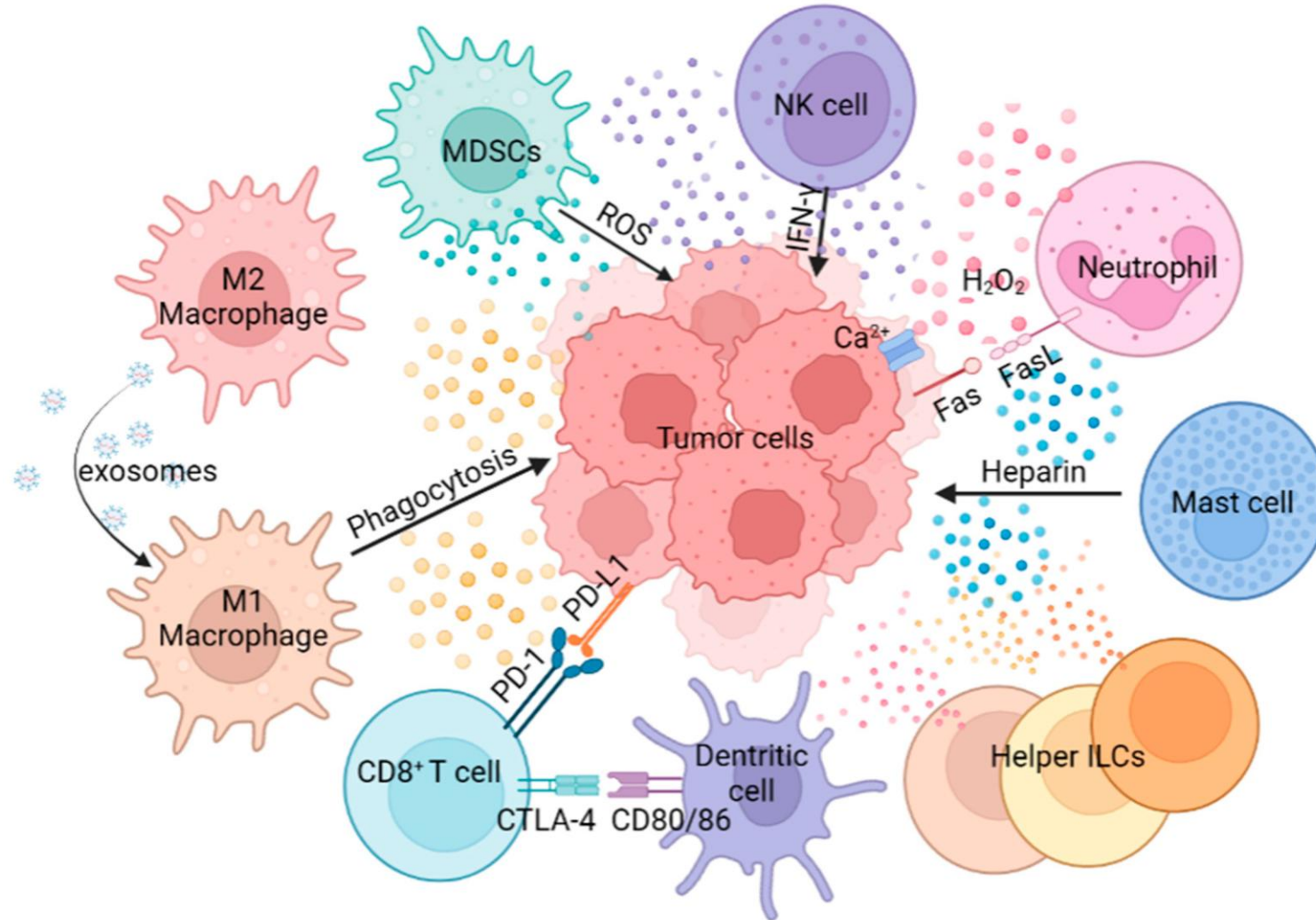
No. at risk:

Pembrolizumab	154	121	106	89	78	73	66	62	54	51	20	0	0
Chemotherapy	151	108	80	61	48	44	35	33	28	26	13	3	0

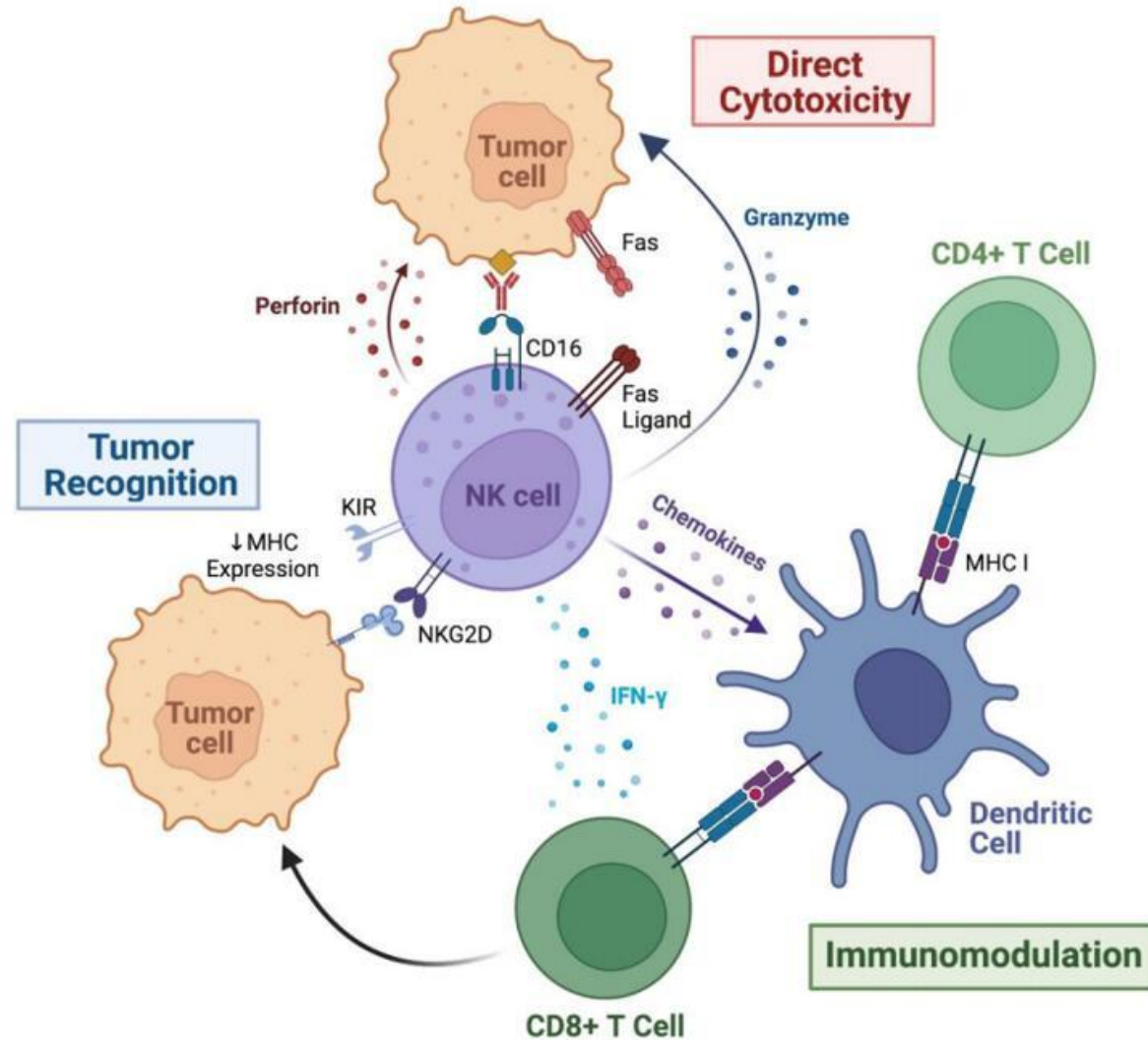
Innate & Adaptive Immunity



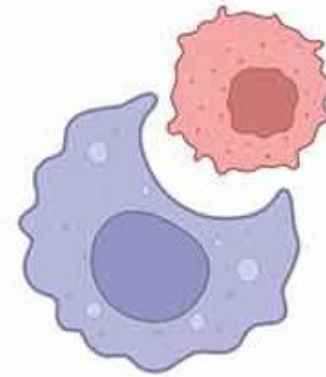
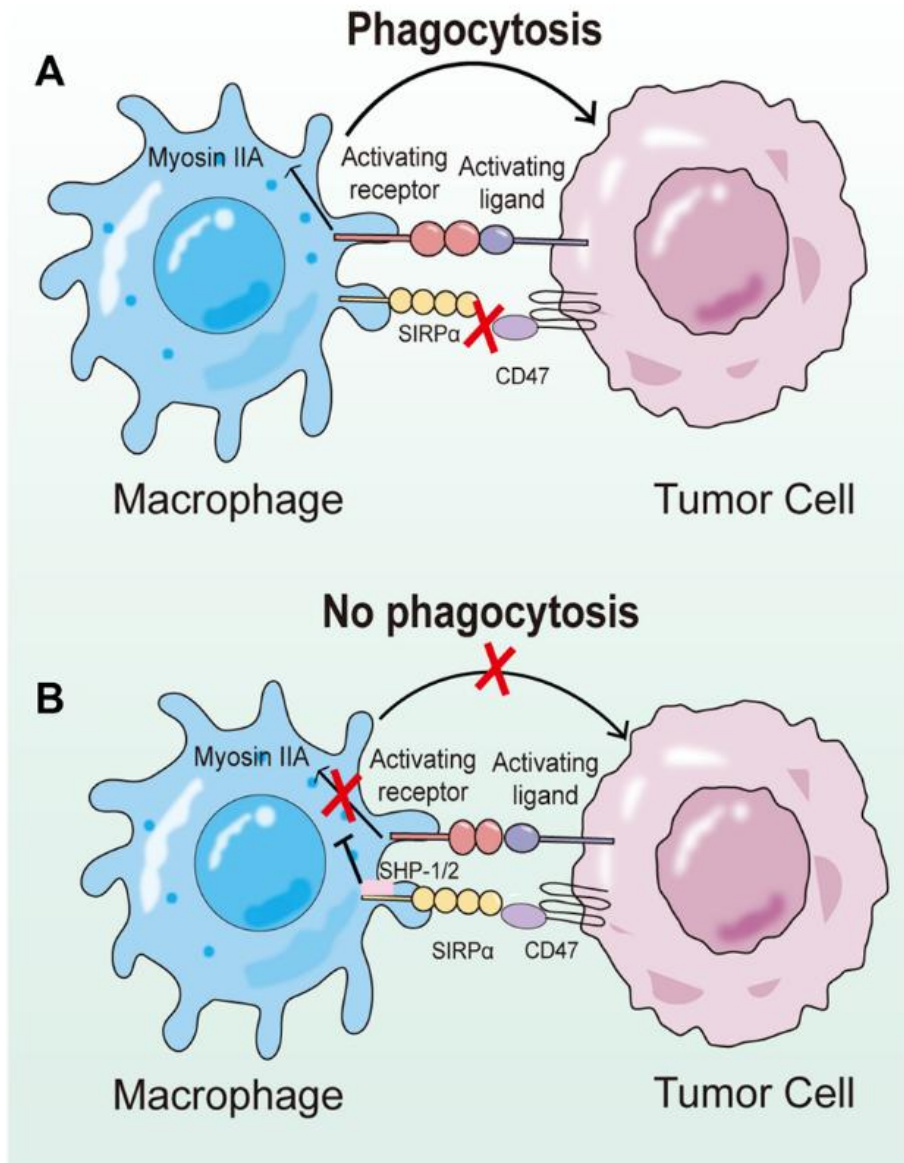
Innate Immunity



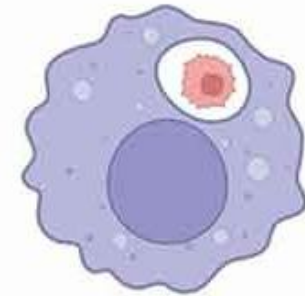
Innate Immunity: NK cell



Innate Immunity: Macrophage

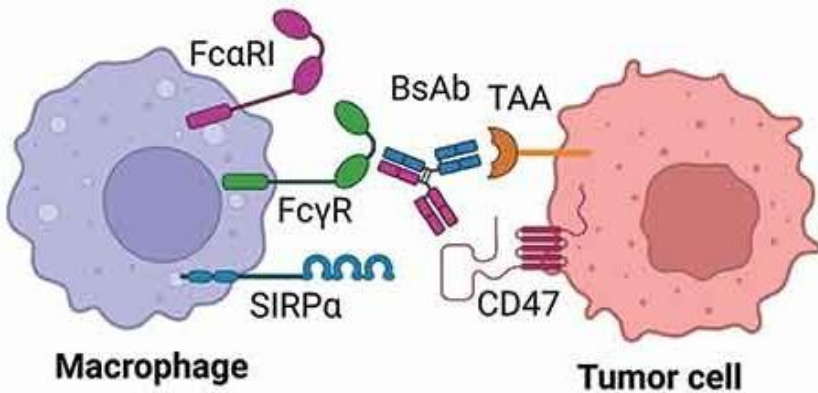
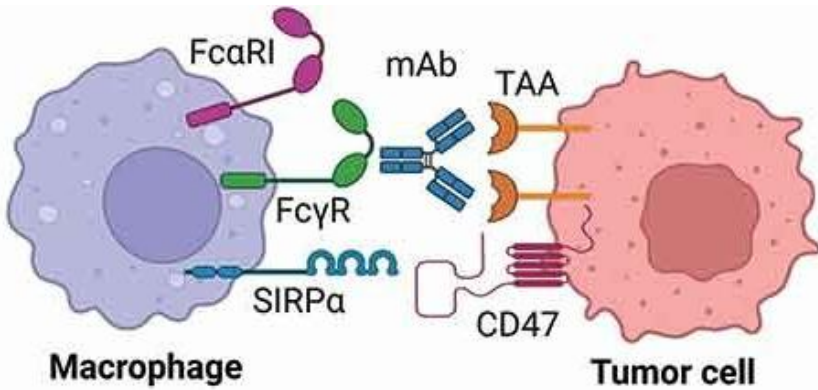


Macrophages engulf the antibody-opsonized tumor cells creating phagosomes

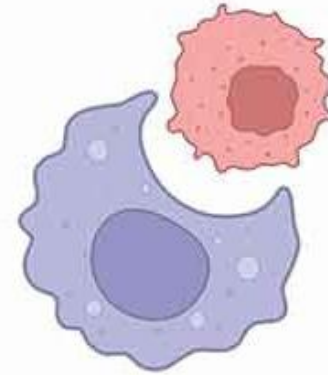


The phagosome fuses with lysosomes leading to acidification of the phagolysosome and degradation of the tumor cell

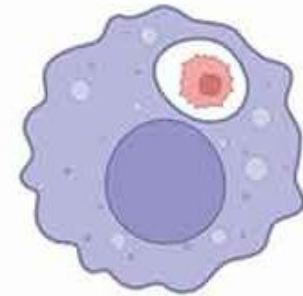
Innate Immunity: Macrophage



Linking of macrophages and tumor cells via antibodies

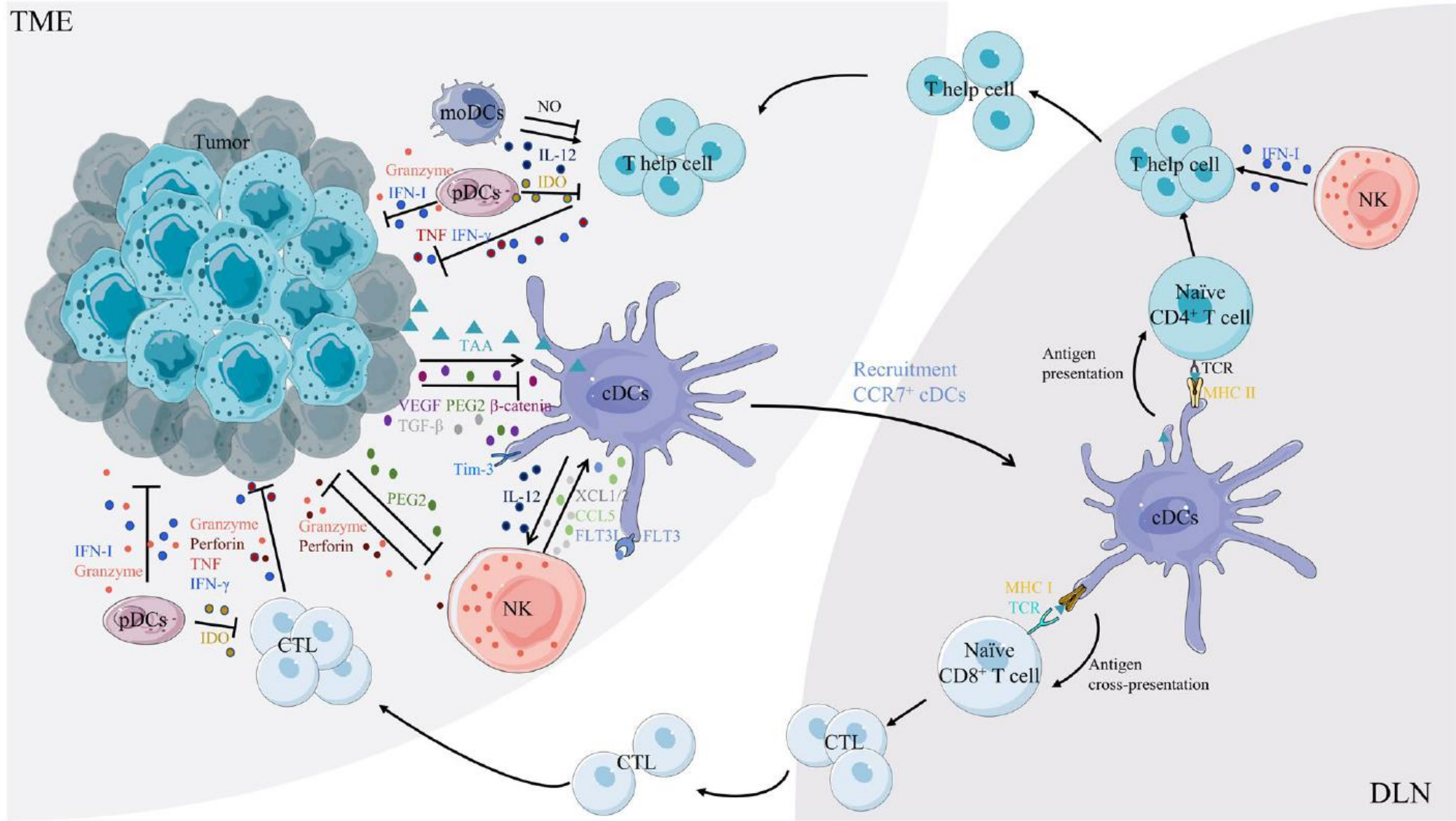


Macrophages engulf the antibody-opsonized tumor cells creating phagosomes



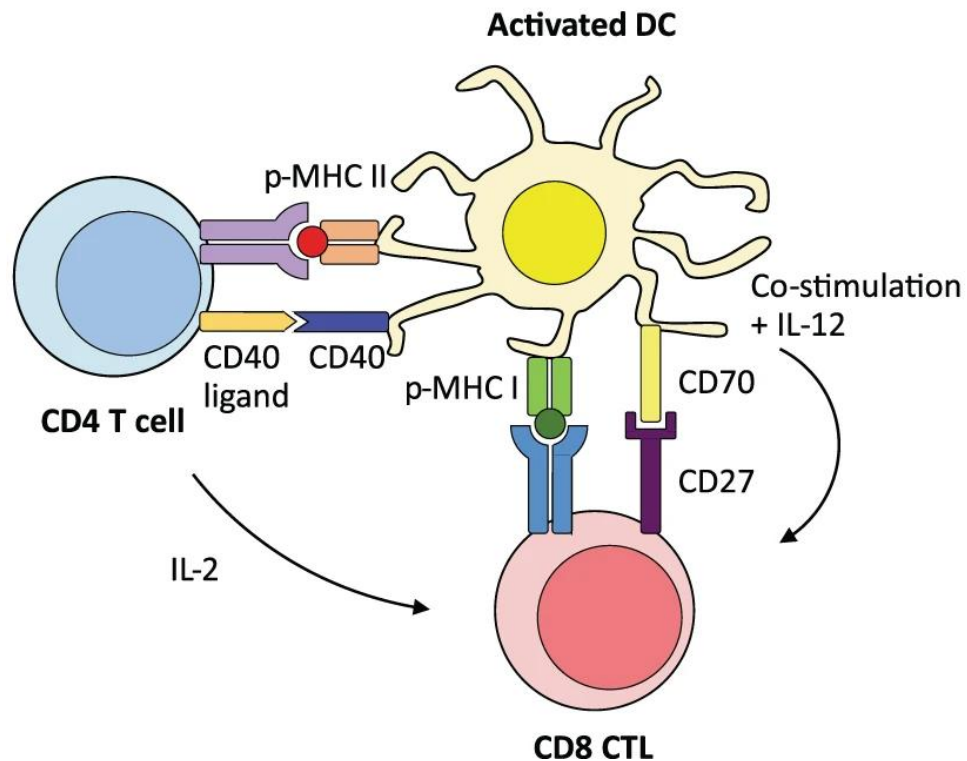
The phagosome fuses with lysosomes leading to acidification of the phagolysosome and degradation of the tumor cell

Antigen Presentation & T-cell Activation

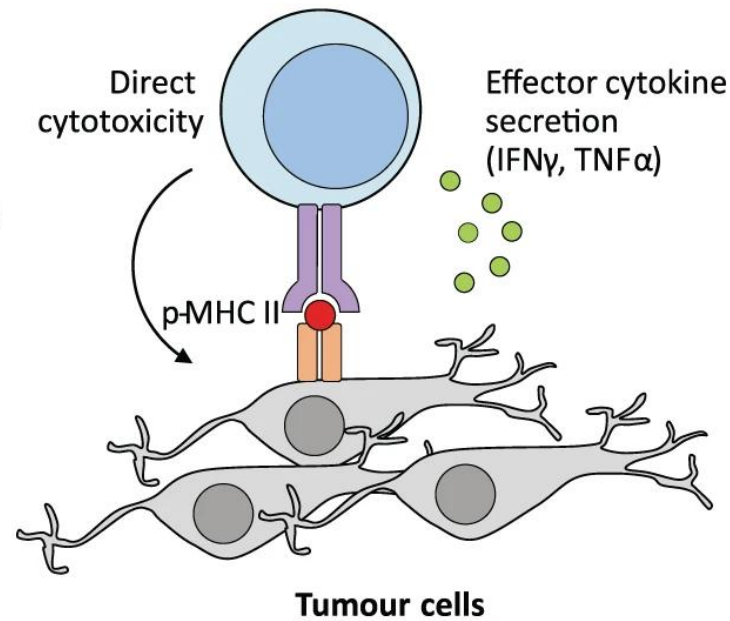


Adaptive Immunity: Helper T-cell

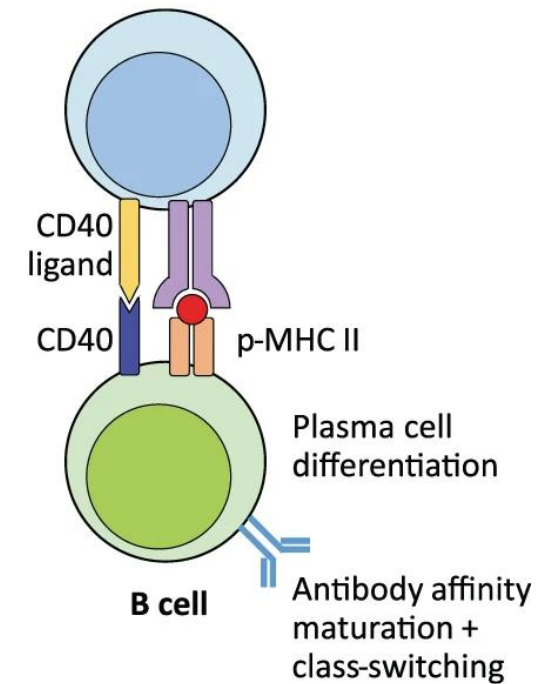
a. Help for CD8 CTLs



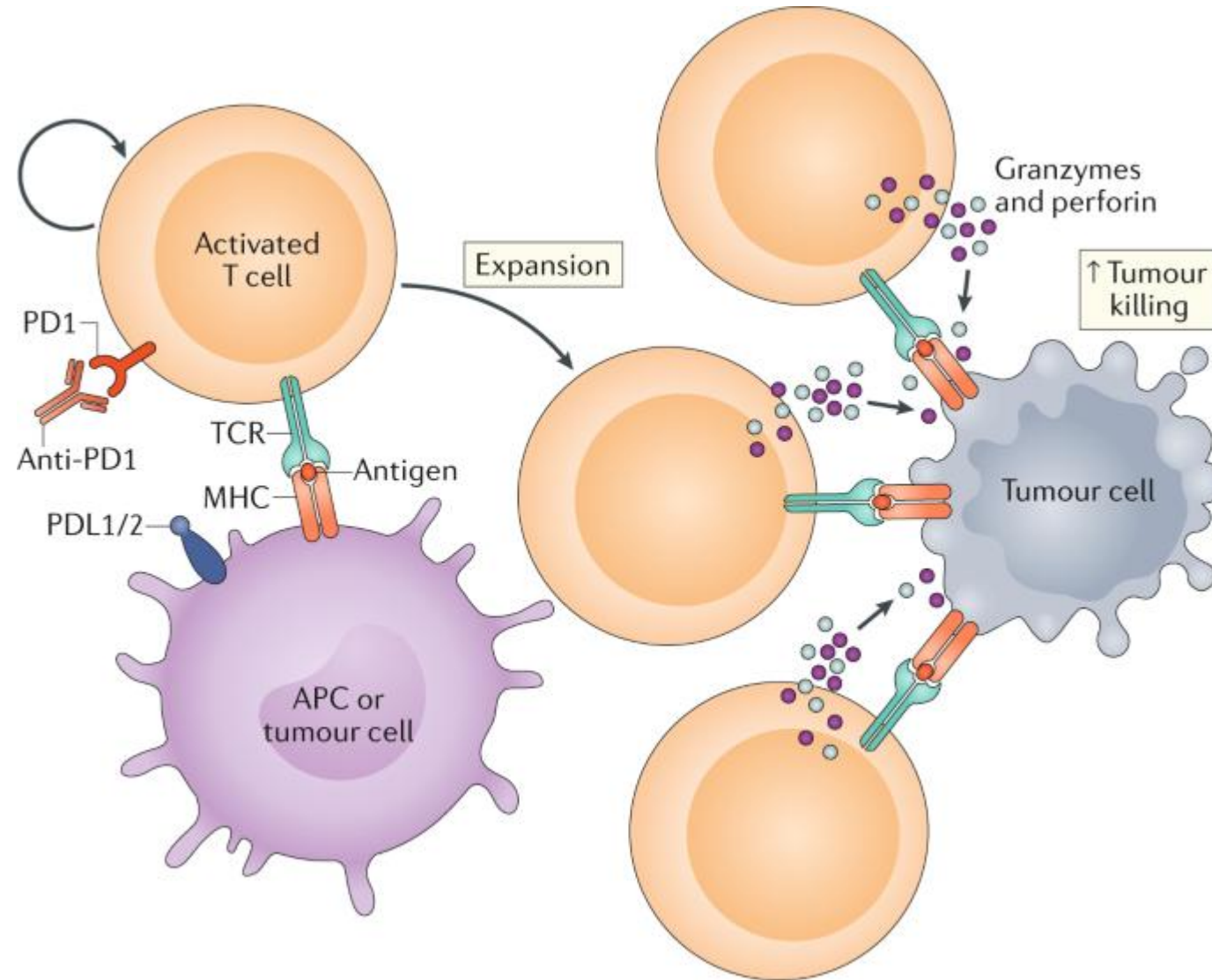
b. Direct anti-tumour activity



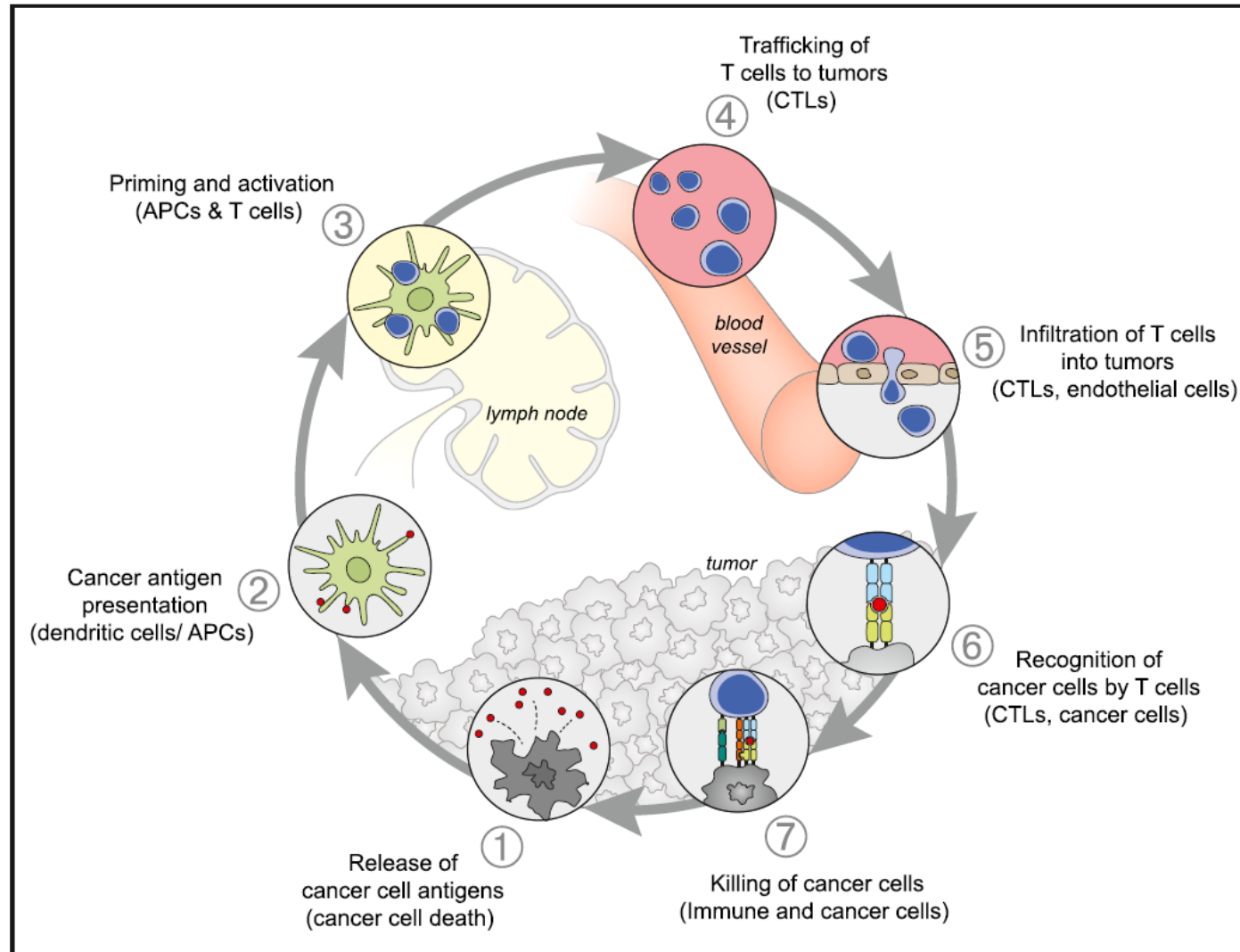
c. Help for B cells producing antibodies



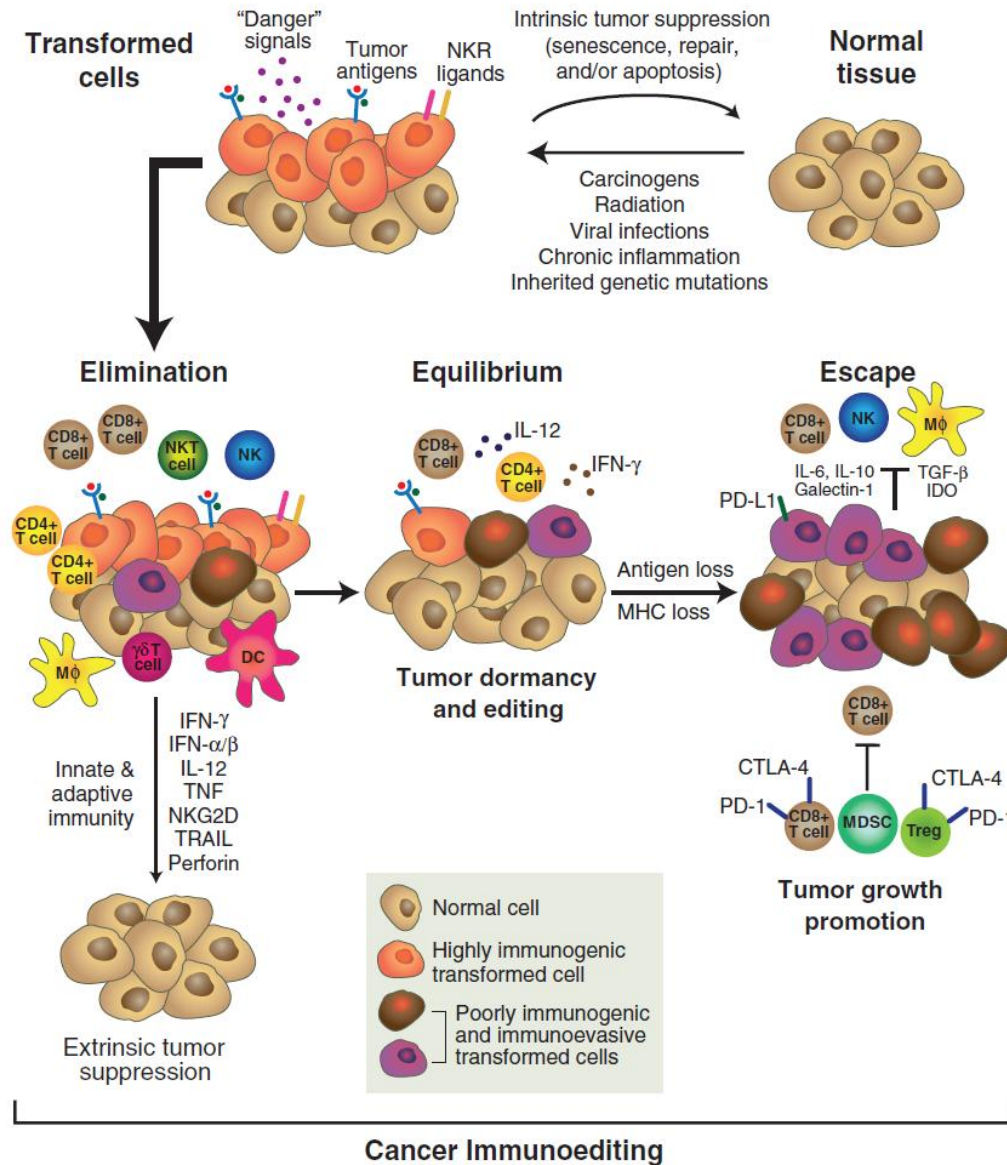
Adaptive Immunity: Cytotoxic T-cell



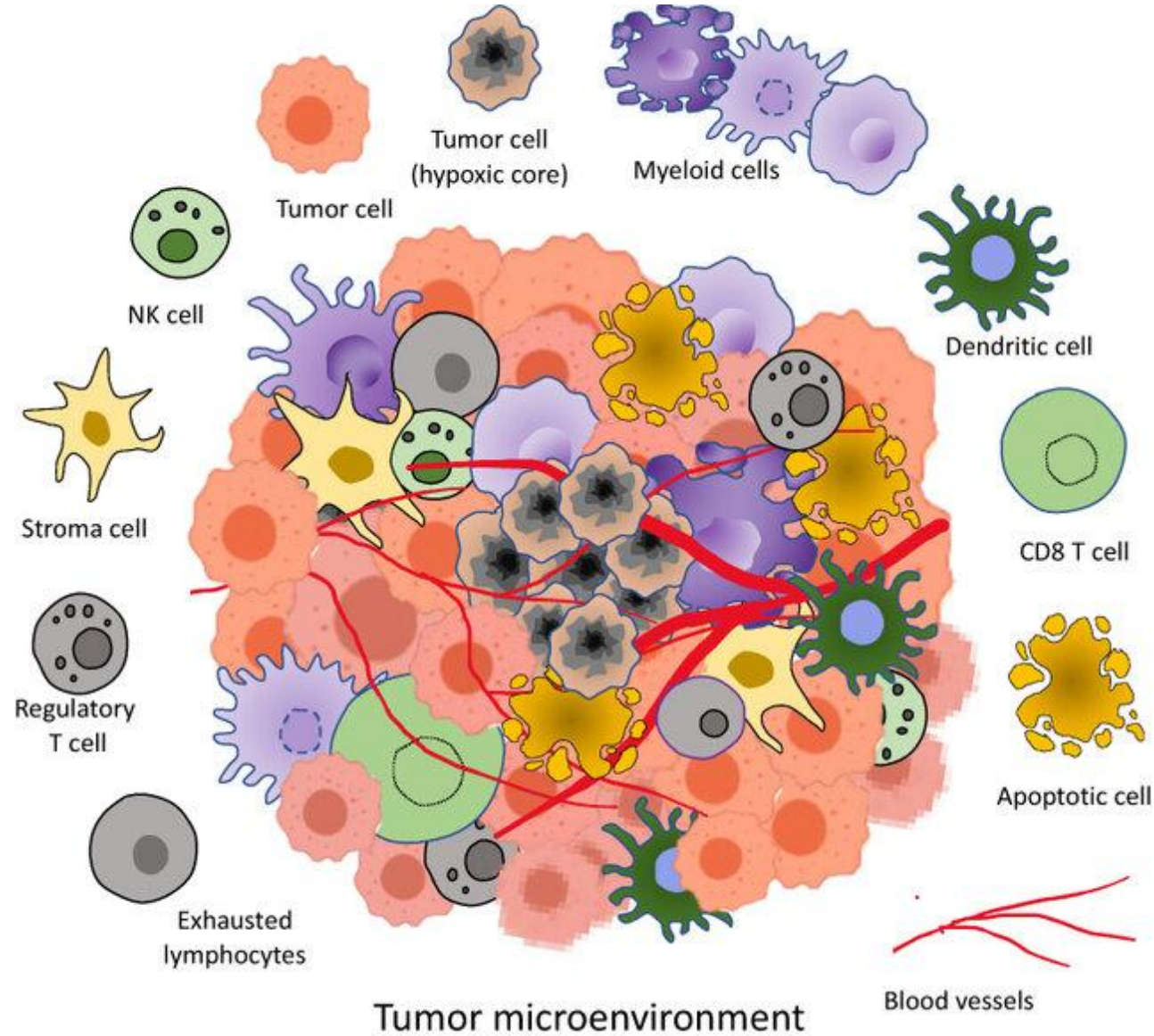
Cancer-Immunity Cycle



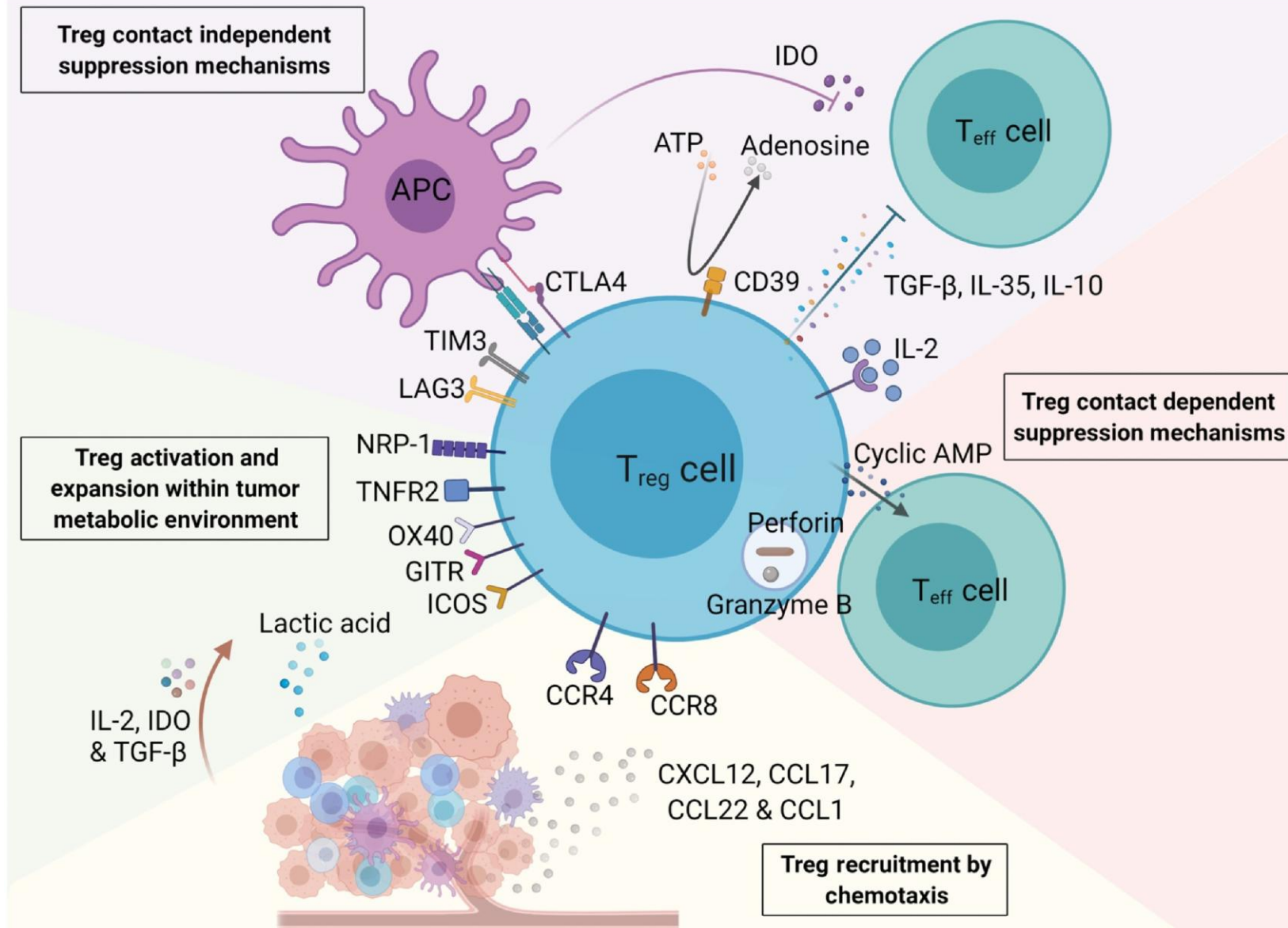
Immune Surveillance & Immunoediting



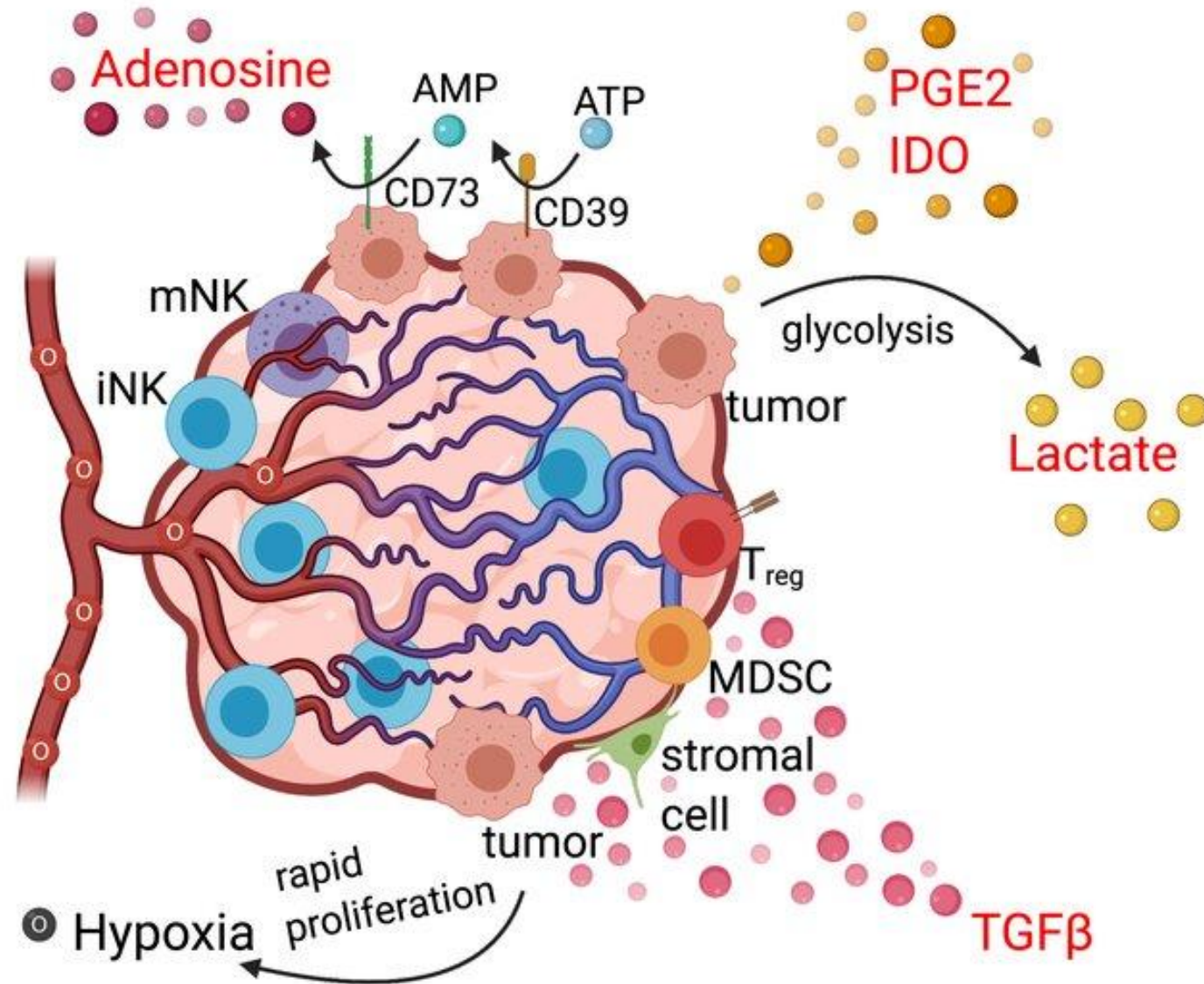
Tumor Micro-environment (TME) Landscape



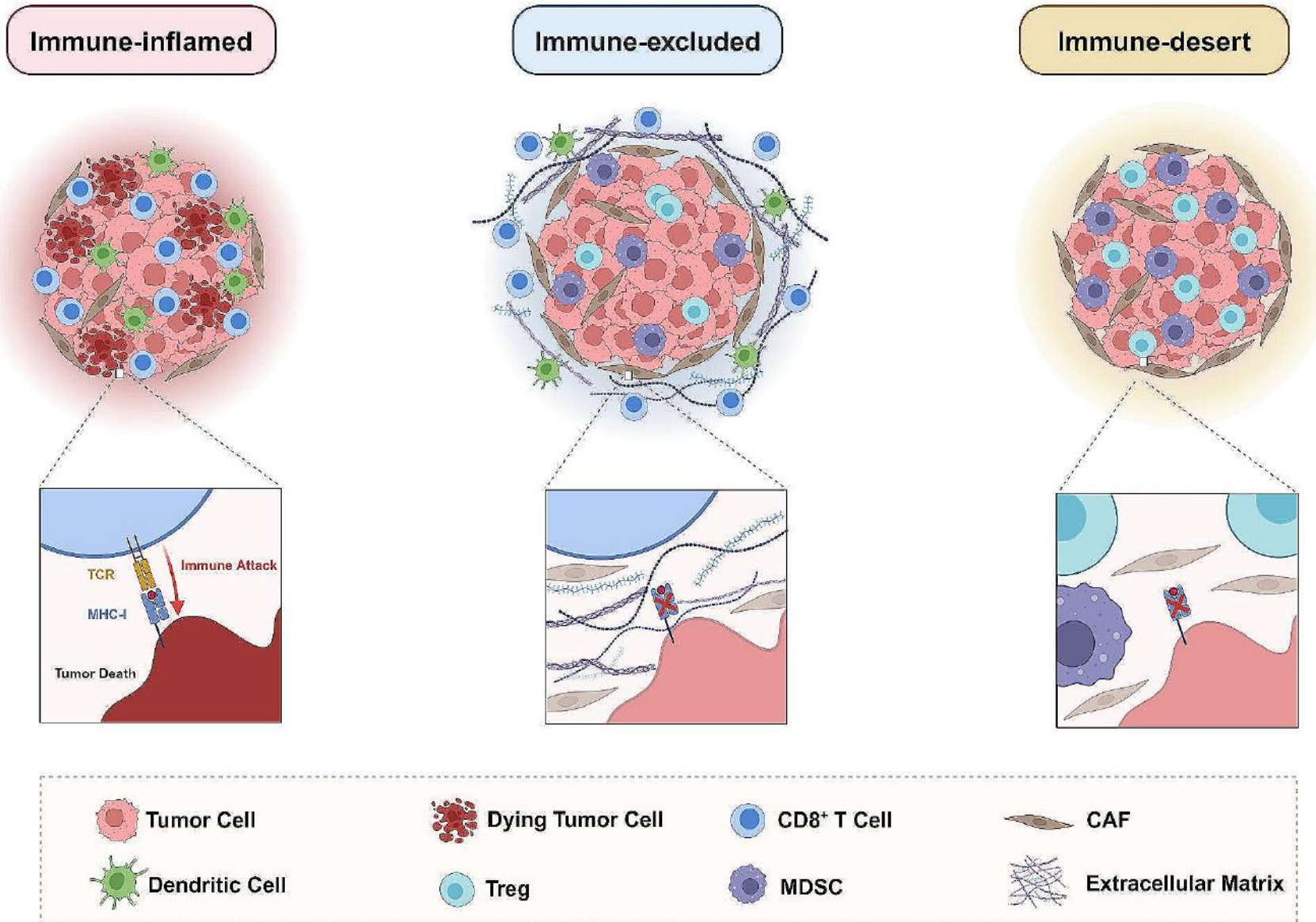
Regulatory T cell



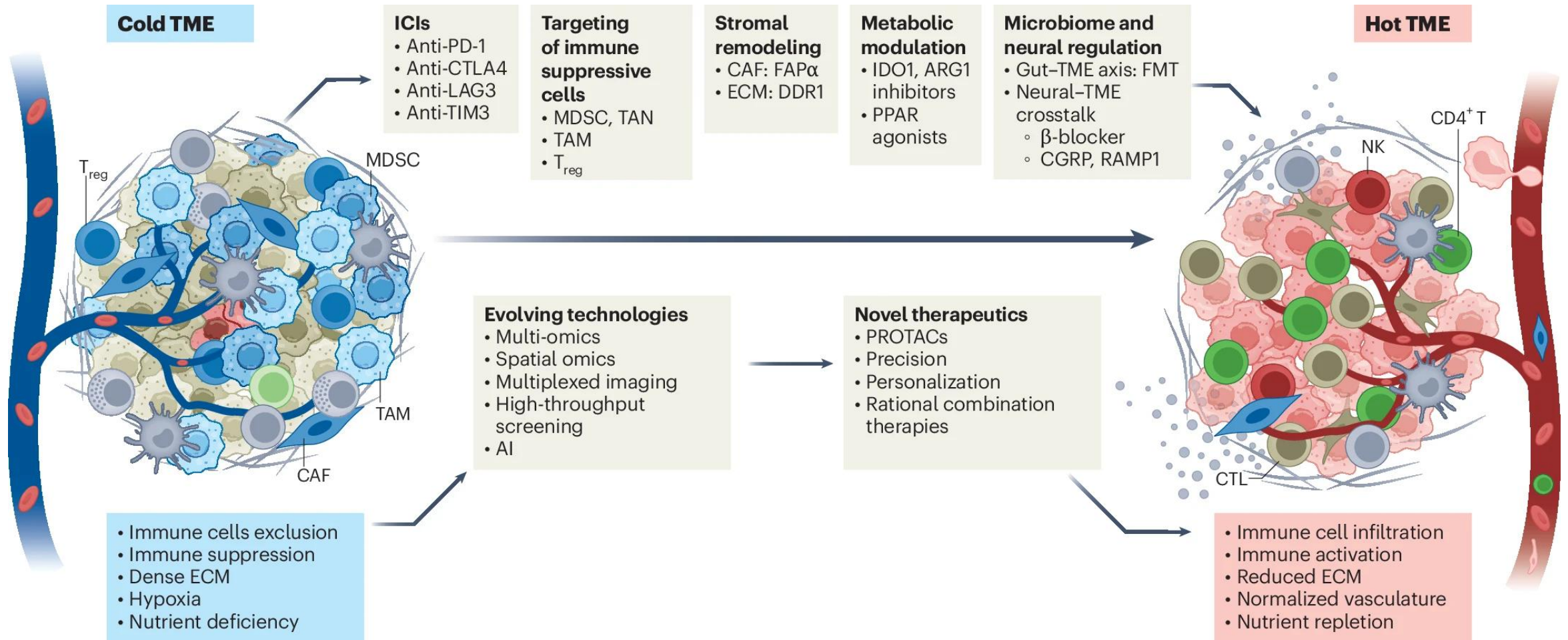
TME Suppressive Network



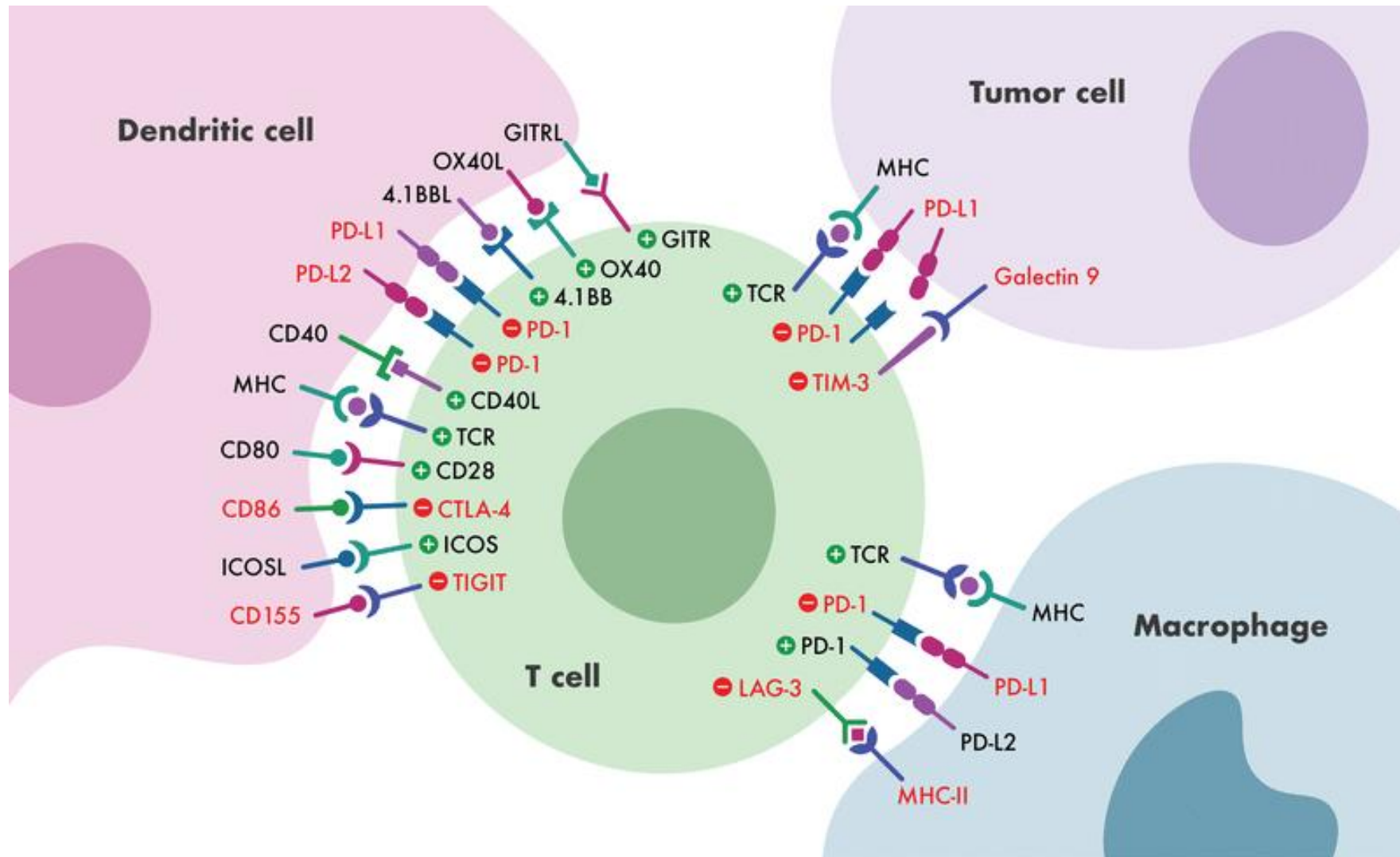
Hot vs Cold Tumor & Warm-up Strategies



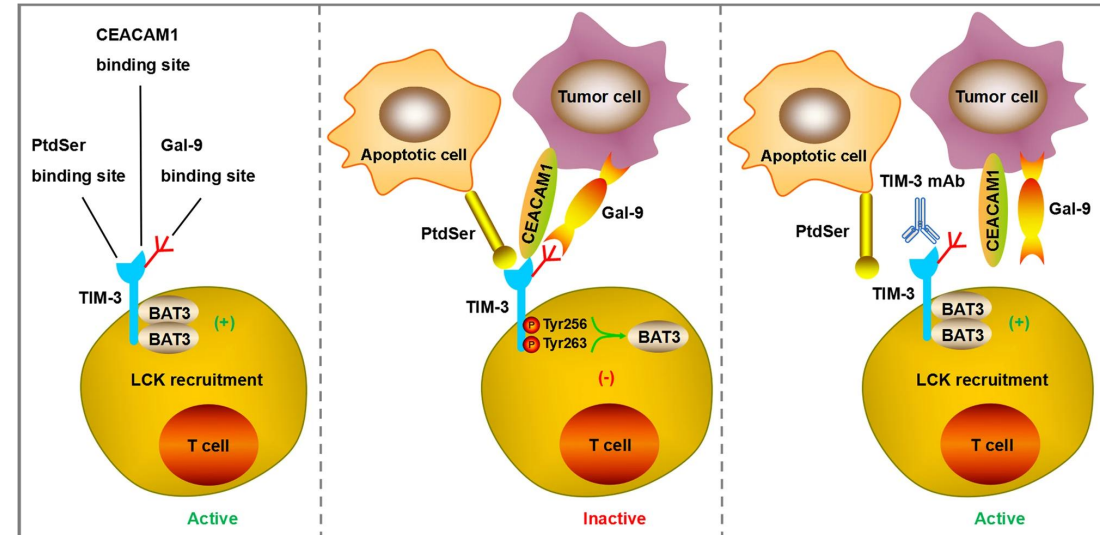
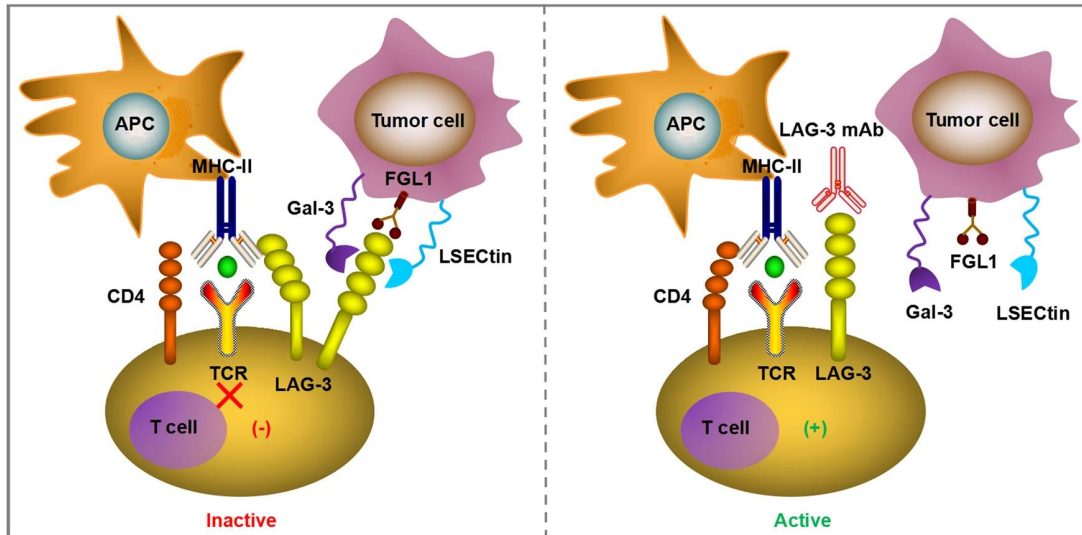
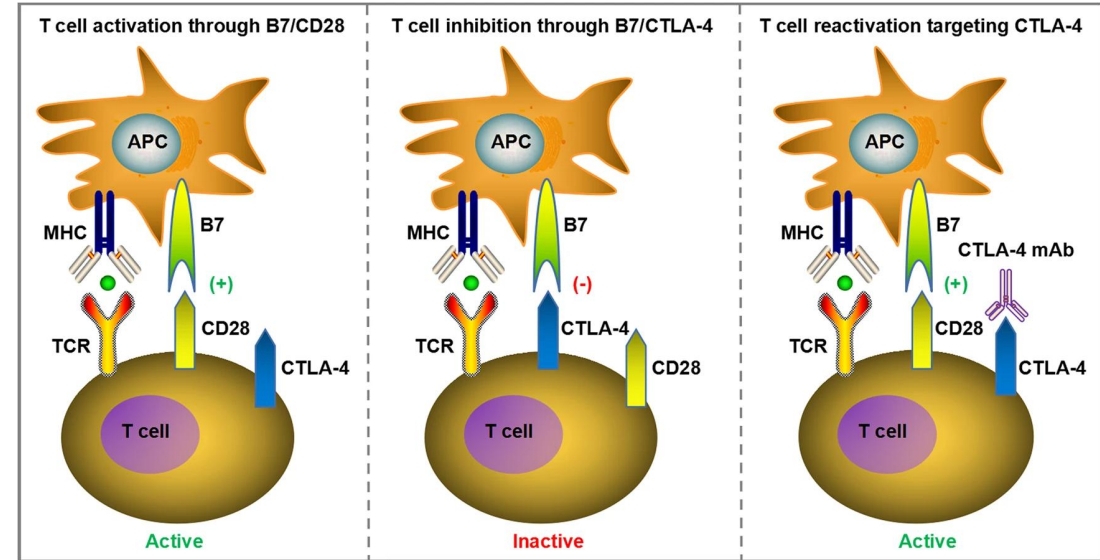
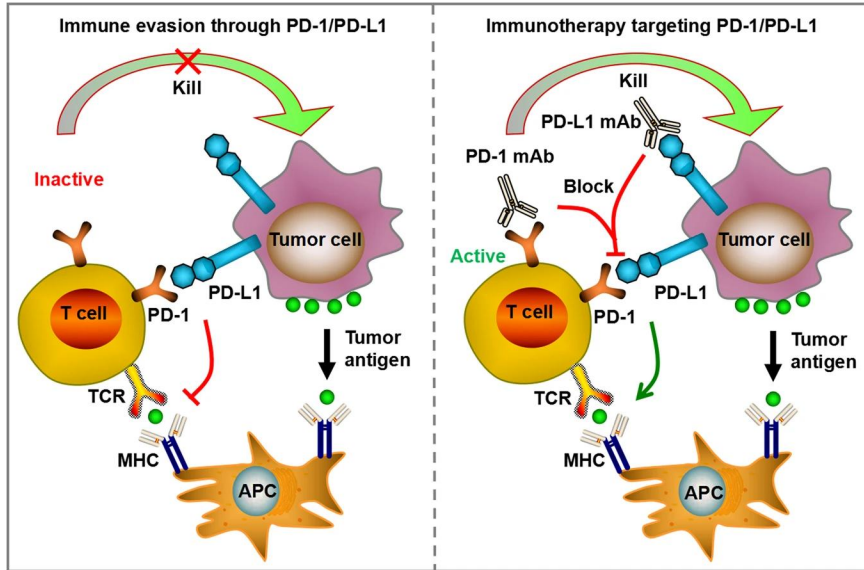
Hot vs Cold Tumor & Warm-up Strategies



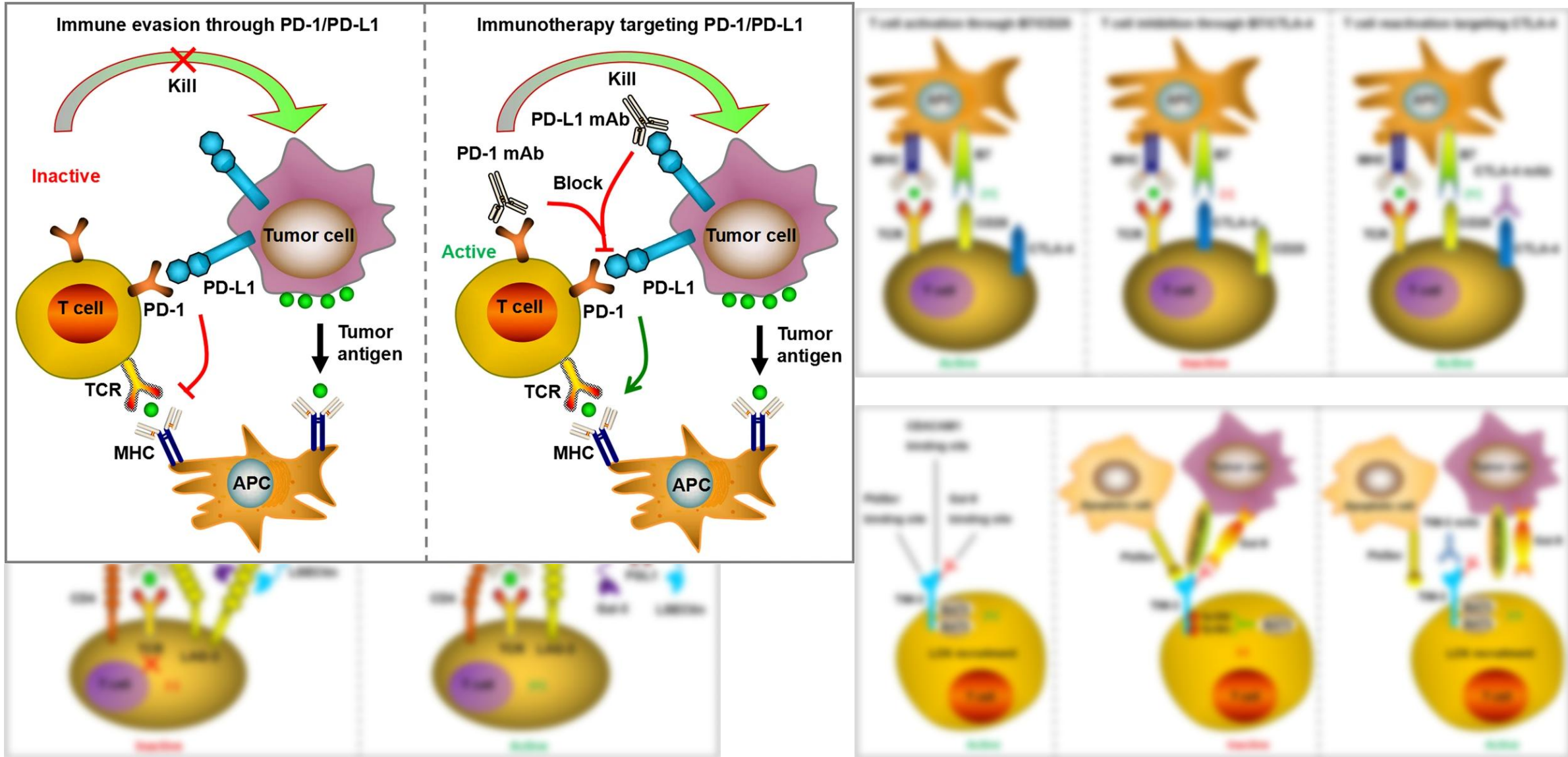
Immune Checkpoints & Evasion Spectrum



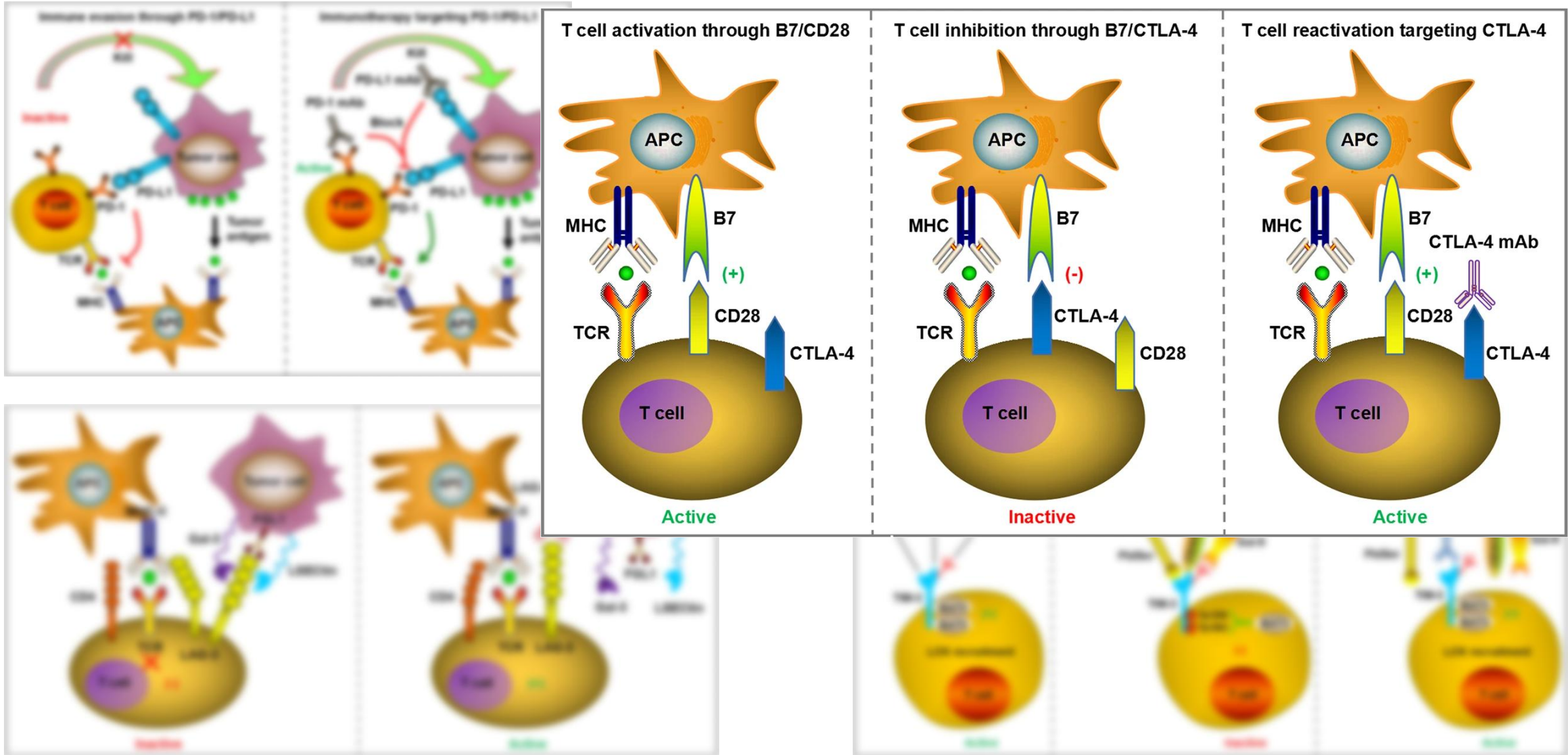
Immune Checkpoint Blockade Mechanism



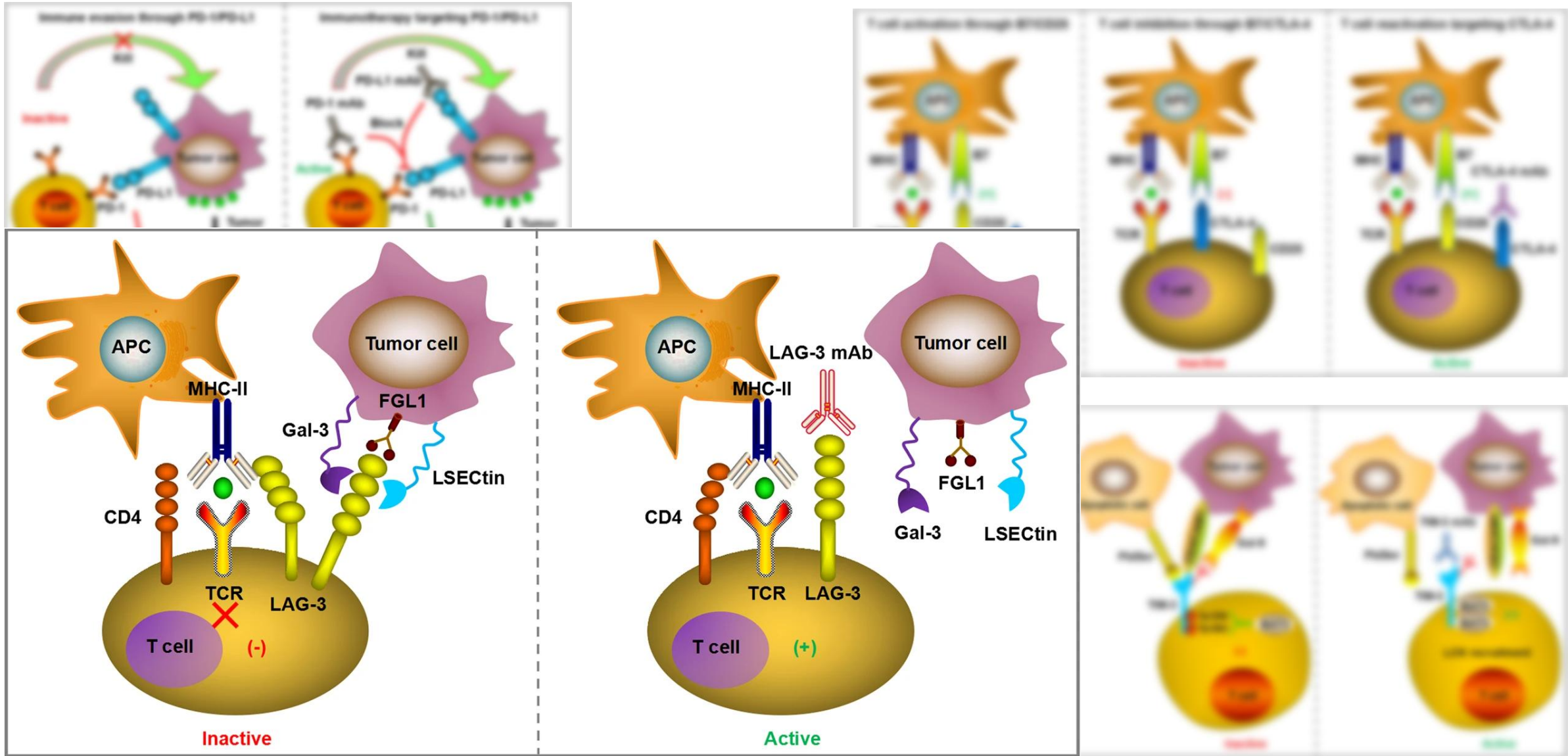
Immune Checkpoint Blockade Mechanism



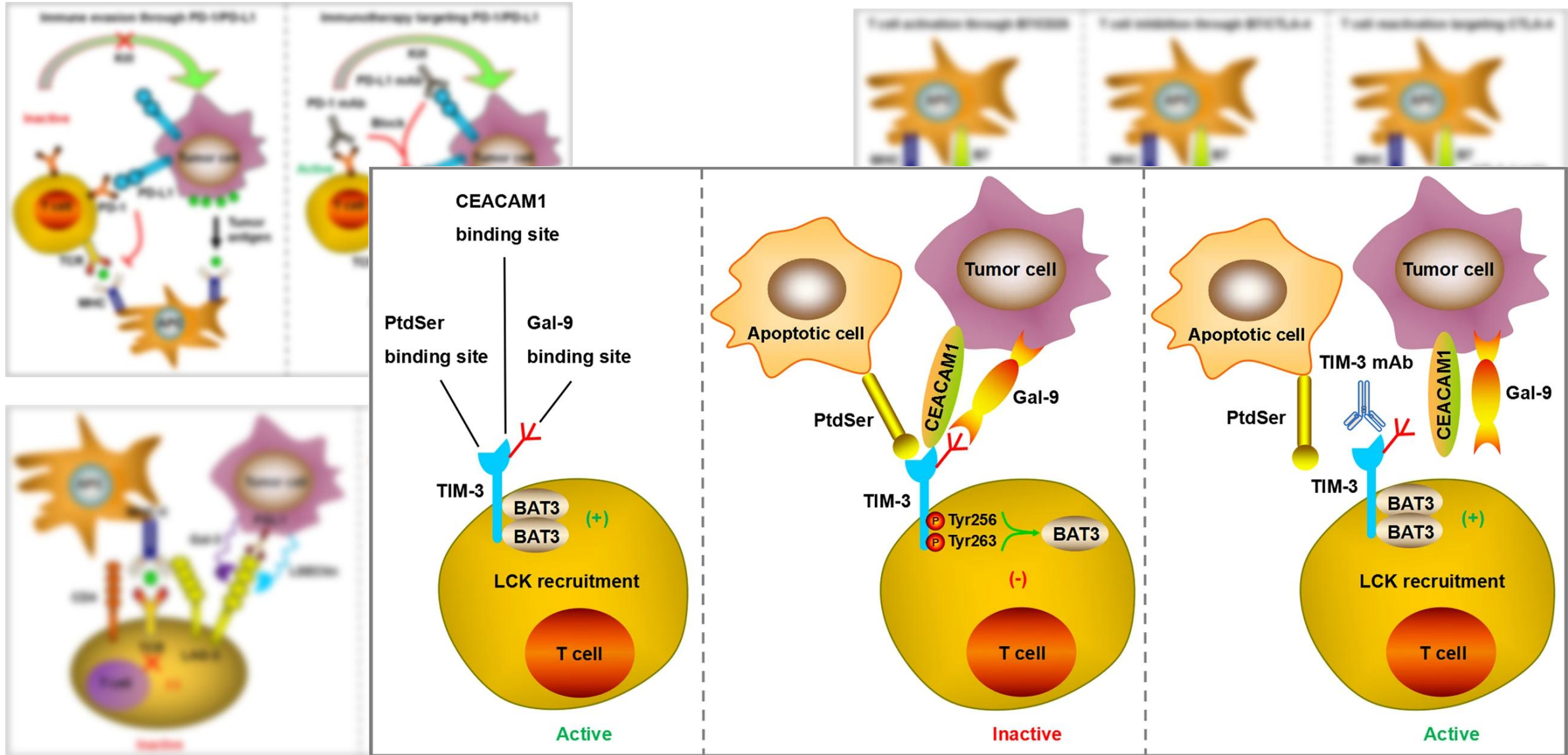
Immune Checkpoint Blockade Mechanism



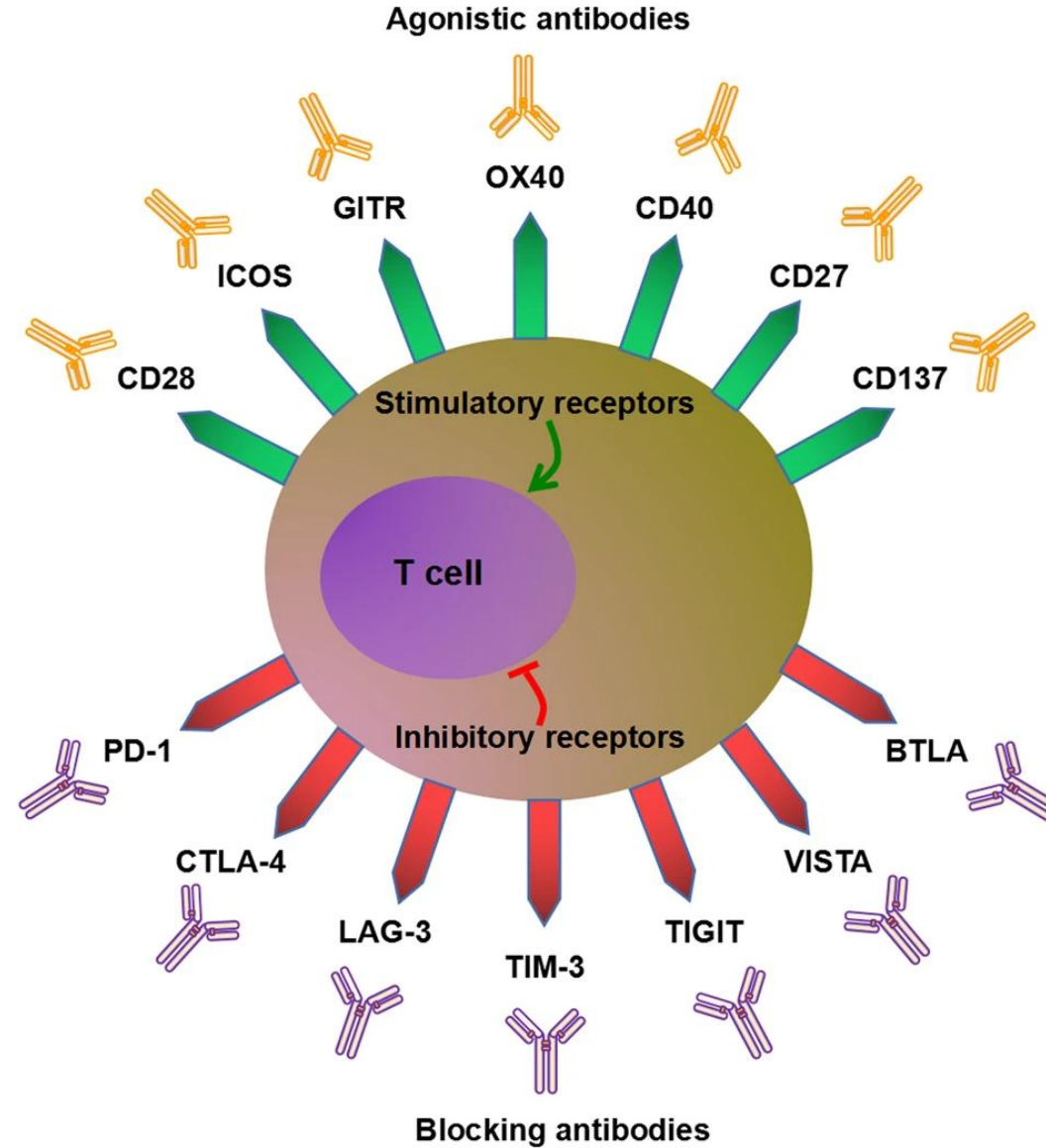
Immune Checkpoint Blockade Mechanism



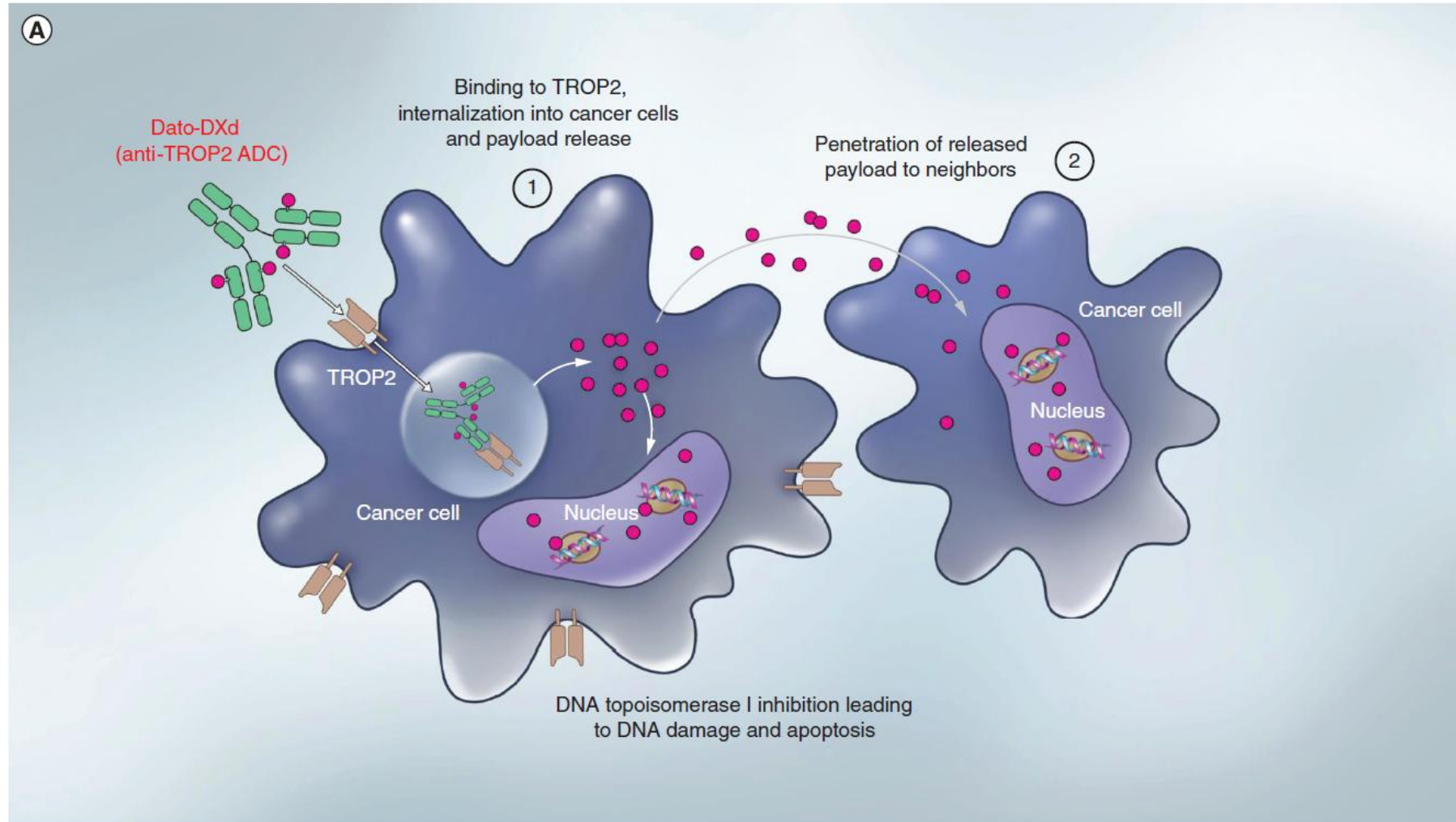
Immune Checkpoint Blockade Mechanism



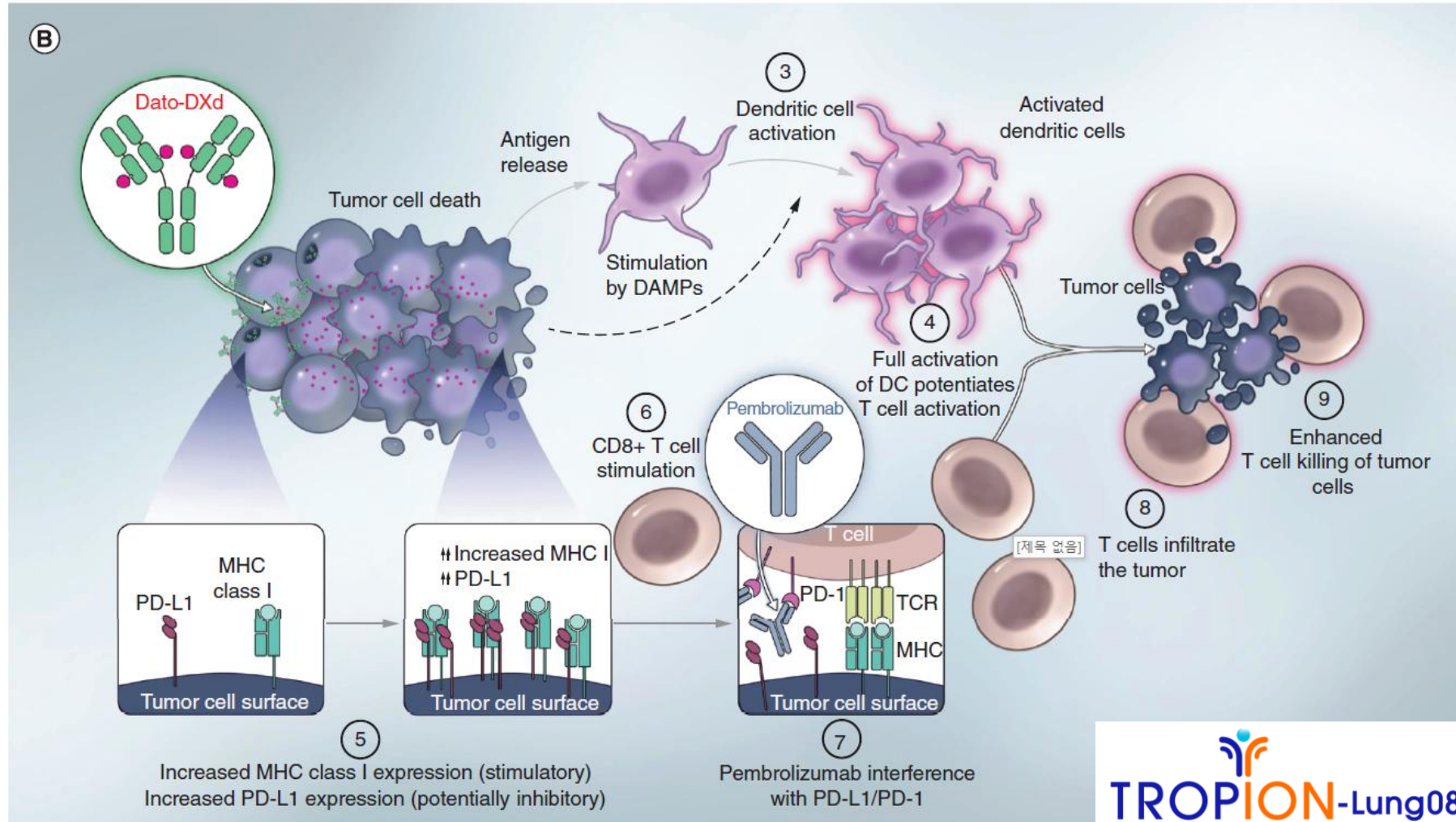
Immune Checkpoint Blockade Mechanism



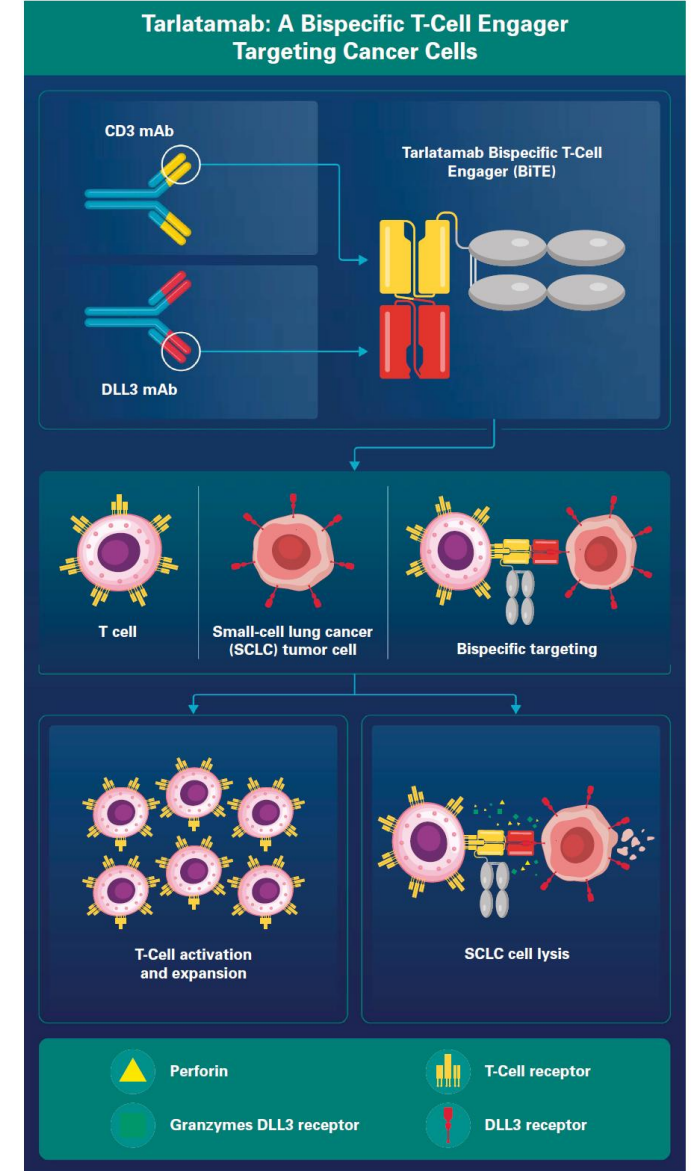
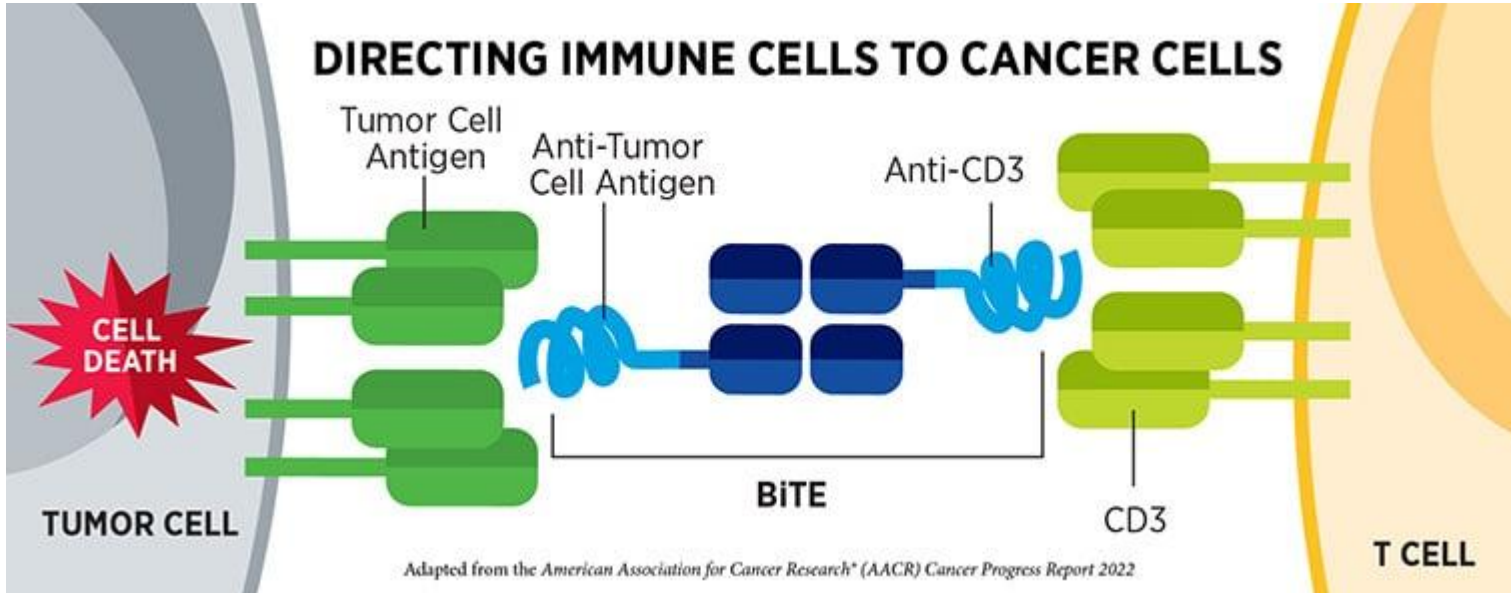
ADC (Antibody-Drug Conjugate)



ADC (Antibody-Drug Conjugate)



BiTE (Bispecific T-cell Engager)



Summary

- Lung cancers often have a high mutational burden, generating many neoantigens that can be recognized by the immune system.
- Immune checkpoint inhibitor doubled OS in PD-L1 high NSCLC, establishing immunity as a central treatment strategy.
- Innate immunity plays a crucial role in the lung cancer development and its progression.
- T-cell priming is the process where antigen-presenting cells (APCs) activate naive T cells, initiating an adaptive immune response.
- Tumors progress from elimination to equilibrium to immune escape by sequentially blocking the seven-step immune cycle.
- Suppressive cells and metabolic barriers dictate “hot” vs “cold” phenotypes and predict ICI efficacy.
- Layered brakes ranging from CTLA-4 and PD-1 to LAG-3, TIGIT, and TIM-3 explain both primary and acquired resistance.
- Standard ICIs, TME-directed agents and emerging platforms such as ADCs and BiTEs enable rational “warm-up” combinations.



Thank you for your attention