

Johns Hopkins Engineering

Immunoengineering

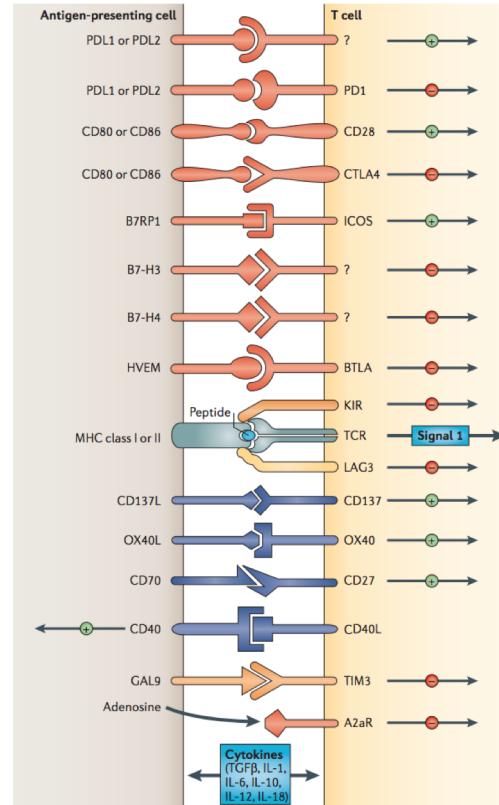
Immunoengineering Cancer: Antibody Therapies



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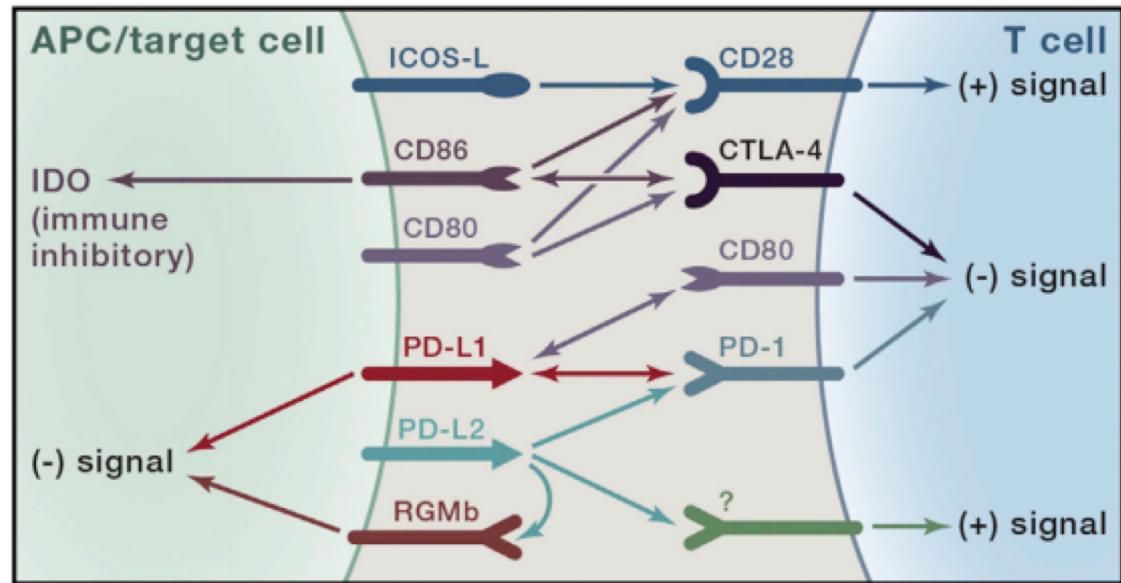
Various Interactions Regulate T cell responses

- Many ligand-receptor interactions between T cells and APCs regulate T cell response in a co-stimulatory or inhibitory manner
- Inhibitory receptors can be blocked with antagonistic antibodies
- Costimulatory receptors can be stimulated with agonist antibodies



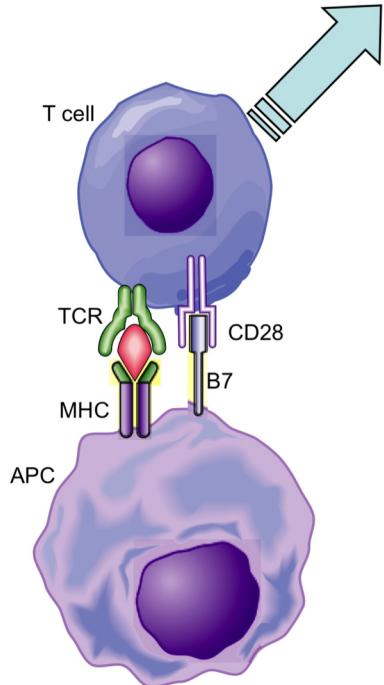
Immune Checkpoint Blockade

- Most successful therapies: anti-PD-1, anti-PD-L1, anti-CTLA4
- Others being explored: TIM-3, LAG-3, BTLA, etc.

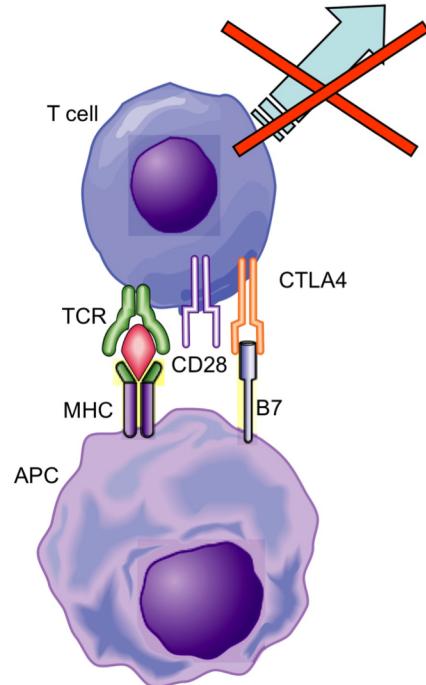


CTLA-4 Blockade

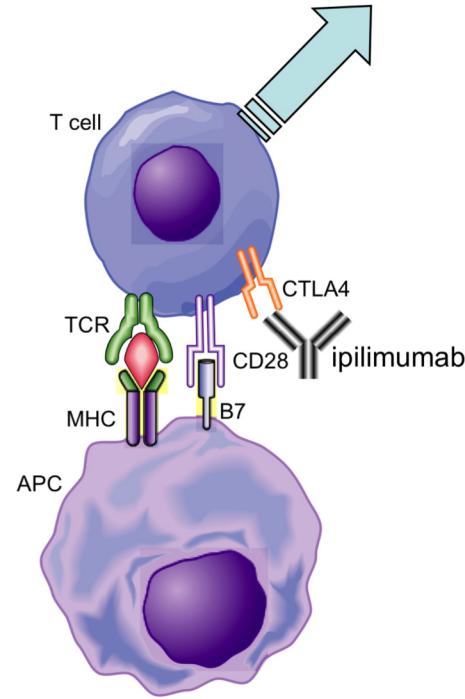
Co-stimulation via CD28:
T-cell activation



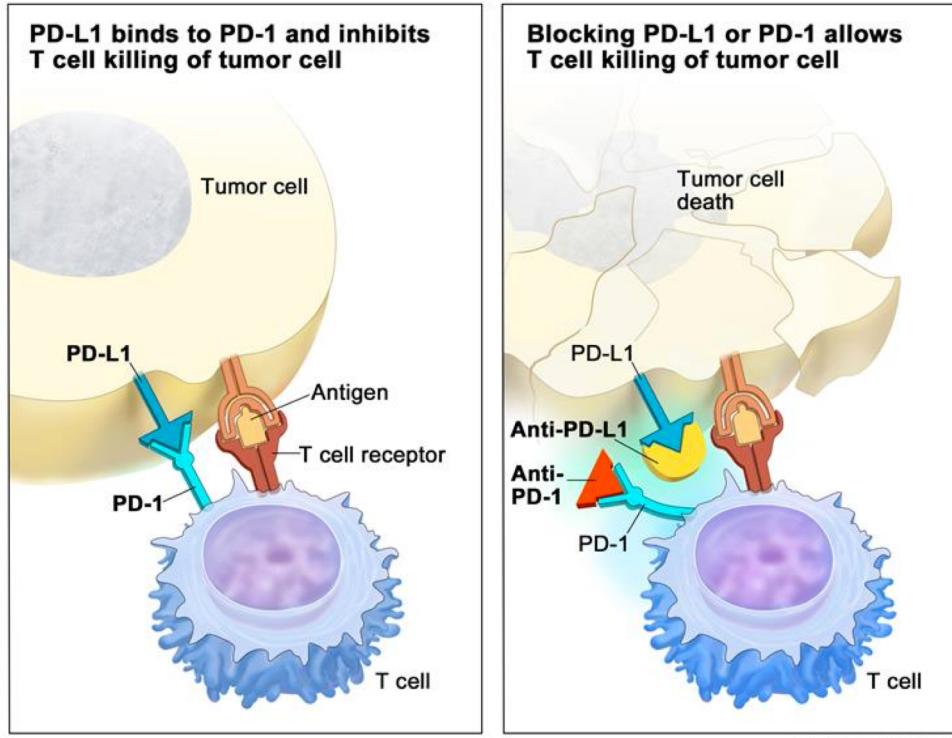
CTLA-4 blocks co-stimulation:
No T-cell activation



Ipilimumab blocks CTLA-4:
T-cell activation

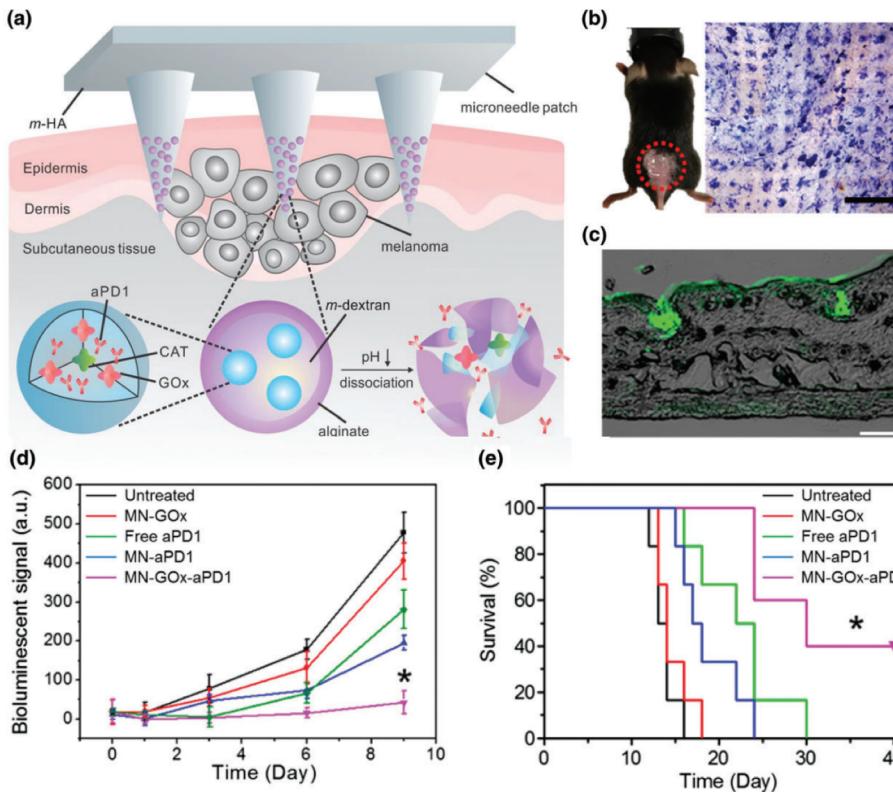


PD-1/PD-L1 Blockade



- FDA approved for several cancer types
- Off-target effects
- Not effective in all cases

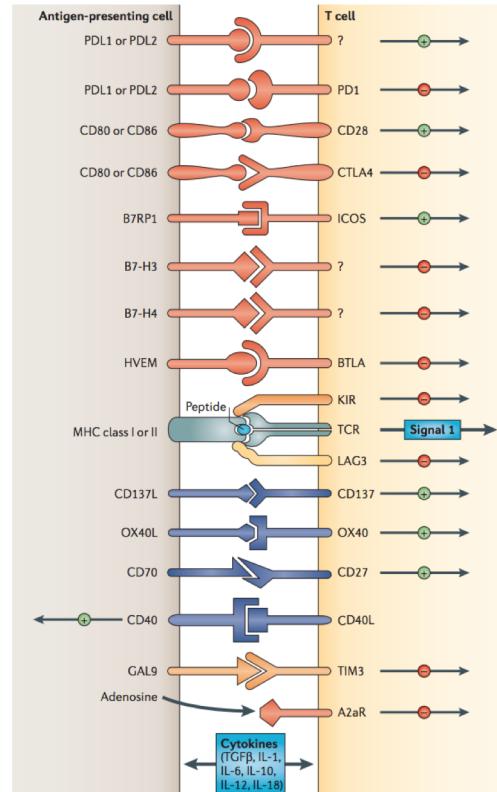
Local Delivery of Checkpoint Inhibitors



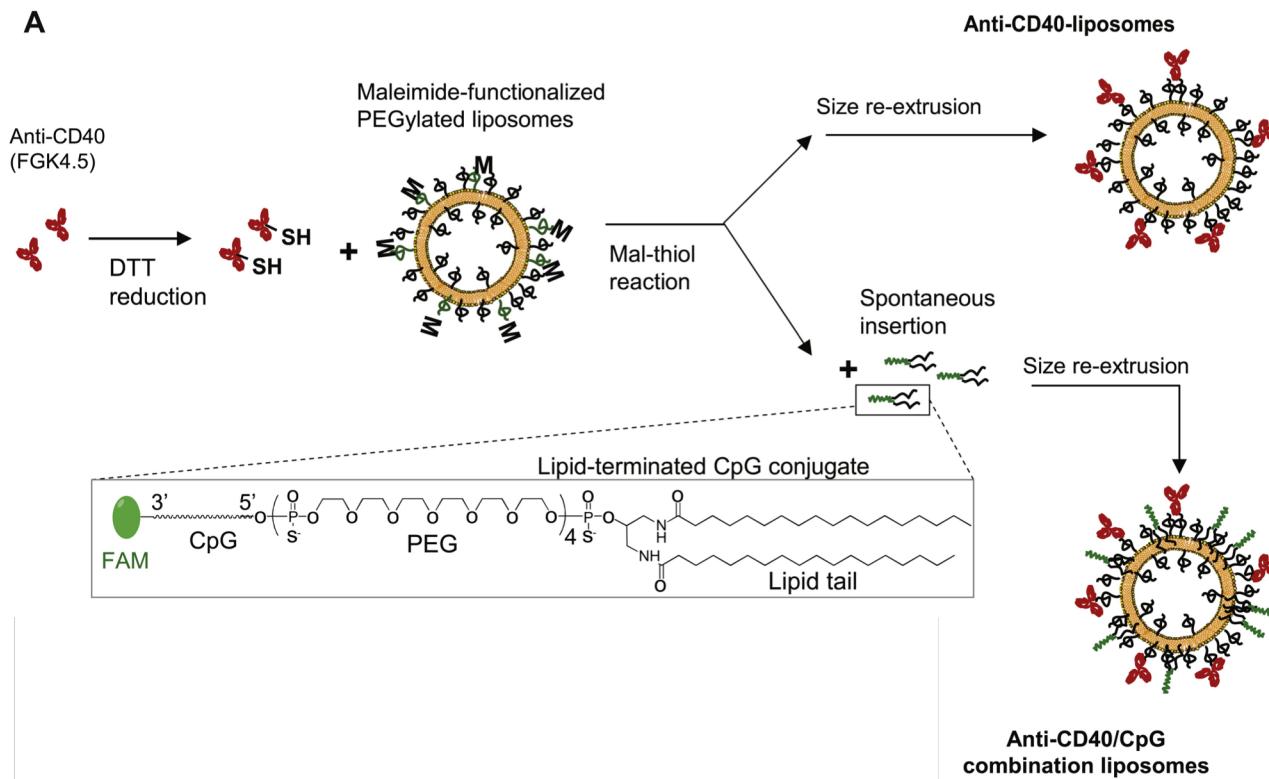
Wang et al. "Enhanced cancer immunotherapy by microneedle patch-assisted delivery of anti-PD1 antibody". *Nano Letters*, 16 (2016): 2334-2340.

Immunostimulatory Antibodies

- Agonist antibodies
- Provide costimulatory signals to prime APCs to activate T cells
- Serious side effects with systemic administration
- Examples: anti-CD40, anti-4-1BB, anti-OX40



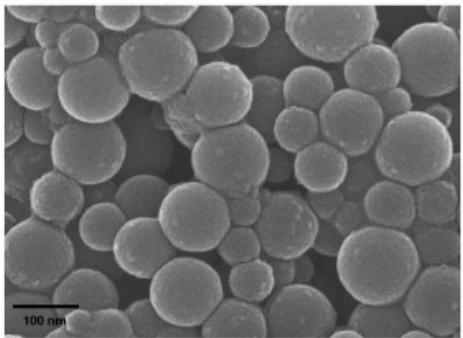
Local Delivery of anti-CD40



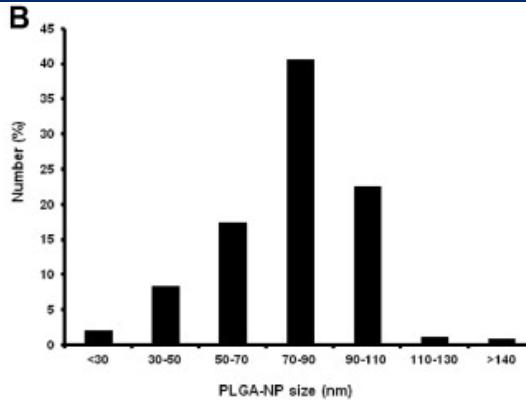
Kwong et al. "Induction of potent anti-tumor responses while eliminating systemic side effects via liposome-anchored combinatorial immunotherapy". *Biomaterials*, 32(22), (2011): 5134-5147

Anti-OX40 Delivery

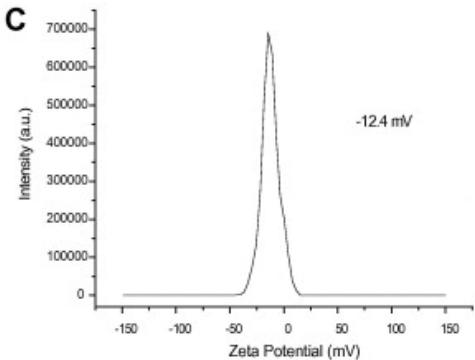
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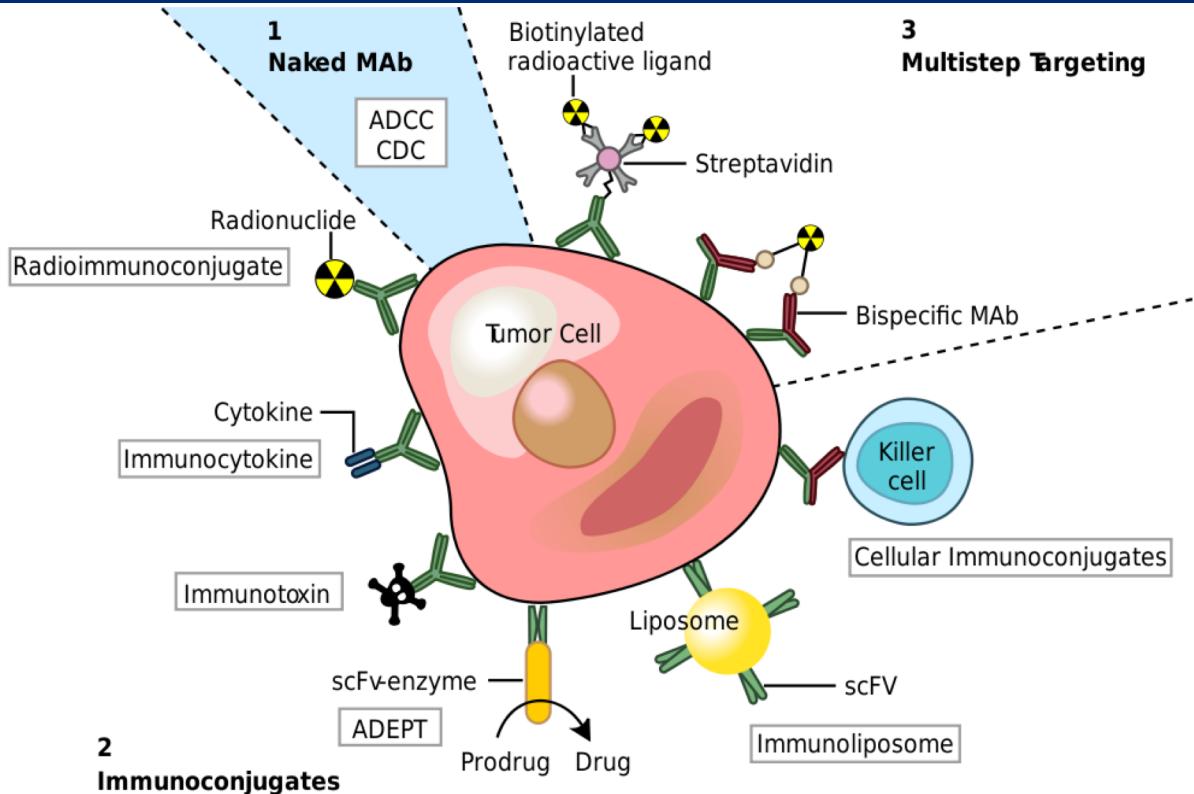
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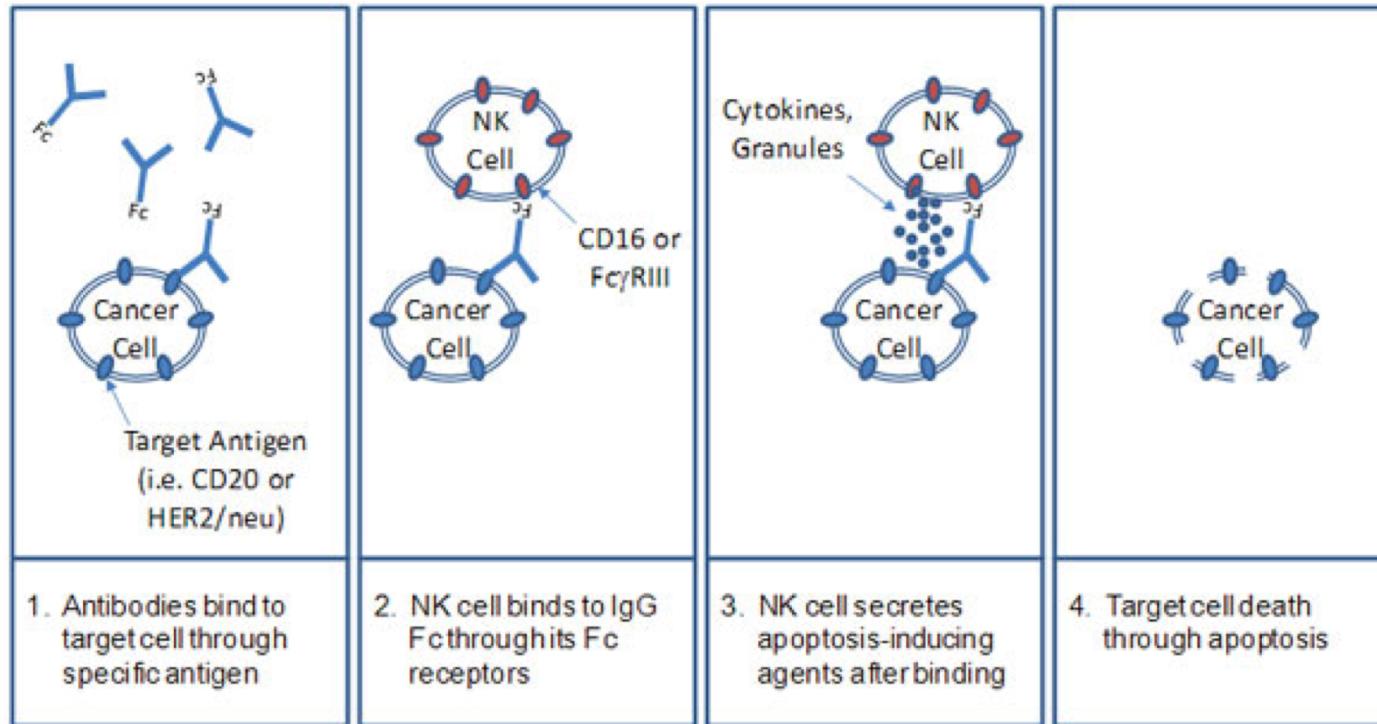
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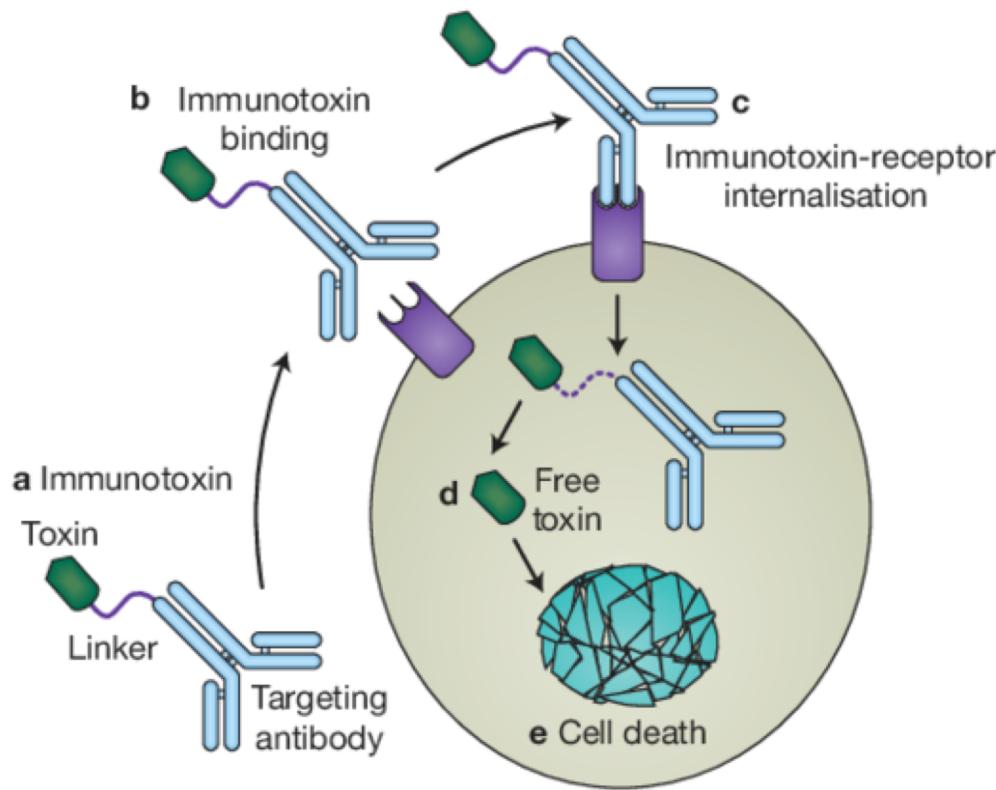
Monoclonal Antibodies: Many Applications



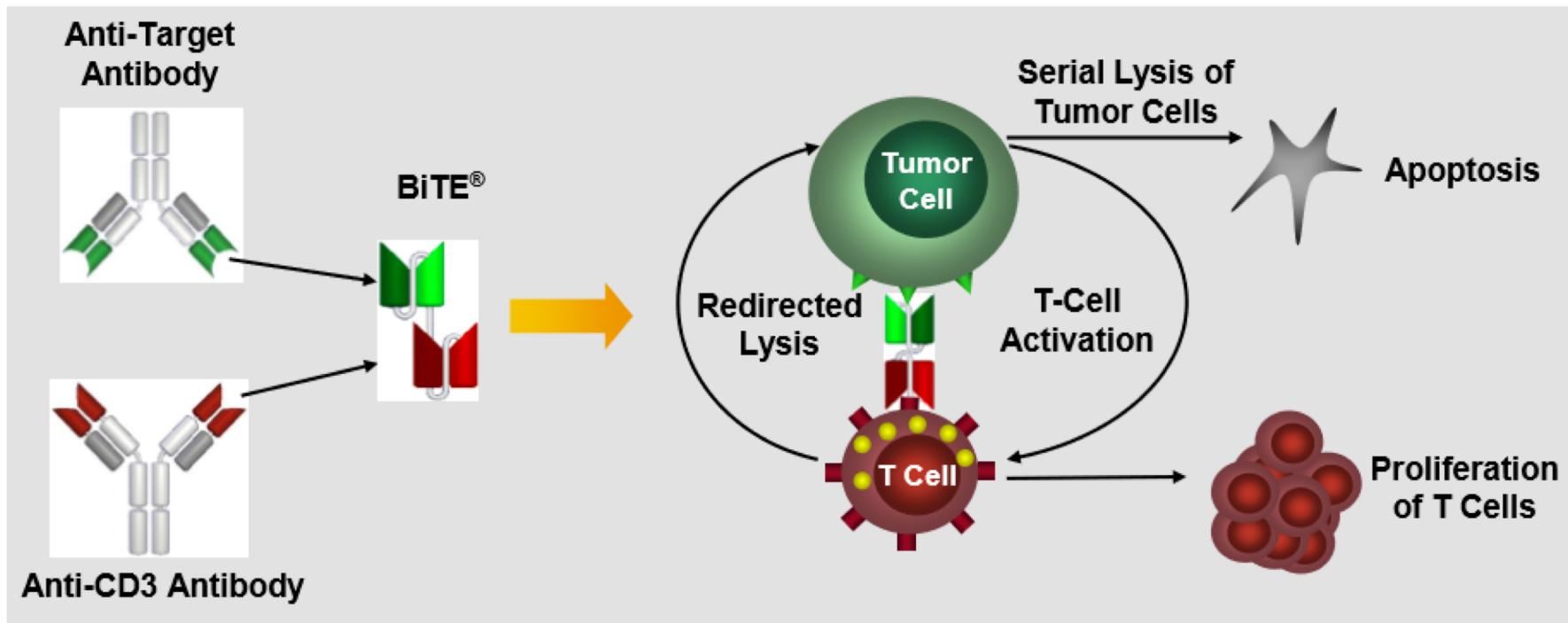
ADCC via Monoclonal Antibody Targeting



Immunotoxins



Bi-specific T-cell Engagers (BiTEs)





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