mRNA Vaccines

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History

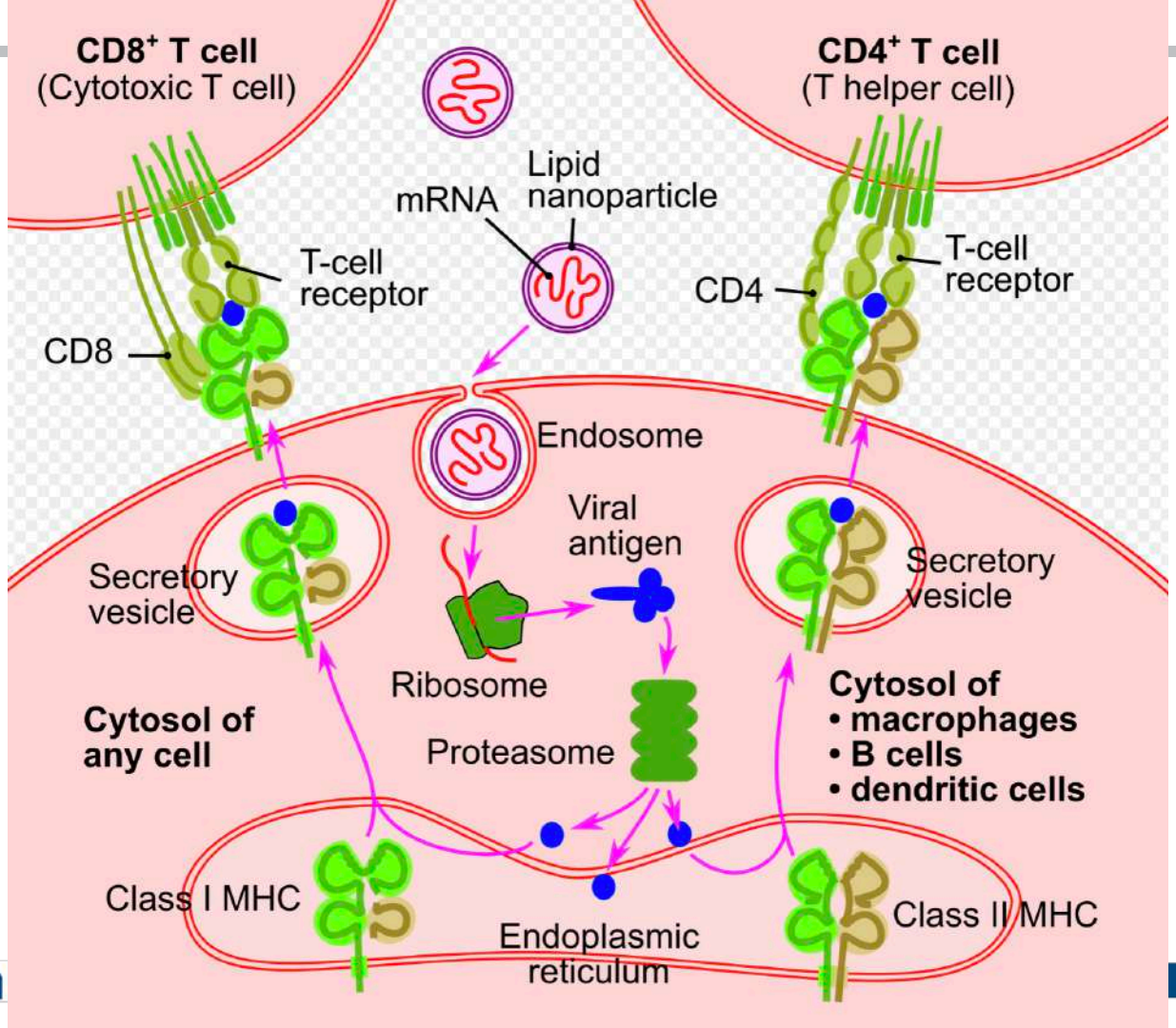
- 1989: liposomal particles can transfect mRNA into cells
- 1993: mRNA can induce cellular immunity
- 1994: mRNA induces both cellular and humoral immunity
- 2005: technique to introduce mRNA into cells without inciting immune response against transfection vehicle
- 2010: both Moderna and BioNTech start research on mRNA vaccines
- 2010-2020: mRNA vaccines created for Zika, rabies, CMV, Flu, and cancer!
    - None are licensed for use at this time
- 2020: Operation Warp Speed
    - Provided significant funding for rapid research and production (little risk for Pharma)
    - Global interest in CV19 sparked significant number of volunteers for study
    - Pandemic allows greater number of patients (unlike Zika, Rabies, etc.)
    - $18B total, $10B for vaccines, $1.5B to Moderna.
    - BioNTech declined (citing too much bureaucracy). Instead, 500M Germany instead

All mRNA Vaccines

- mRNA is transcription of DNA used by ribosomes to create proteins
- Viral genome for mRNA of a specific genome is replicated and placed into lipid nanoparticles to evade our immune system
- These lipid nanoparticles enter our cells and deliver the mRNA into cytoplasm
- Ribosomes translate the mRNA & create the specific proteins
- All mRNA in cytoplasm is degraded by our natural mechanism within 2-3 days

COVID-19 mRNA Vaccines

- The proteins created by this specific mRNA sequence is for the viral spike proteins
    - Spike proteins are on surface of viruses and allow the viruses to enter cells
- The spike proteins are then expressed on our own cells
- Our immune system recognizes these viral spike proteins as foreign and create immune reaction
- The spike proteins on our cells are then degraded over the course of 1-2 weeks


CD8+ T cell
(Cytotoxic T cell)
CD4+ T cell
(T helper cell)
mRNA
Lipid nanoparticle
T-cell receptor
CD8
CD4
T-cell receptor
Endosome
Viral antigen
Secretory vesicle
Secretory vesicle
Ribosome
Cytosol of any cell
Proteasome
Cytosol of
• macrophages
• B cells
• dendritic cells
Class I MHC
Endoplasmic reticulum
Class II MHC

mRNA Vaccines

Pros	Cons
Rapid production of new vaccines (Ebola, Zika, etc.), or mutations of existing targets	Instability of mRNA vaccines
Rapid production of volume of vaccines	Minimal long-term data
Inexpensive production	Public confusion of DNA vs RNA => fear
Very specific	Historical challenge of delivery system
Potential use in oncology	Can cause too much immune response
Potential against challenging viruses: HIV, HSV, RSV, other	
Excellent humoral AND cellular immunity	