Immunology and vaccination

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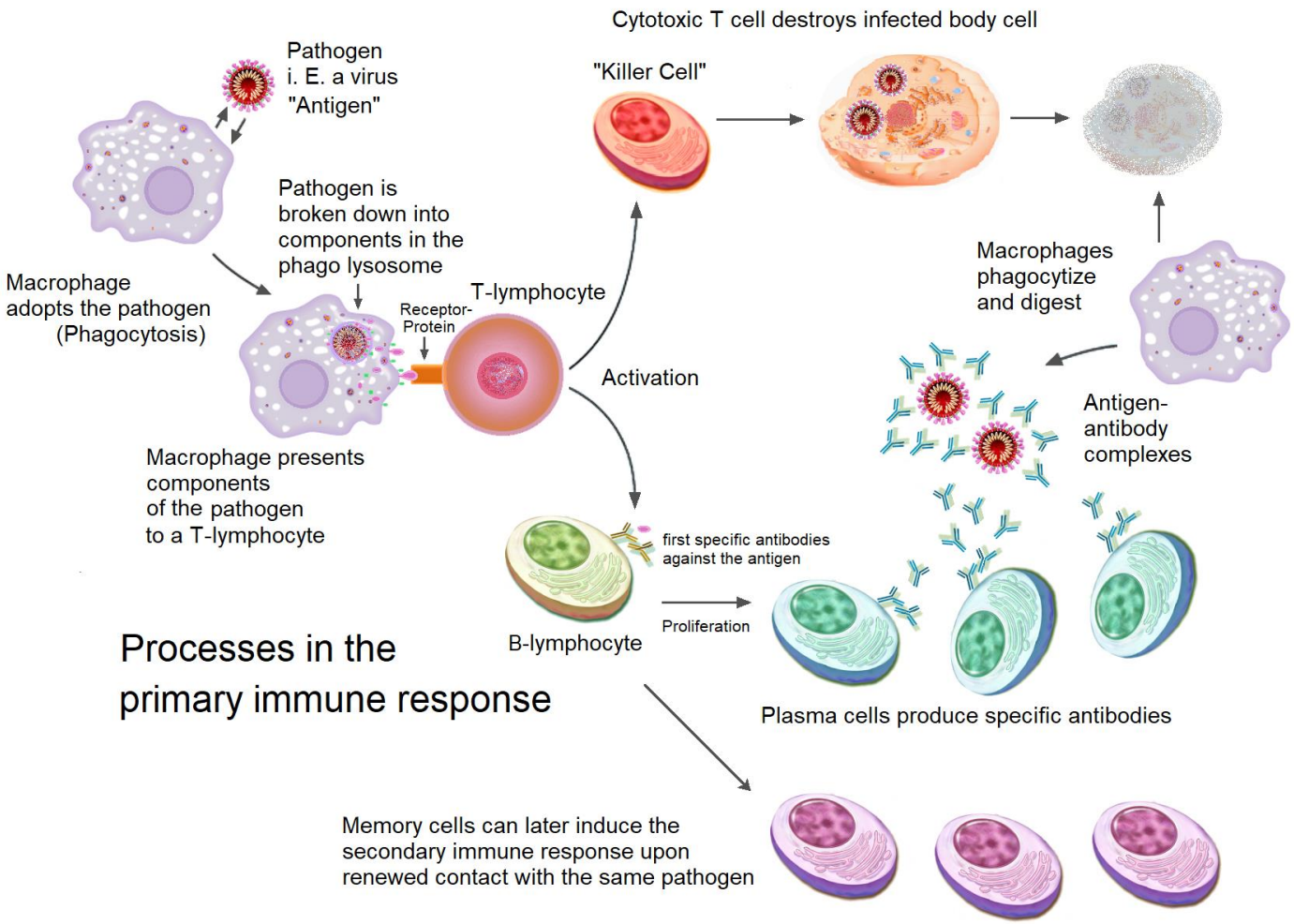
Immunity system

- **recognizes** harmful from harmless and **protects** organism

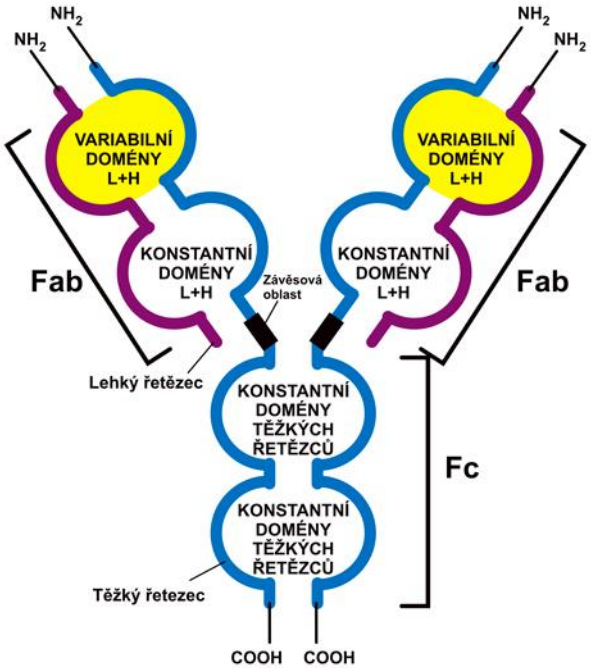
- **innate** immunity (antigen nonspecific):
  - ✓ cellular: phagocytes, macrophages, NK cells
  - ✓ humoral: complement, interferons
  - ✓ reactions in minutes, without memory

- **specific** immunity (acquired adaptive):
  - ✓ cellular: T-lymphocytes
  - ✓ humoral: B-lymphocytes -> antibodies

Immunity system



Antibodies

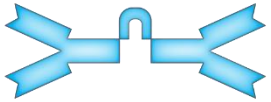


STRUKTURA MONOMERU IMUNOGLOBULINU

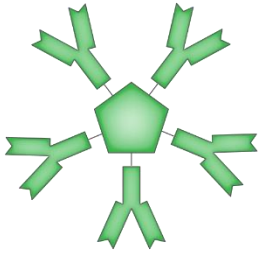
CC: Malmstajn

CC: bandlee86

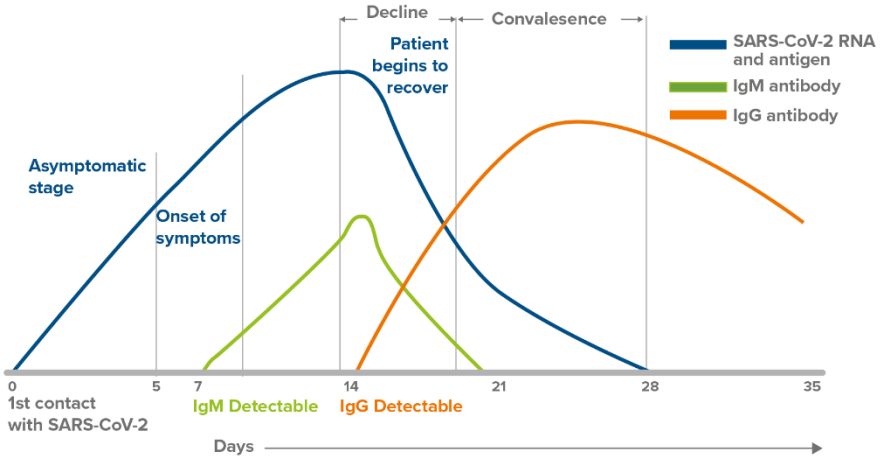
Monomer
IgD, IgE, IgG



Dimer
IgA



Pentamer
IgM



https://dianax.eu/covid-19-testing/

Immunization (vaccination)

- **Active**: induction of specific immunity against a antigen (after infection or vaccination) = body itself *forms* the Ab
- **Pasive**: administration of Ab (body si *not forming* them) – either natural (IgG from mother) or artifical way

Edward Jenner – May 14th 1796

- farmers do not suffer from smallpox
- transfer of material from cowpox
- 8 yrs old James Phipps – infected after 6 weeks and OK
- lat. *vacca* = cow

- 1980 – WHO - eradication

pic.: © https://commons.wikimedia.org/wiki/File:E.Jenner.jpg

Active immunization

Types of vaccine:

1. **attenuated**: alive and weakened by passaging (it losses pathogenicity – cultivation in medium or cells) – e.g. measles, rubella, mumps, Sabin poliovaccine peroral - 1957, BCG vaccine *(Mycobacterium bovis* weakened – Bacillus Calmette-Guérin; intraderm. until 2010 in CZ) – advantage is multiplication of causing organism
2. **dead**: dead viruses or bacteria, conserved antigen structure (flu, pertussis, hepatitis A,…) – inactivation with heat of chemicals – there are usually adverse effects, booster doses are necessary – but unlike (1) will not convert to disease; better stability and easier distribution

Active immunization

Types of vaccine:

3. **toxoids (anatoxins)**: bacterial toxins with reduced toxicity, but with conserved antigens – tetanus (revaccination after injury), diphteria – toxicity reduced with formaldehyde or heat
4. **subunits**: digested and purified viral particles (fewer AE flu e.g.) – isolation of imunogens from cellular organisms (must be the correct part)
    a) **conjugated**: polysaccharide antigen bound with immunogenic protein (carrier) – suitable for children – e.g. pneumococcus, meningococcus, *Haemophilus influenzae* type B
    b) **recombinant**: production in a yeast clone (acellular vaccine against pertussis)
    c) **synthetic** (peptides; prototypes)

Pasive immunization

Types of antibodies:

- animal: heterologous, xenogenic globulins
- human: homologous globulins – normsl or hyperimmune (from donors with high titer of Ab)

Examples:

- ✓ botulismus immune globulin
- ✓ antitetanic globulin
- ✓ antirabies globulin – in case of bite or injury from animal suspected of being infected

Types of vaccination in CZ

1. **regular** – decree no. 355/2017 Coll. – vaccination calnedar – compulsory for children: **hexavaccine** (diphteria, tetanus, pertussis, hepatitis B, poliomyelitis, *Haemophilus infl.* B), **MMR** (measles, rubella, mumps)
2. **special** – for people with higher risks at work (hepatitis B for medical professionals and rabies for vets)
3. **exceptional** – e.g. in flooded areas
4. **travelling** into/from several countries (yellow fever, typhoid fever, etc.)
5. **injury** – tetanus, rabies
6. **on request**:
   - ❖ tick-borne encephalitis, flu, rotavirus, hepatitis A (recommended = not reimbursed)
   - ❖ *pneumococcus, papillomavirus, meningococcus* (voluntary = non-compulsory, but reimbursed)

Adverse effects

- **local** reaction: edema, redness, painfullness
- **general**: higher temperature, fever, headache, joint and muscle ache
- **unusual**: absces in place of injection, t>38°C, meningeal irritation, postvaccine encefalitis

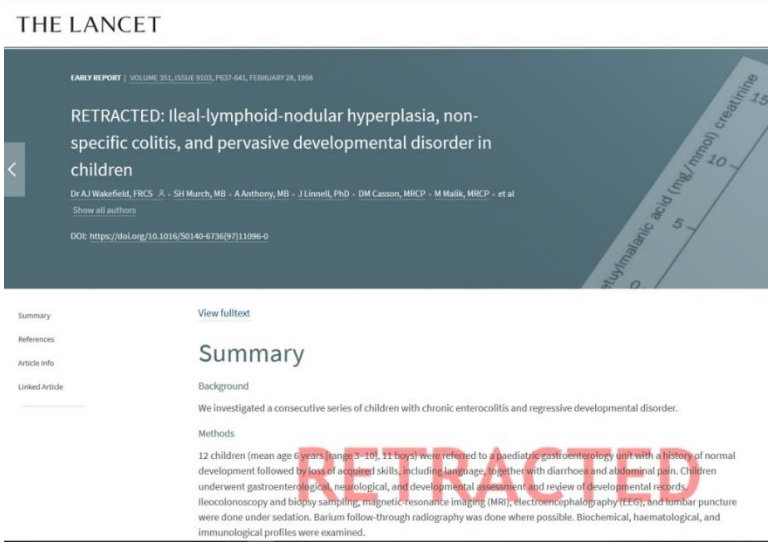
Unusual AE must be reproted to SUKL – data from 2017: total 794 reports (mainly hexa; most cases higher temperature, fever, painfullness; minor neurological symptoms)

Antivax

- non-compliance with obligation: 10 000 CZK fee (400 €)
- Jan 2016 decision of CC – can be refused due to freedom of conscience (certain conditions!)
- cca 1% of parents refuse vacc. totally
- public health protection ✖ parent's right for upbringing
- herd immunity – spread of a disease (at least 95% vacc.)
- MMR in same age as 1st symptoms of autism (3rd year)

MMR vaccine and autism – article retracted

in 2010 pro dishonesty and ethical issues


THE LANCET

EARLY REPORT | VOLUME 351, ISSUE 9103, P637-641, FEBRUARY 28, 1998

RETRACTED: Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children

Dr AJ Wakefield, FRCS · SH Murch, MB · A Anthony, MB · J Linnell, PhD · DM Casson, MRCP · M Malik, MRCP · et al

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DOI: https://doi.org/10.1016/S0140-6736(97)11096-0

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Summary

References

Article Info

Linked Article

Summary

Background

We investigated a consecutive series of children with chronic enterocolitis and regressive developmental disorder.

Methods

12 children (mean age 6 years [range 3–10], 11 boys) were referred to a paediatric gastroenterology unit with a history of normal development followed by loss of acquired skills, including language, together with diarrhoea and abdominal pain. Children underwent gastroenterological, neurological, and developmental assessment and review of developmental records. Ileocolonoscopy and biopsy sampling, magnetic resonance imaging (MRI), electroencephalography (EEG), and lumbar puncture were done under sedation. Barium follow-through radiography was done where possible. Biochemical, haematological, and immunological profiles were examined.

RETRACTED

Covid-19

vaccines approved in EU (on 29th Nov reported 9379; 129 deaths):

- ✓ Comirnaty (Pfizer/BioNtech) – mRNA enveloped in liposomes (21st Dec 2020 – emergency conditional reg.)
- ✓ Spikevax (Moderna) – mRNA in liposomes
- ✓ Vaxzevria (AstraZeneca) – vector (adenovirus ChAdOx1) – 2 doses
- ✓ Janssen (Johnson&Johnson) – vector (adenovirus Ad26)

in process:

- ✓ Nuvaxovid (Novavax) – protein, adjuvanted
- ✓ Sputnik V (Gam-COVID-Vac) – vector (adenovirus)
- ✓ VERO CELL (Sinovac) – inactivated viral

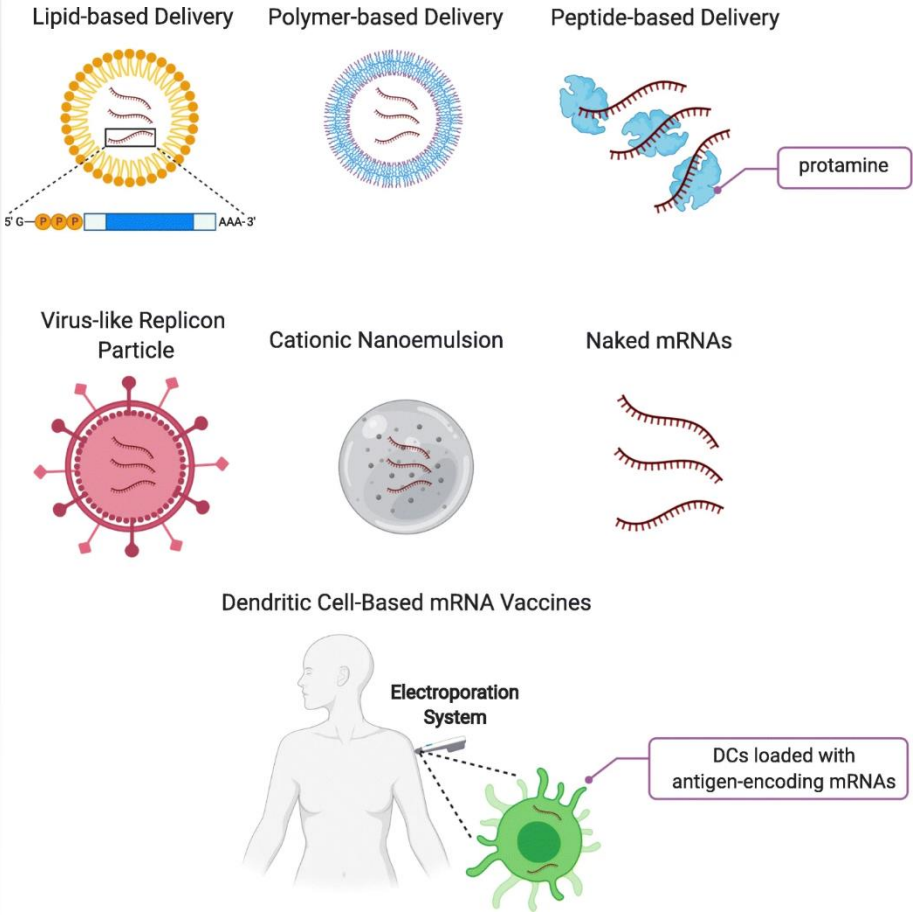
mRNA vaccines

- ✓ 1961: Discovery of mRNA (Brenner; Watson)
- ✓ 1993: liposome+mRNA stimul. of T-lymphocytes in mice
- ✓ 2001: *ex vivo* dendritic cells – transfection – clinical study on humans for cancer treatment
- ✓ 2013: first clinical trial with mRNA vaccine against infection (rabies)

- ✓ intramuscular injection (mRNA coding S-protein)
- ✓ mRNA must get **into cells** – too large for **diffusion**, also **negative charge** (electrostatic repulsion), **RNases** on skin and in blood
- ✓ *ex vivo* methods × *in vivo* methods
- ✓ during distribution: - 80°C

- ✓ efficacy in clinical trials upto 95%

mRNA vaccines



Pfizer/BioNTech:

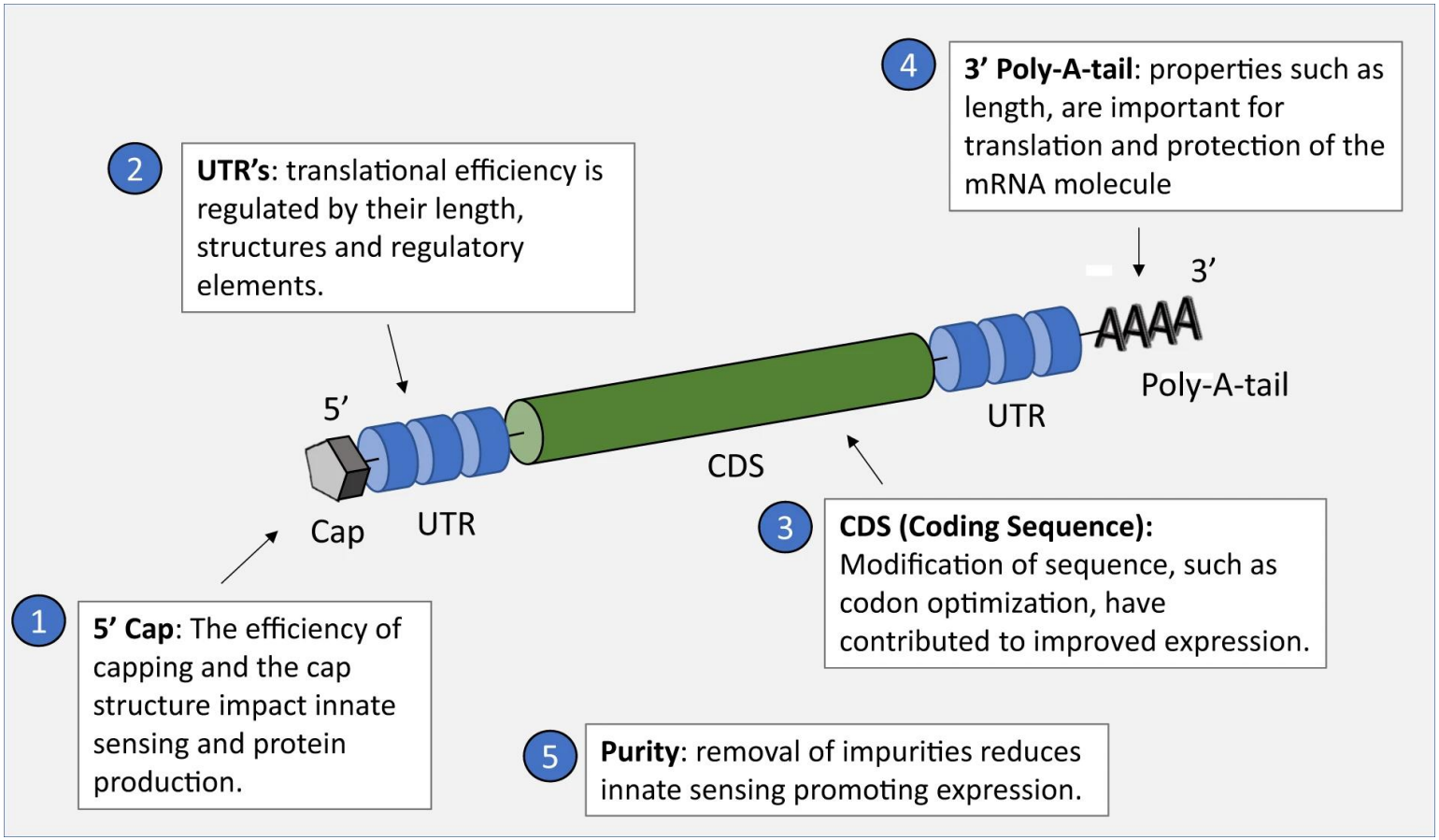
((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate)

2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide

1,2-distearoyl-sn-glycero-3-phosphocholine

cholesterol

mRNA vaccines



CC: Guest2625

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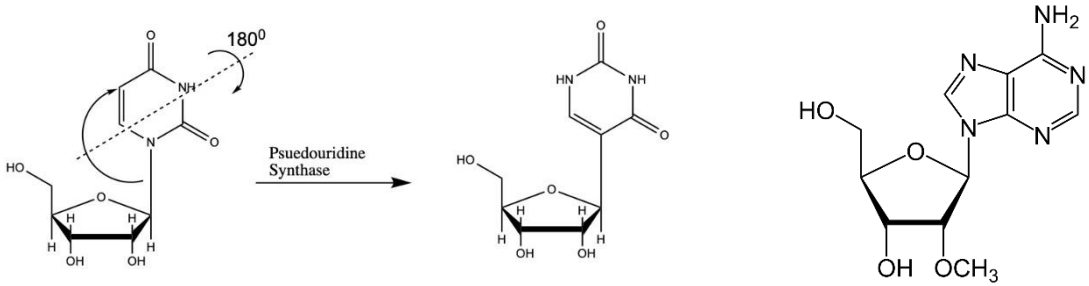
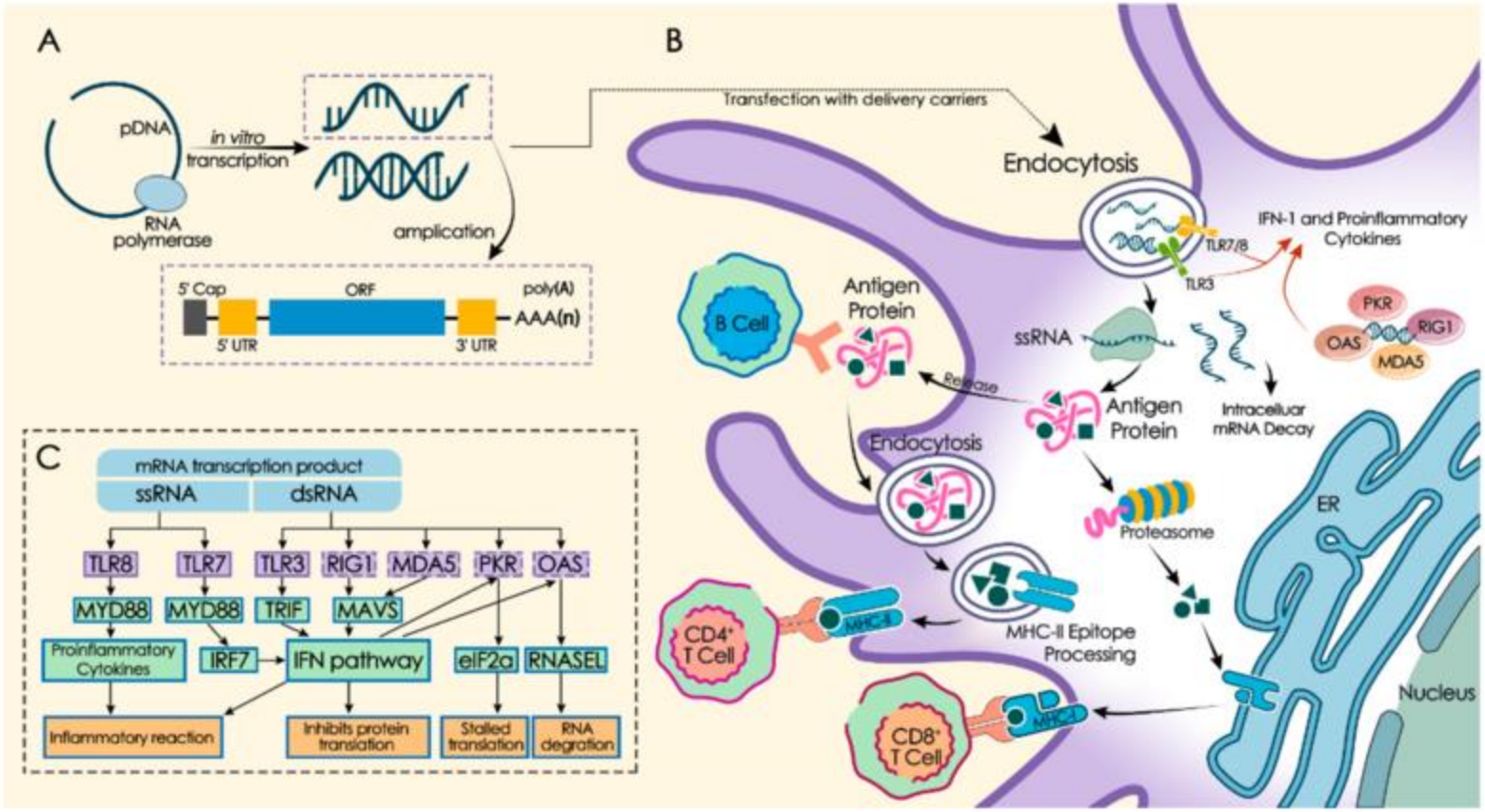


mRNA vaccines



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mRNA vaccines +/-

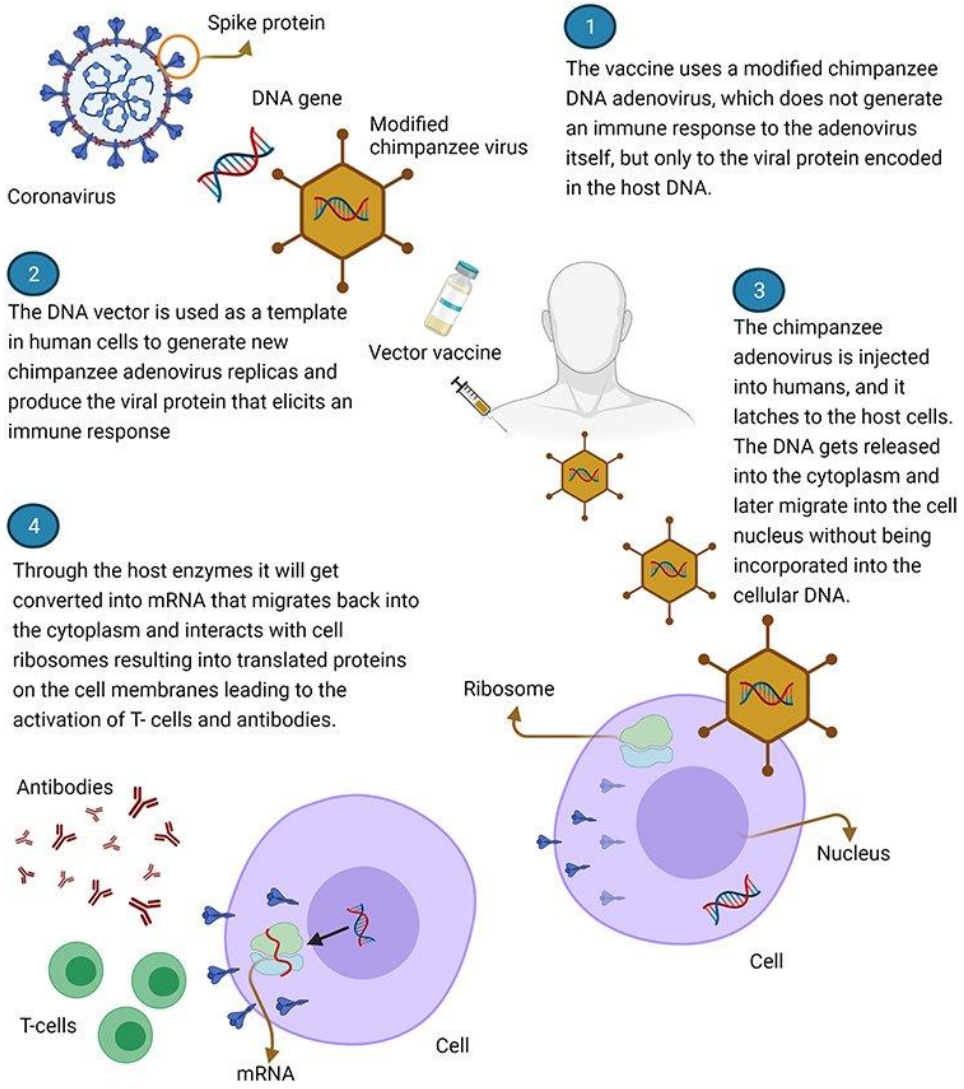
- ✓ noninfectious as it is
- ✓ activates cellular and humoral response
- ✓ production and design advantage (Moderna designed mRNA in 2 days; production as it self takes 22 days)
- ✓ production in cytosol (not entering the nucleus)
- ✓ stability increased with modifications
- ✓ „protein made by cells in the body“

- ✓ mRNA is very very unstabile
- ✓ unknown effects and riscs (reverse transcriptase? – similiar risk during infection and in vaccination)

Adenovirus vector vaccines

- ✓ viral vector (harmless adenovirus): contains DNA for S-protein of virus
- ✓ **adenovirus**: non-enveloped dsDNA virus – respirátory infections
- ✓ great rate of transdukce, broad tropism
- ✓ disadvantage in existing immunity after previous exposure – chimpanzee viruses
- ✓ Oxford-AstraZeneca – 2 doses, efficacy 81%; questions about blood clotting – EMA: 222 cases in April 2021 in 447 mil. humans)

Adenovirus vector vaccines



https://doi.org/10.2147/IDR.S315727

Vaccine against malaria

- ✓ Oct 2021: **Mosquirix** (RTS,S/AS01) – approved WHO
- ✓ recombinant vakccine (efficacy in children: 26 – 50%) – clinical trials in Africa – 4 injections
- ✓ paid from non-profit sources (PATH iniciativa, nadace Gatesových)

CC: Cmglee