ImmunoScience Academy

Partnering for Education & Optimizing Treatment in ImmunoScience

COVID-19 vaccinations: the immunology behind and are they delivering on expectations?

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de Duve Institute
Universtity of Louvain

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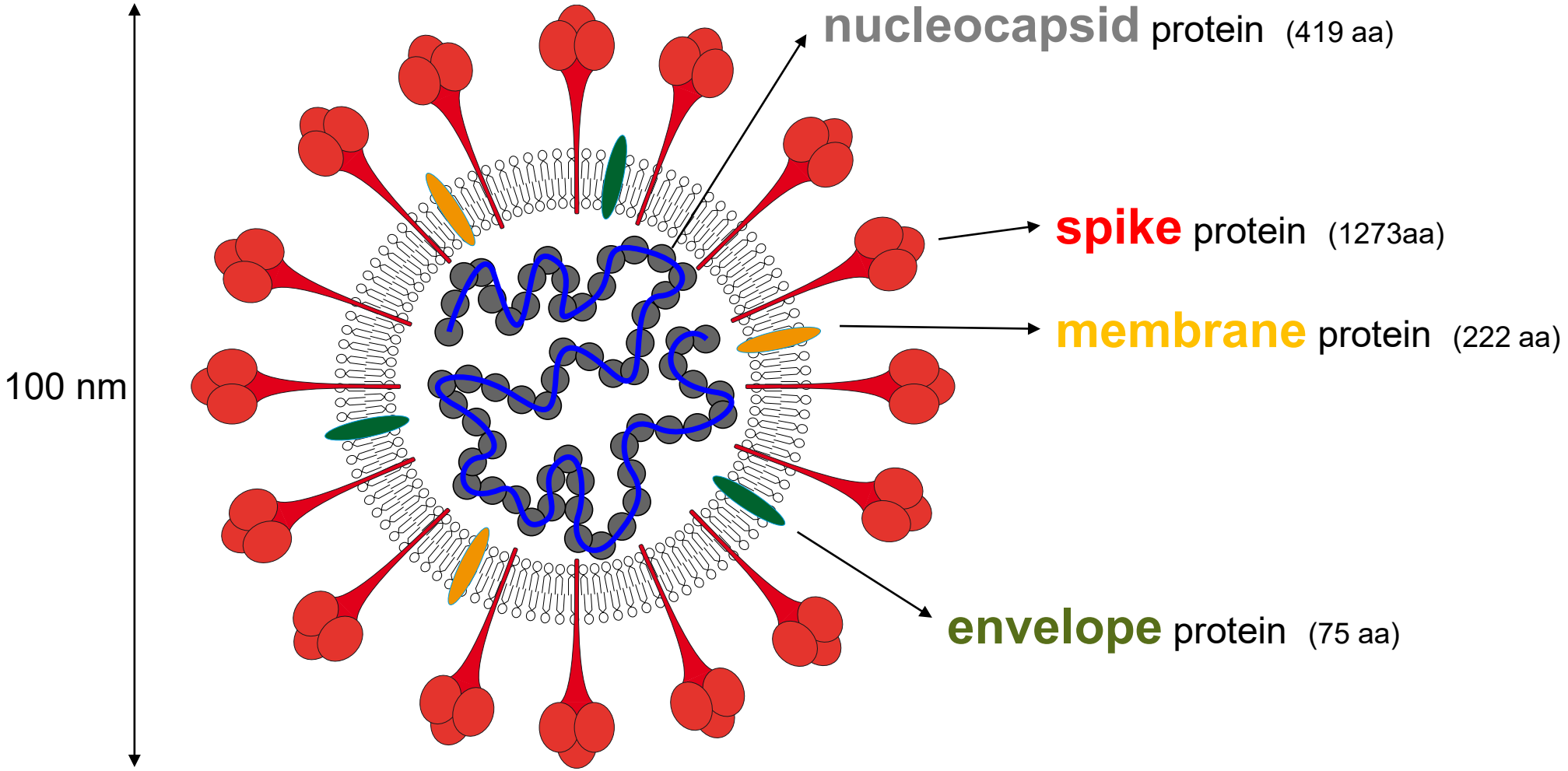
SARS-CoV-2 structural proteins



1. Wu A, et al. Cell Host Microbe 2020;27:325-328; 2. Huang Y, et al. Acta Pharmacol Sin 2020;41:1141-1149; 3. Walls A, et al. Cell 2020;181:281-292.e6.

SARS-CoV-2 structural proteins

	Worldwide	Belgium
Number of cases	240 x 10^6	1.28 x 10^6
Number of confirmed deaths	4.9 x 10^6	25,750
Number of vaccinations	6,650 x 10^6	16.7 x 10^6
Number of vaccinees	3,750 x 10^6	8.65 x 10^6

https://ourworldindata.org (accessed Oct 2021)

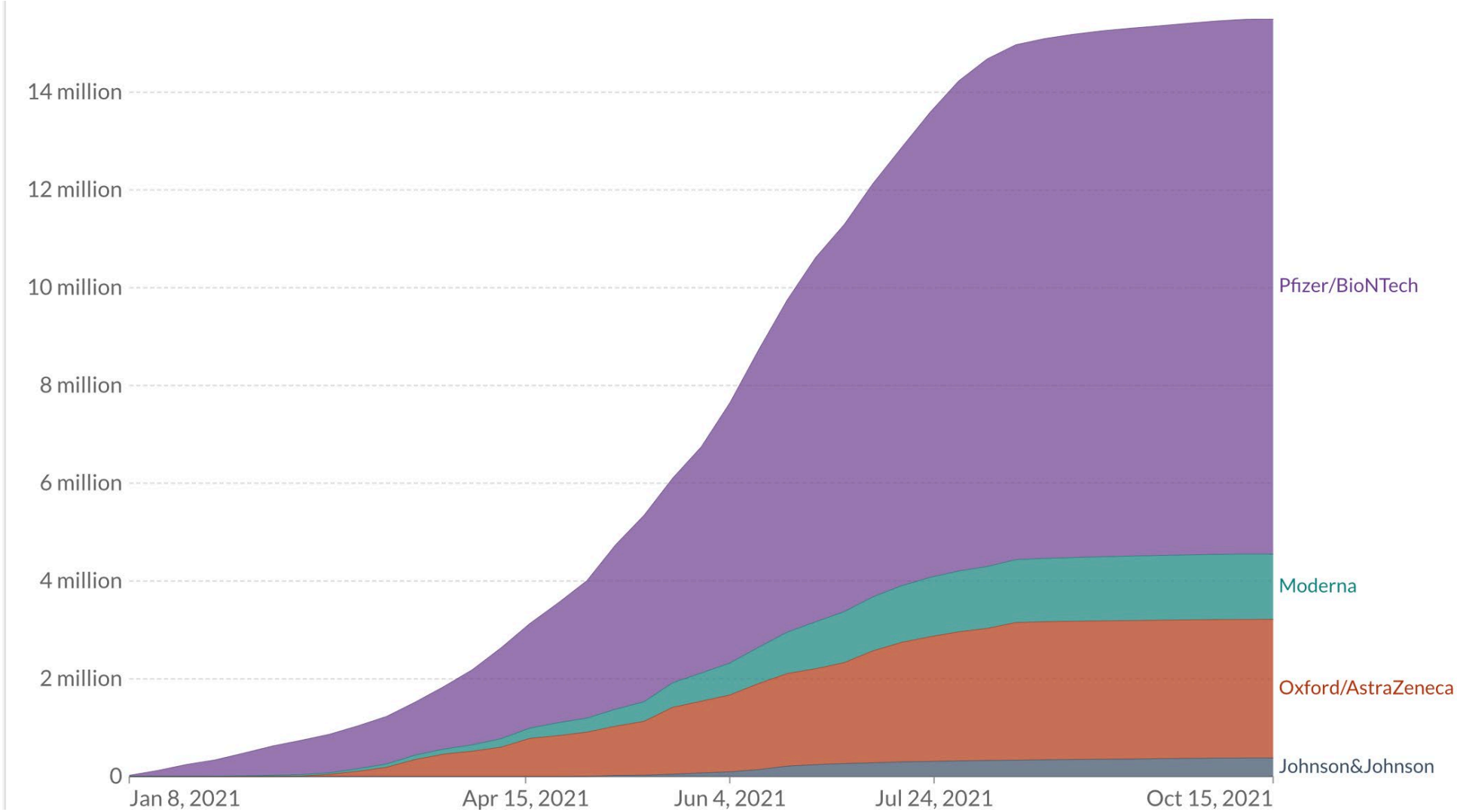
- **Anti-SARS-CoV-2 S vaccines in Belgium**
- Adaptive immune response to these vaccines
- Towards better vaccines ?

Anti-SARS-CoV-2 S vaccines in Belgium (oct 2021)

	Targeted antigen	Vehicle	Dose	Schedule	Storage
Pfizer-BioNTech[1] Comirnaty	SARS-CoV-2 S	mRNA in lipid nanoparticles	30 µg mRNA	2x 3w	- 70°C 9m
Moderna[2] Spikevax	SARS-CoV-2 S	mRNA in lipid nanoparticles	100 µg mRNA	2x 4w	- 20°C 7m
Astra Zeneca[3] Vaxzevria	SARS-CoV-2 S	defective (replication deficient) chimpanzee adenovirus	5 x 10^{10} viral particles	2x 4-12w	4°C 6m
Johnson & Jonhson[4] Janssen COVID-19 Vaccine	SARS-CoV-2 S	defective (replication deficient) human adenovirus 26	5 x 10^{10} viral particles	1x	4°C 6m

1. Polack F, et al. N Engl J Med 2020;383:2603-2615; 2. Baden R, et al. N Engl J Med 2021;384:403-416; 3. Ramasamy M, et al. Lancet 2021;396:1979-1993;
4. Sadoff J, et al. N Engl J Med 2021;384:1824-1835.

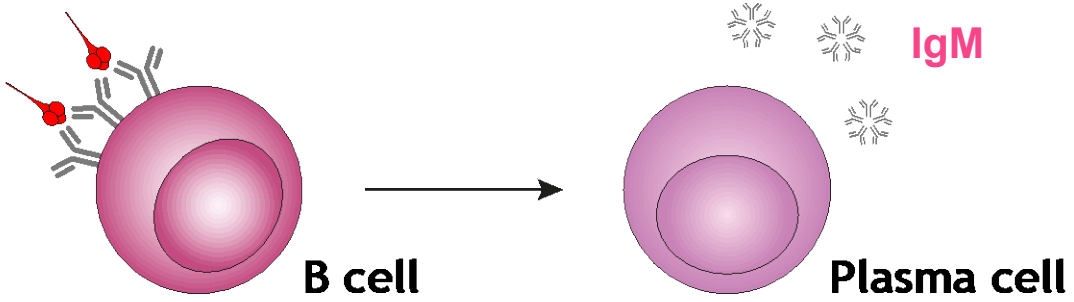
COVID-19 vaccines in Belgium



https://ourworldindata.org/grapher/covid-vaccine-doses-by-manufacturer?country=~BEL

- Anti-SARS-CoV-2 S vaccines in Belgium
- **Adaptive immune response to these vaccines**
- Towards better vaccines ?

Adaptive immune response to adenovirus- or mRNA-based anti-SARS-CoV-2 S vaccines



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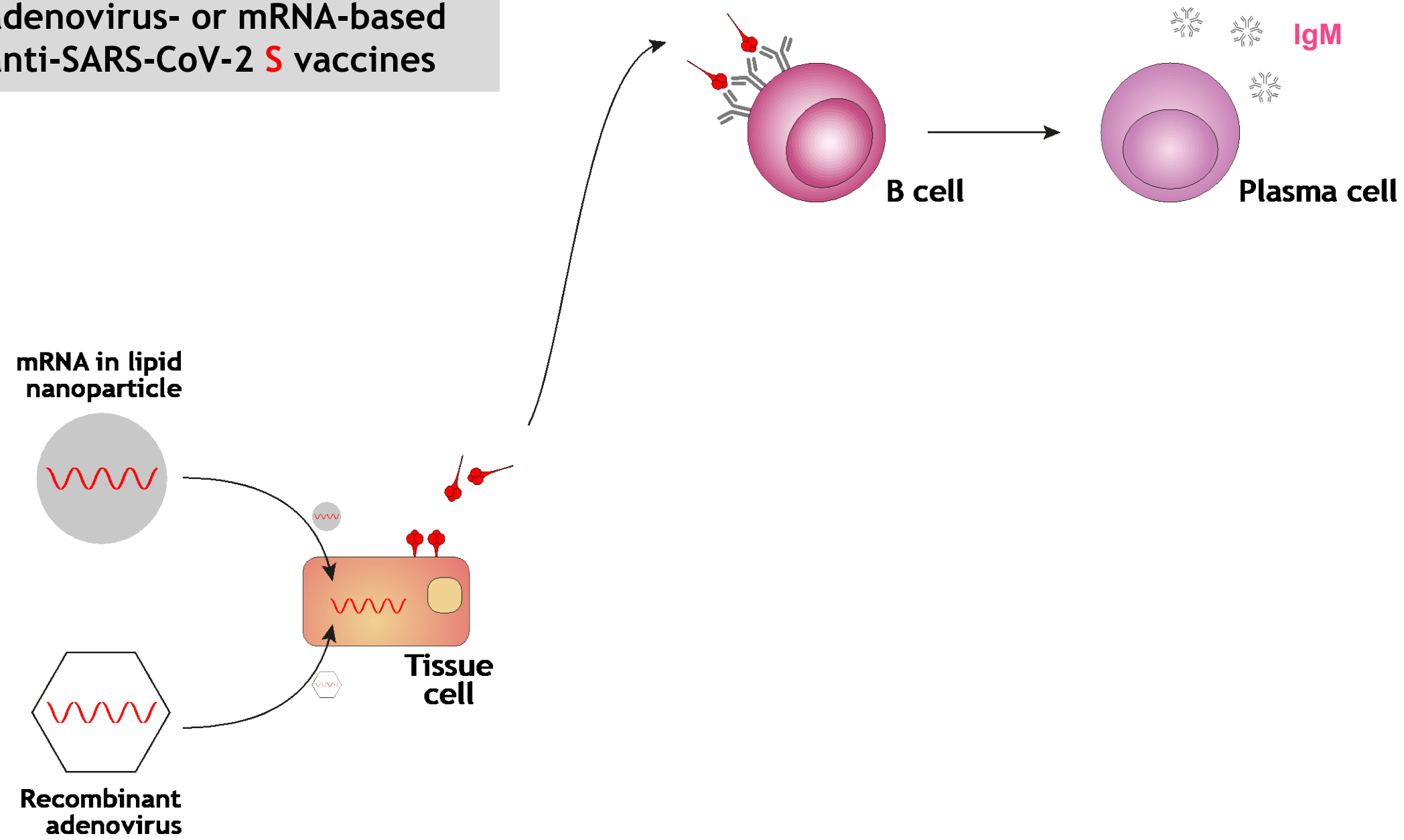

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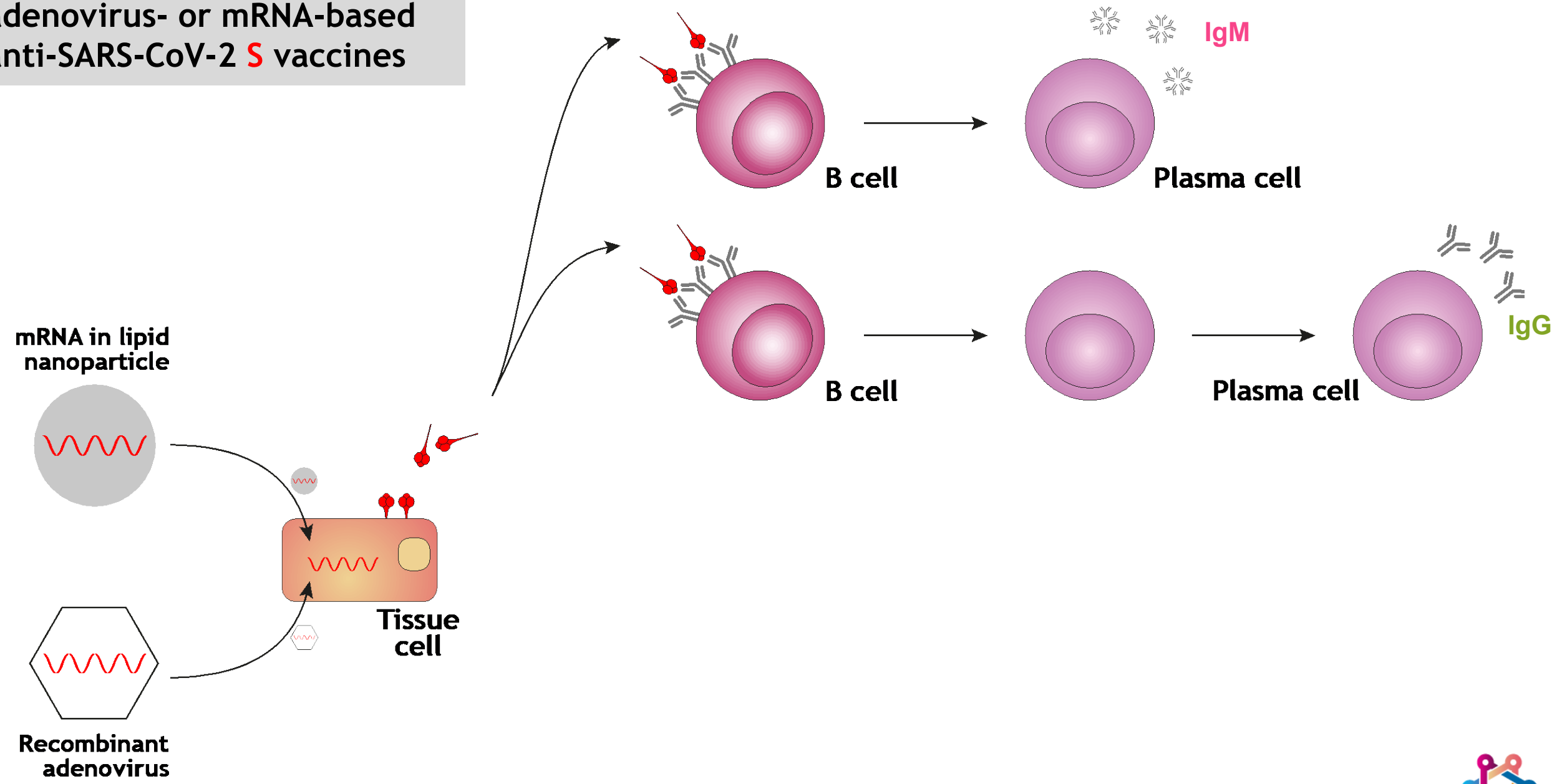

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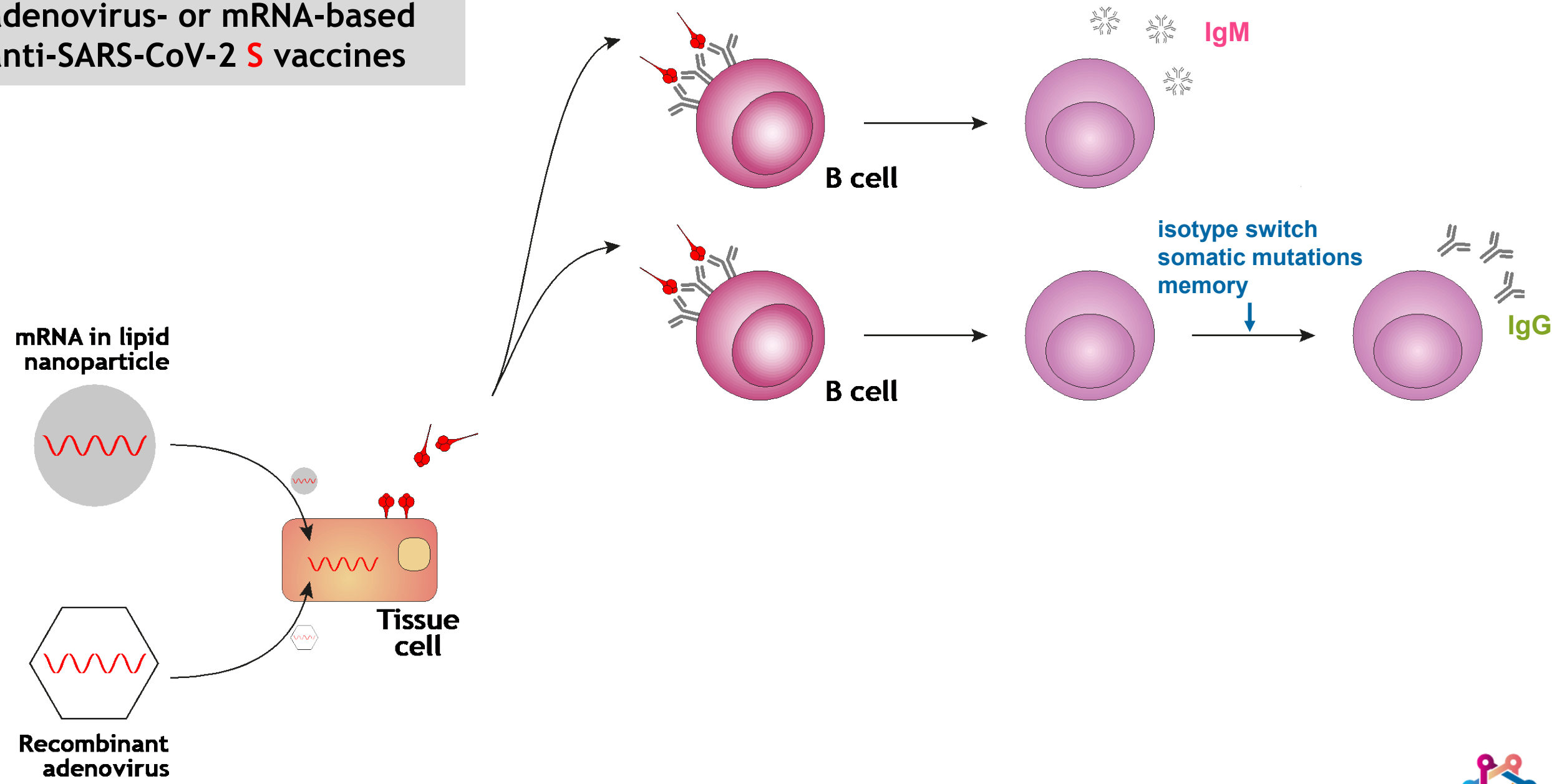

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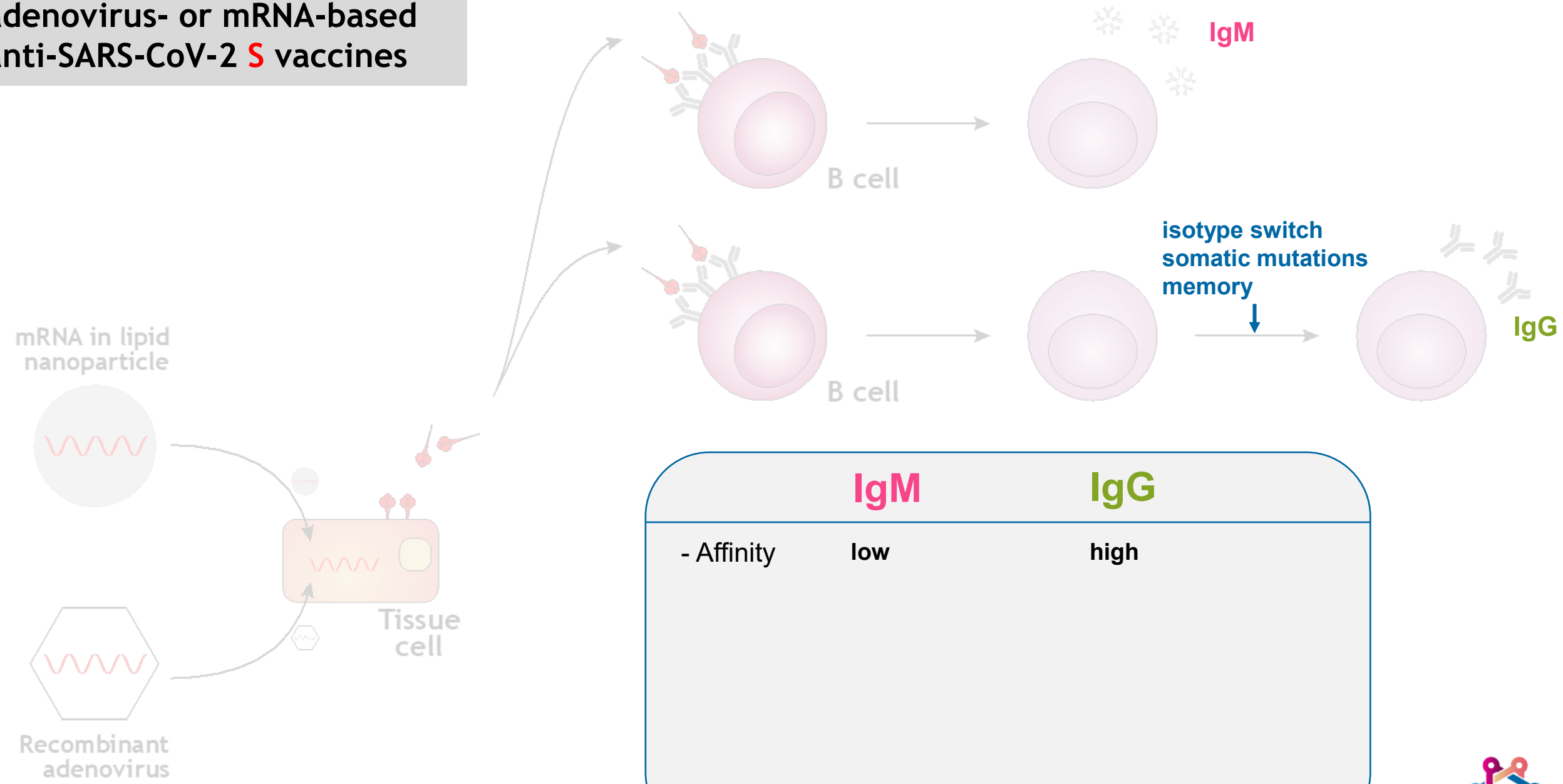

	IgM	IgG
- Affinity	low	high

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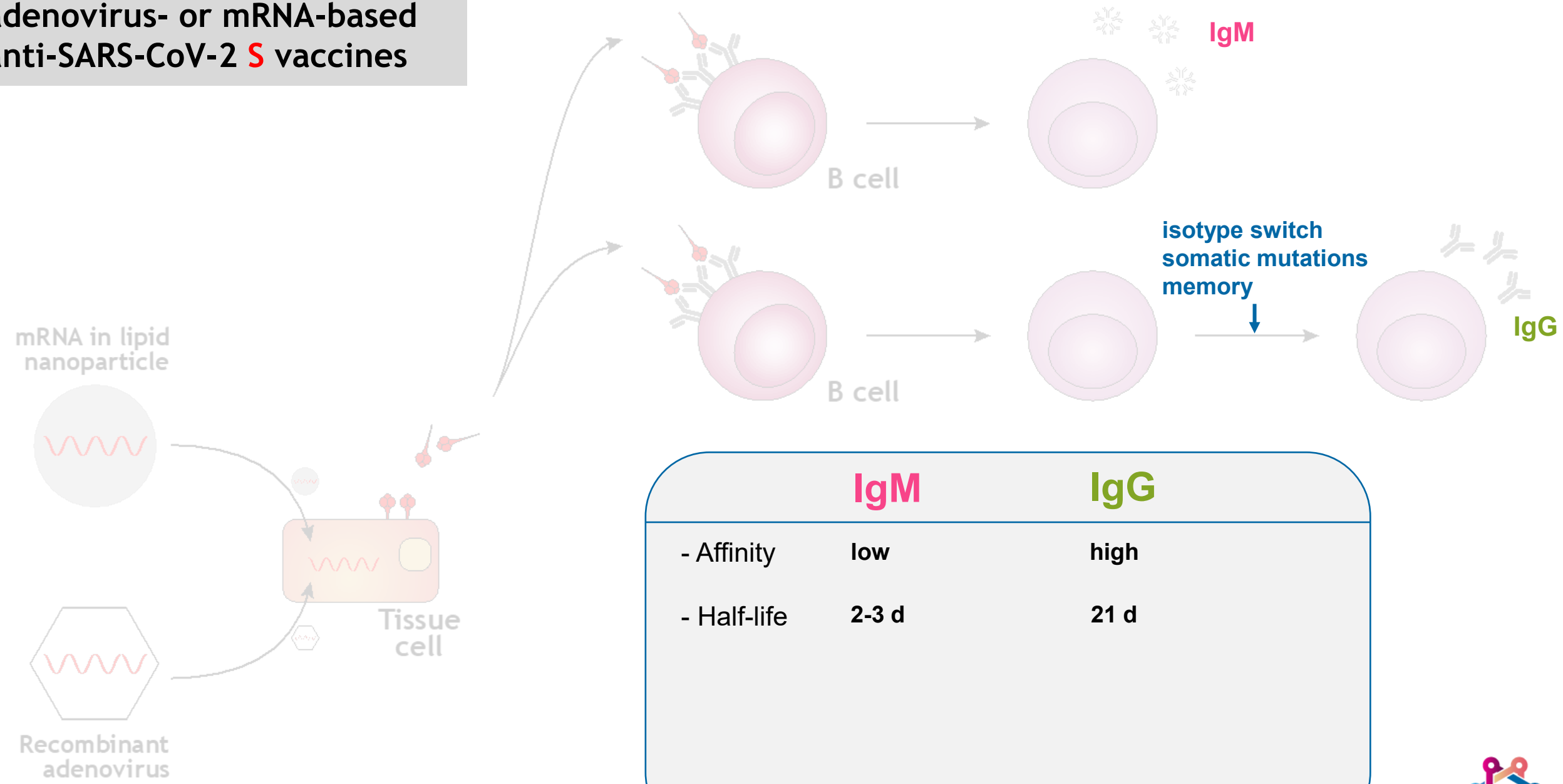

	IgM	IgG
- Affinity	**low**	**high**
- Half-life	**2-3 d**	**21 d**

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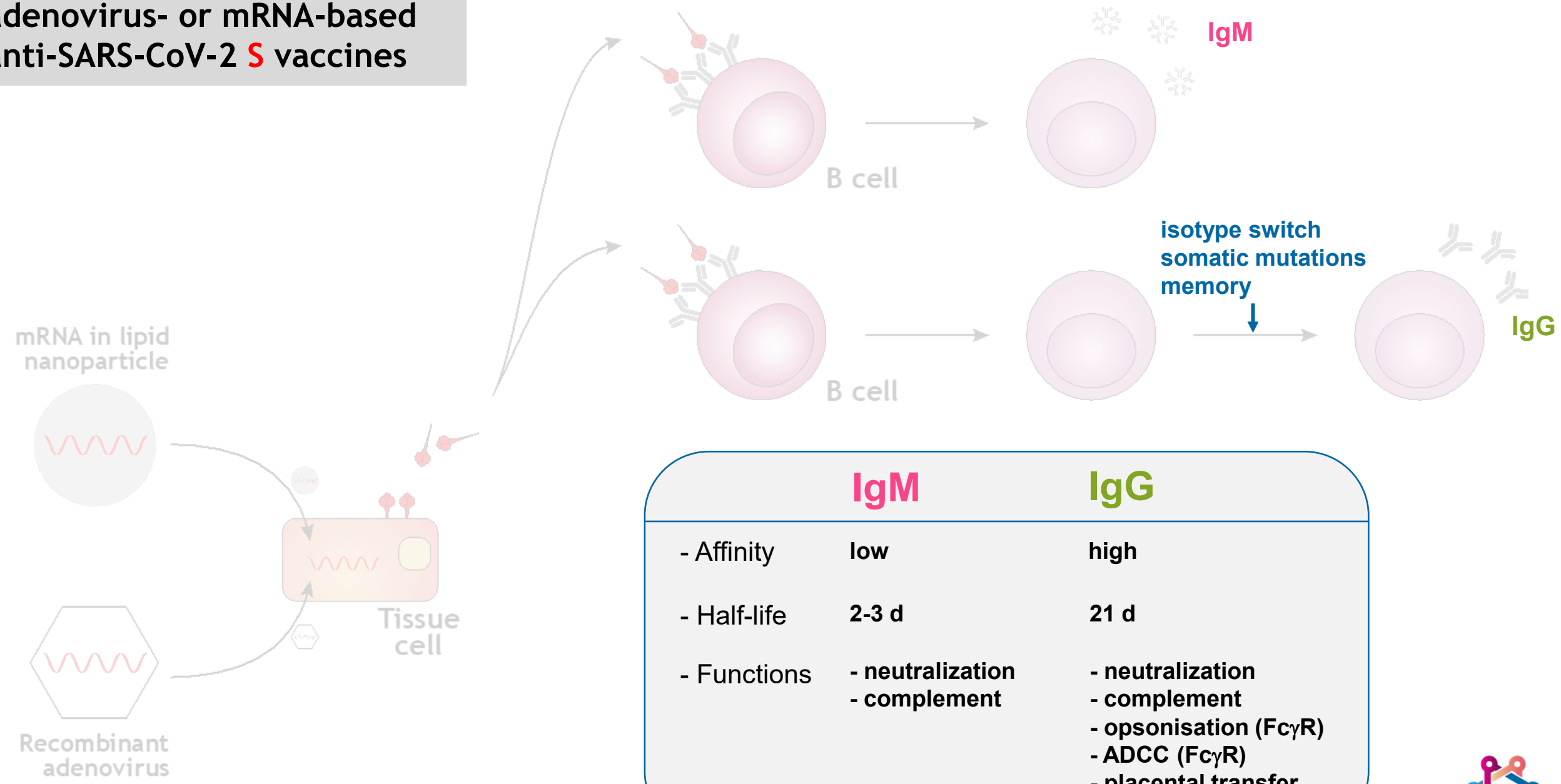

	IgM	IgG
- Affinity	**low**	**high**
- Half-life	**2-3 d**	**21 d**
- Functions	**- neutralization** **- complement**	**- neutralization** **- complement** **- opsonisation (FcγR)** **- ADCC (FcγR)** **- placental transfer**

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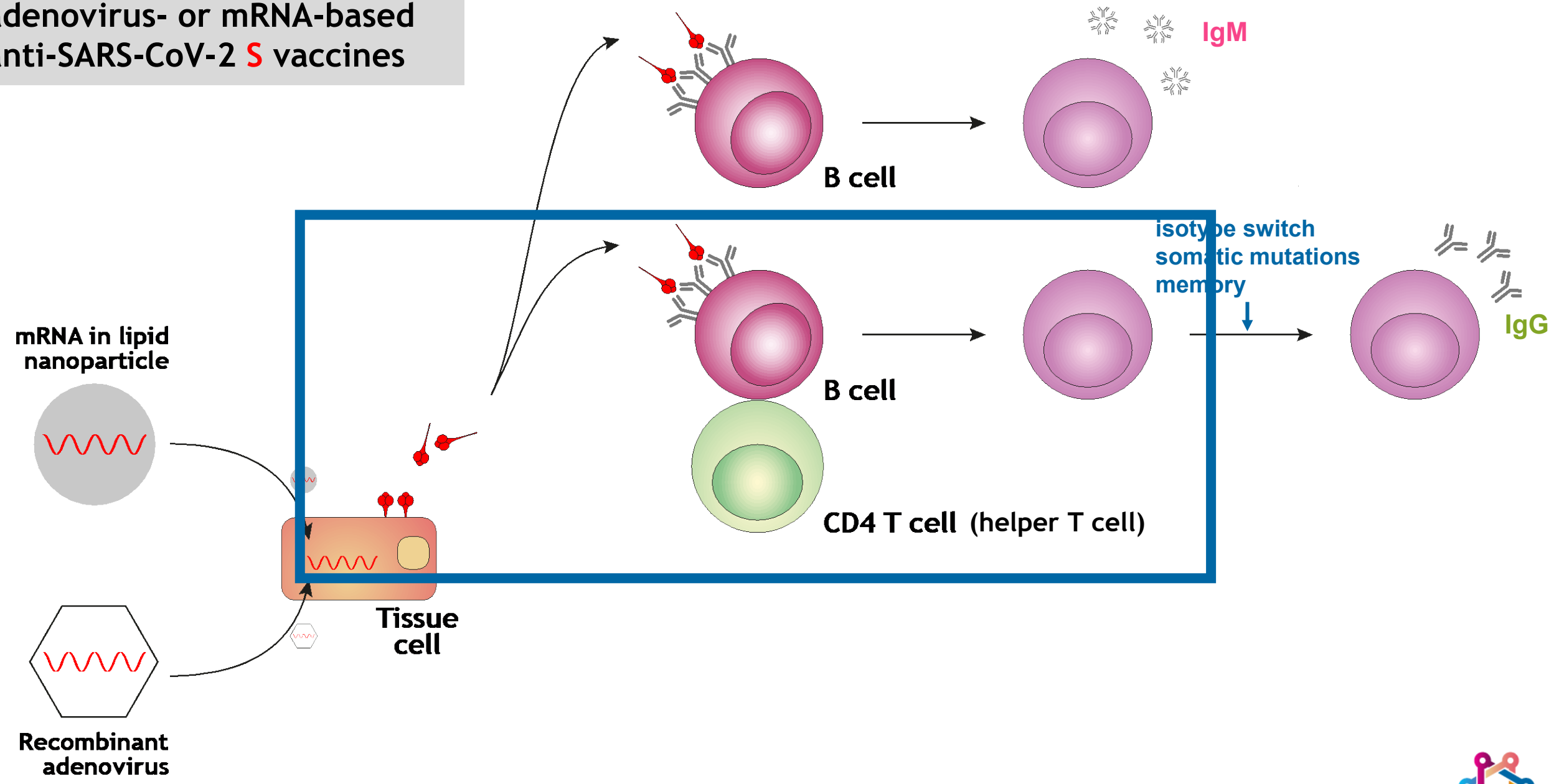

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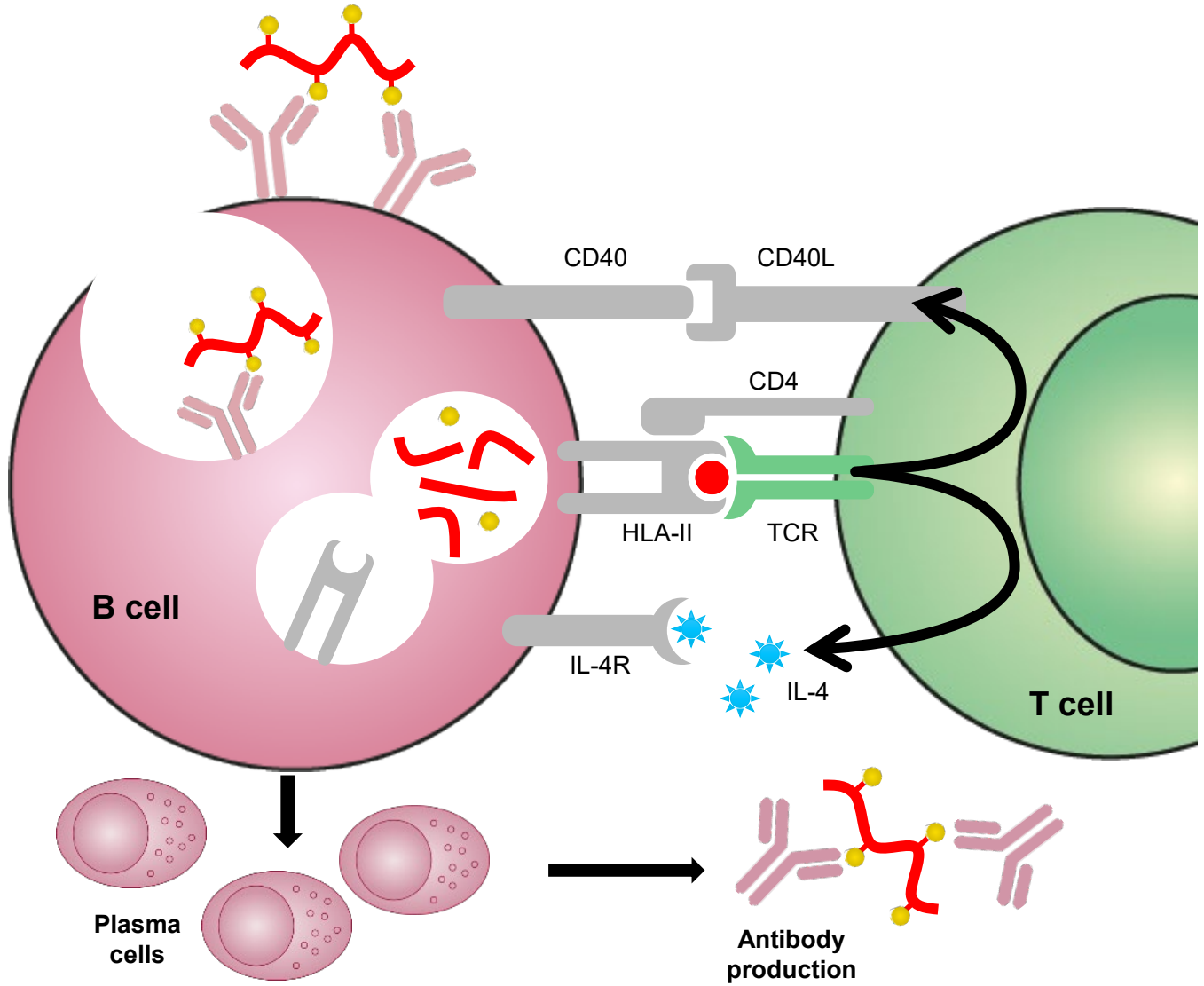
T-B collaboration

- The surface immunoglobulin that serves as the BCR has two roles in B-cell activation:
  - BCR binds antigen (a hapten-carrier complex), leading directly to the intracellular signaling cascade
  - BCR delivers the antigen to intracellular sites where it is degraded and returned to the B-cell surface as peptides bound to HLA class II molecules
- The peptide:HLA class II complex is recognized by helper T cells, stimulating them to express CD40L and secrete IL-4, which stimulates B-cell proliferation and differentiation into Ab-secreting cells



Ab, antibody; BCR, B-cell antigen receptor; CD40L, CD40 ligand; HLA, human leukocyte antigen; IL-4R, interleukin-4 receptor; TCR, T-cell receptor.

Janeway et al. Immunobiology: The Immune System in Health and Disease, 5th edn, 2001. Available from: https://www.ncbi.nlm.nih.gov/books/NBK27142/. Accessed April 2020;
Alberts et al. Molecular Biology of the Cell. 4th edn, 2002. Available from: https://www.ncbi.nlm.nih.gov/books/NBK2682/. Accessed April 2020.

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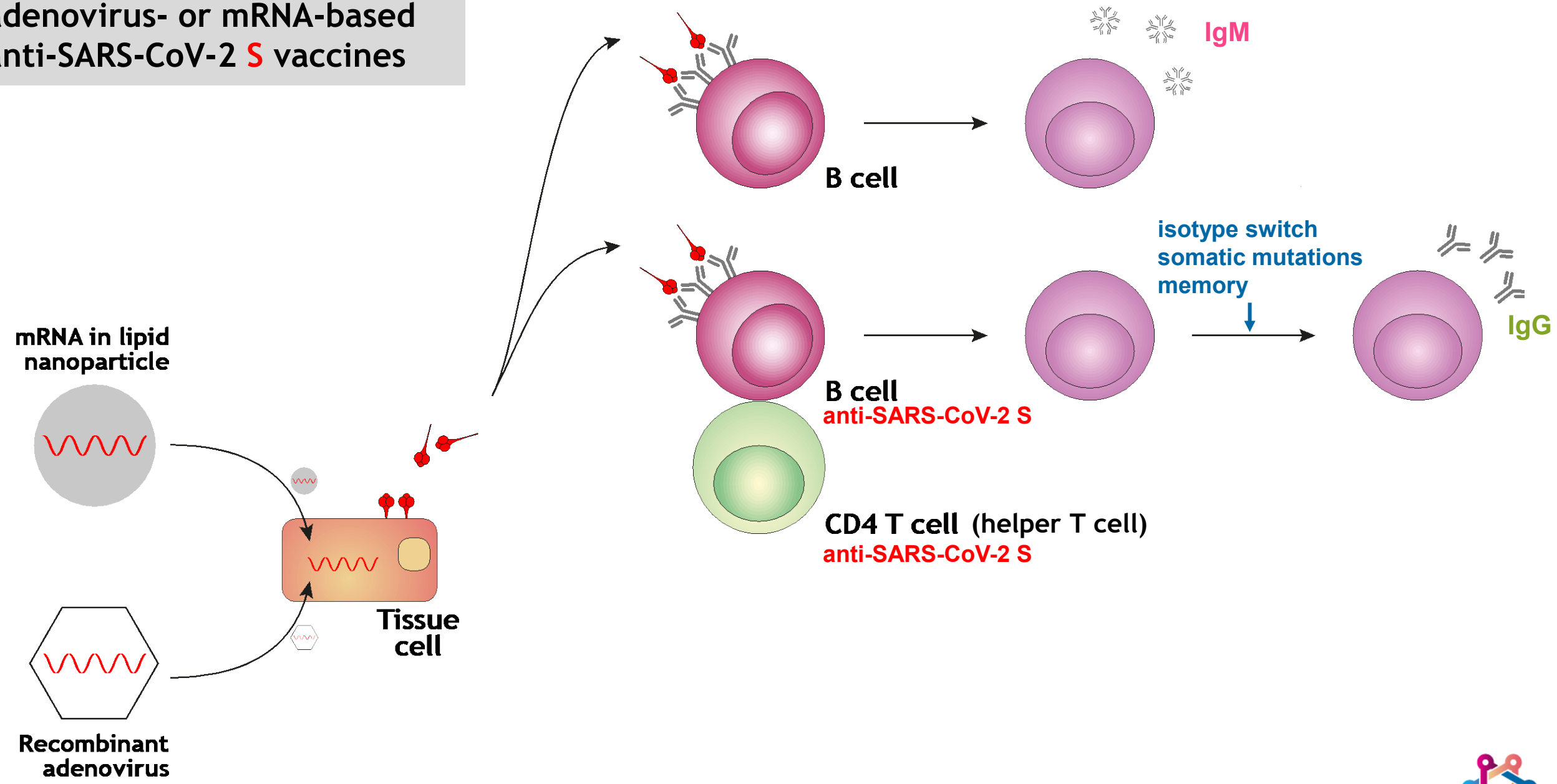

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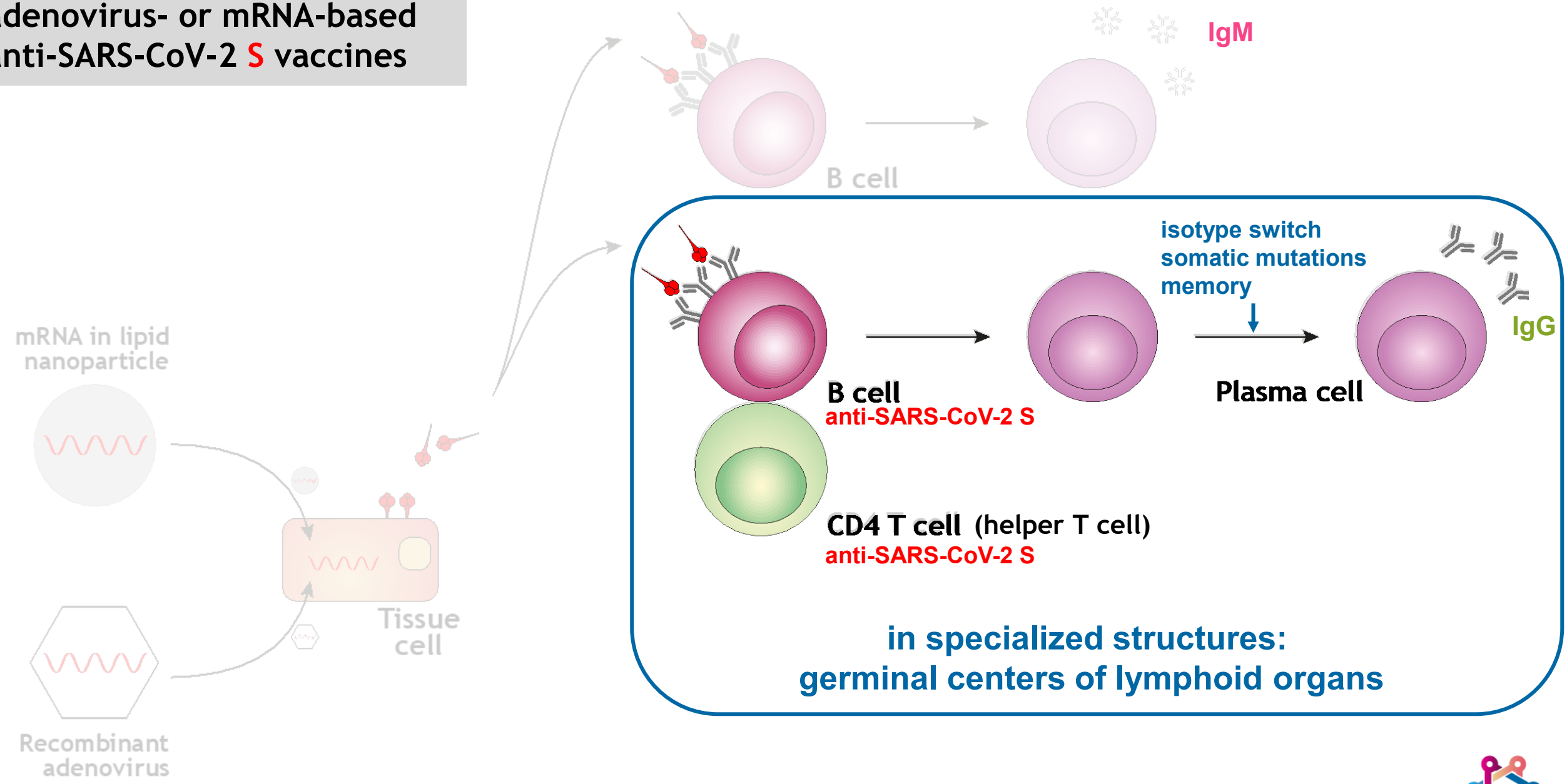

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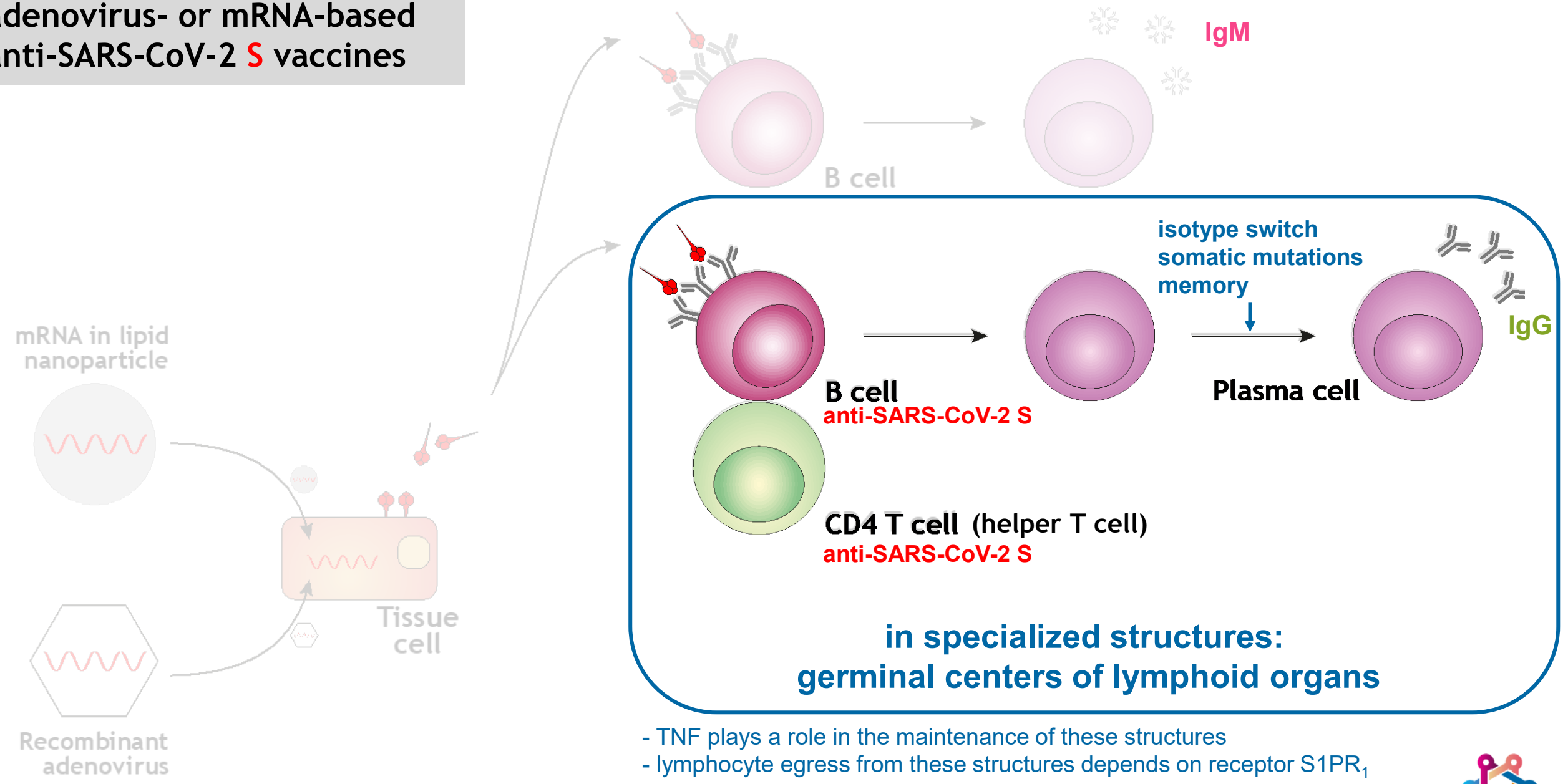

- TNF plays a role in the maintenance of these structures
- lymphocyte egress from these structures depends on receptor $S1PR_1$

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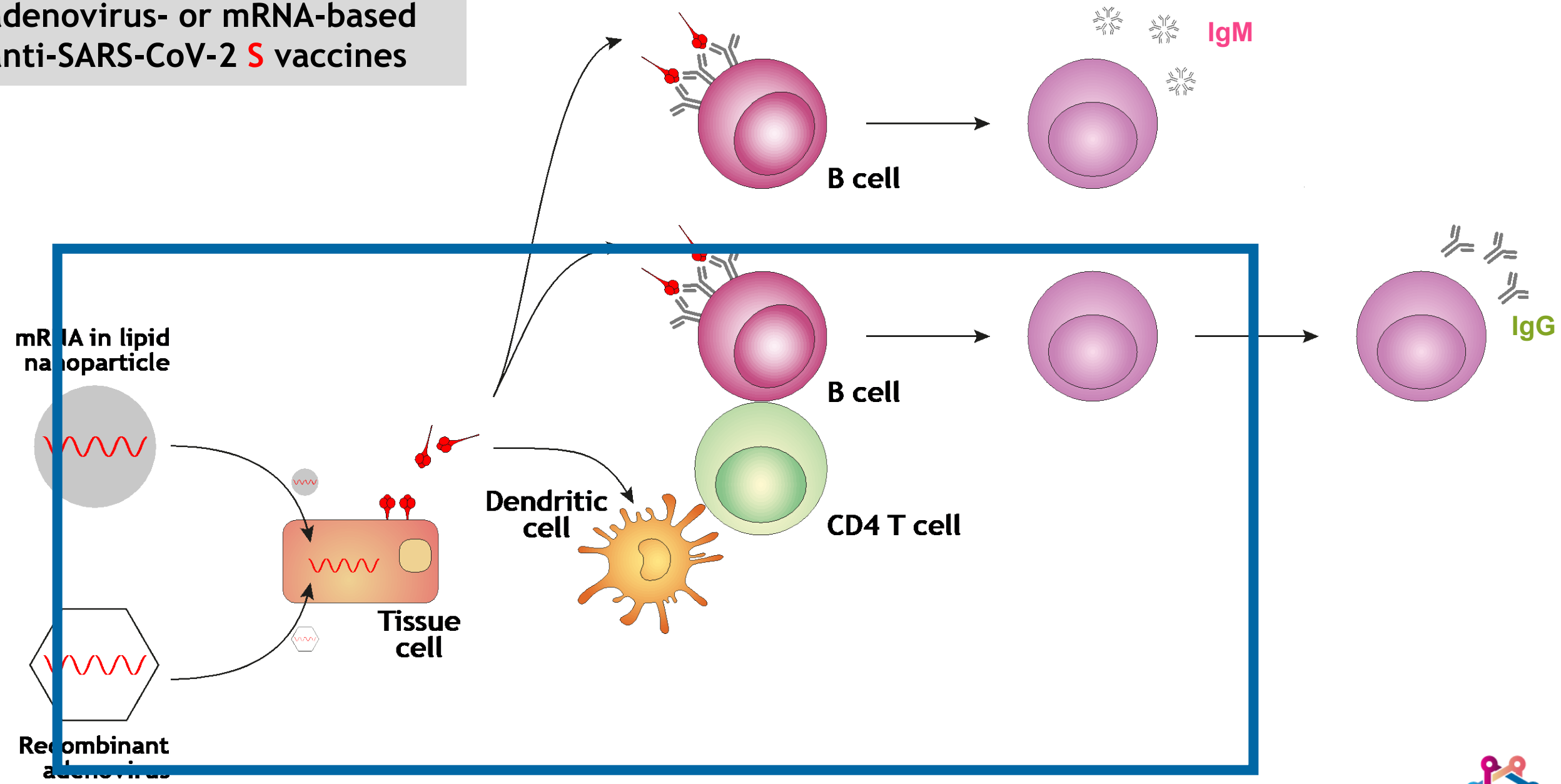

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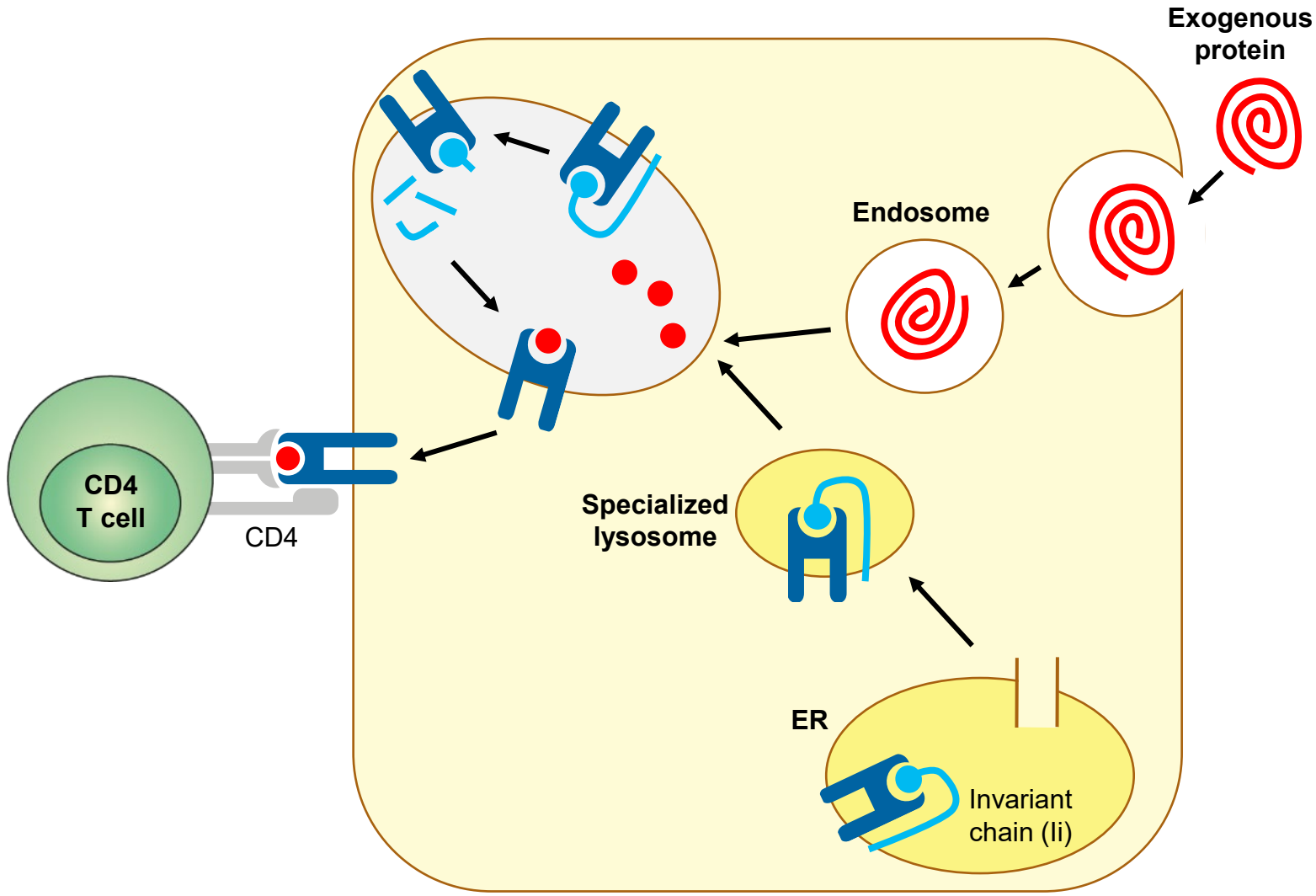
Canonical HLA class II antigen processing pathway

- HLA class II α- and β-chains assemble in the ER and form a complex with the invariant chain
- The heterotrimer is transported through the Golgi to the HLA class II compartment
- Endocytosed proteins and Ii are degraded by resident proteases
- The Ii fragment in the peptide-binding groove is exchanged for an antigenic peptide
- HLA class II molecules are transported to the plasma membrane to present antigenic peptides to CD4+ T cells



ER, endoplasmic reticulum; HLA, human leukocyte antigen; Ii, invariant chain; TAP, transporter associated with antigen presentation.
Neefjes et al. Nat Rev Immunol 2011;11:823–36.

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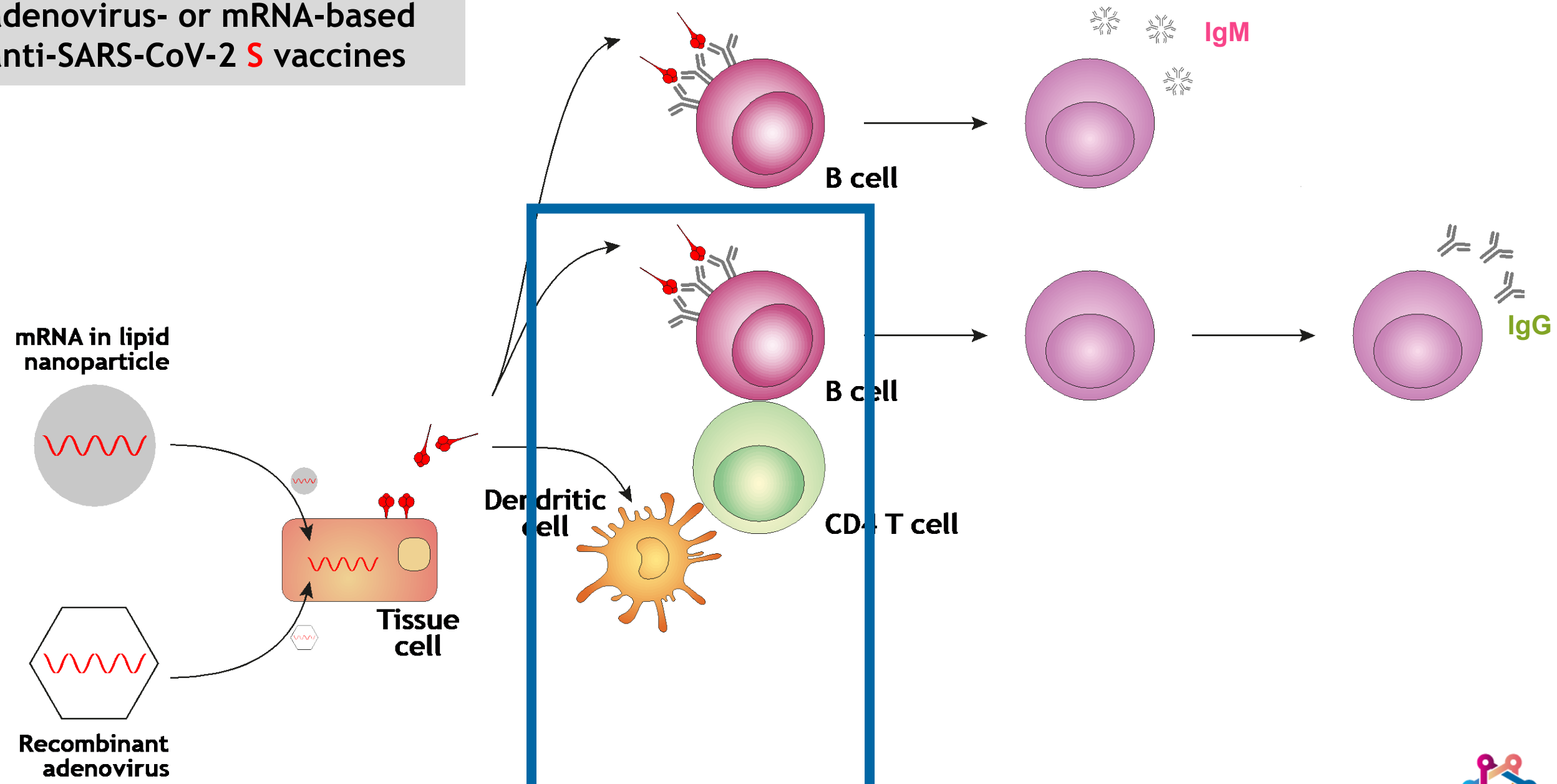

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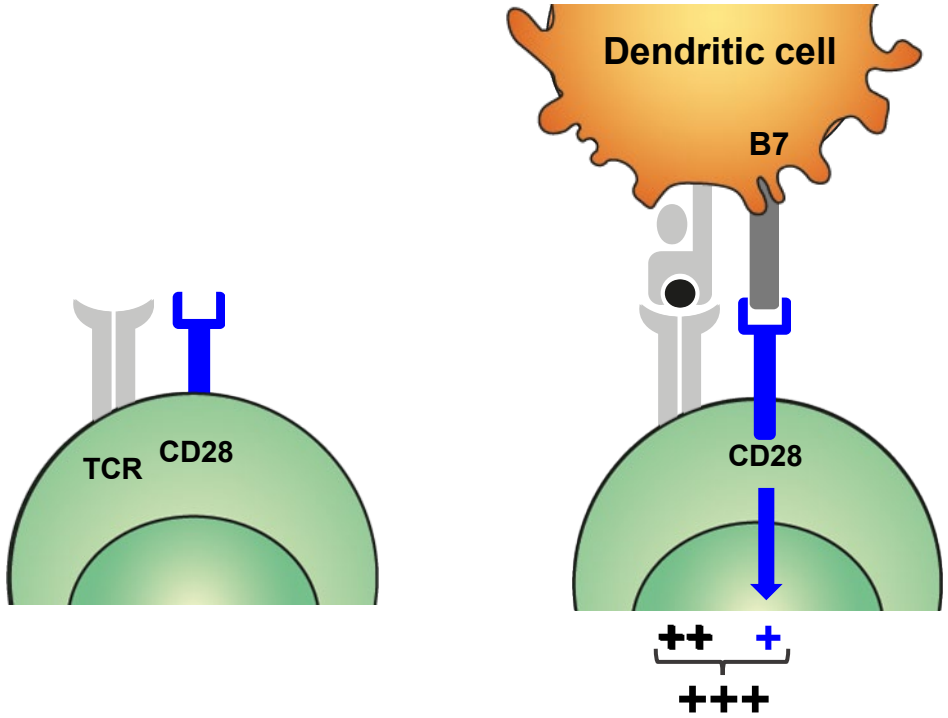
CD28: a stimulatory coreceptor required for T-cell priming

Naive T cell → **Priming** (first activation) → Proliferation, differentiation → **Antigen-experienced T cell**



CTLA-4, cytolytic T-lymphocyte-associated protein 4; DC, dendritic cell; PD-1, programmed cell death 1; PD-L1, programmed death-ligand 1; TCR, T-cell receptor.

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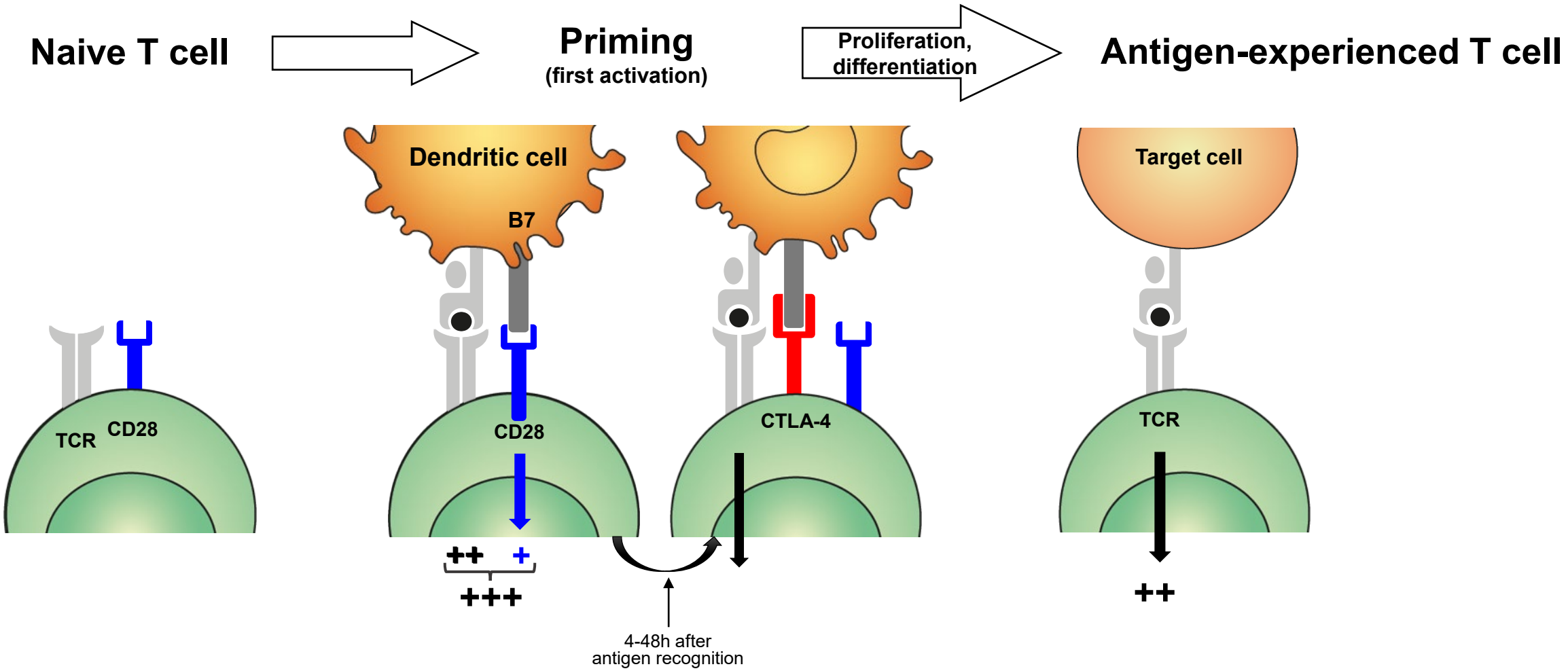

APC, antigen-presenting cell; CTLA-4, cytolytic T-lymphocyte-associated protein 4; DC, dendritic cell; PD-1, programmed cell death 1; PD-L1, programmed death-ligand 1; TCR, T-cell receptor.

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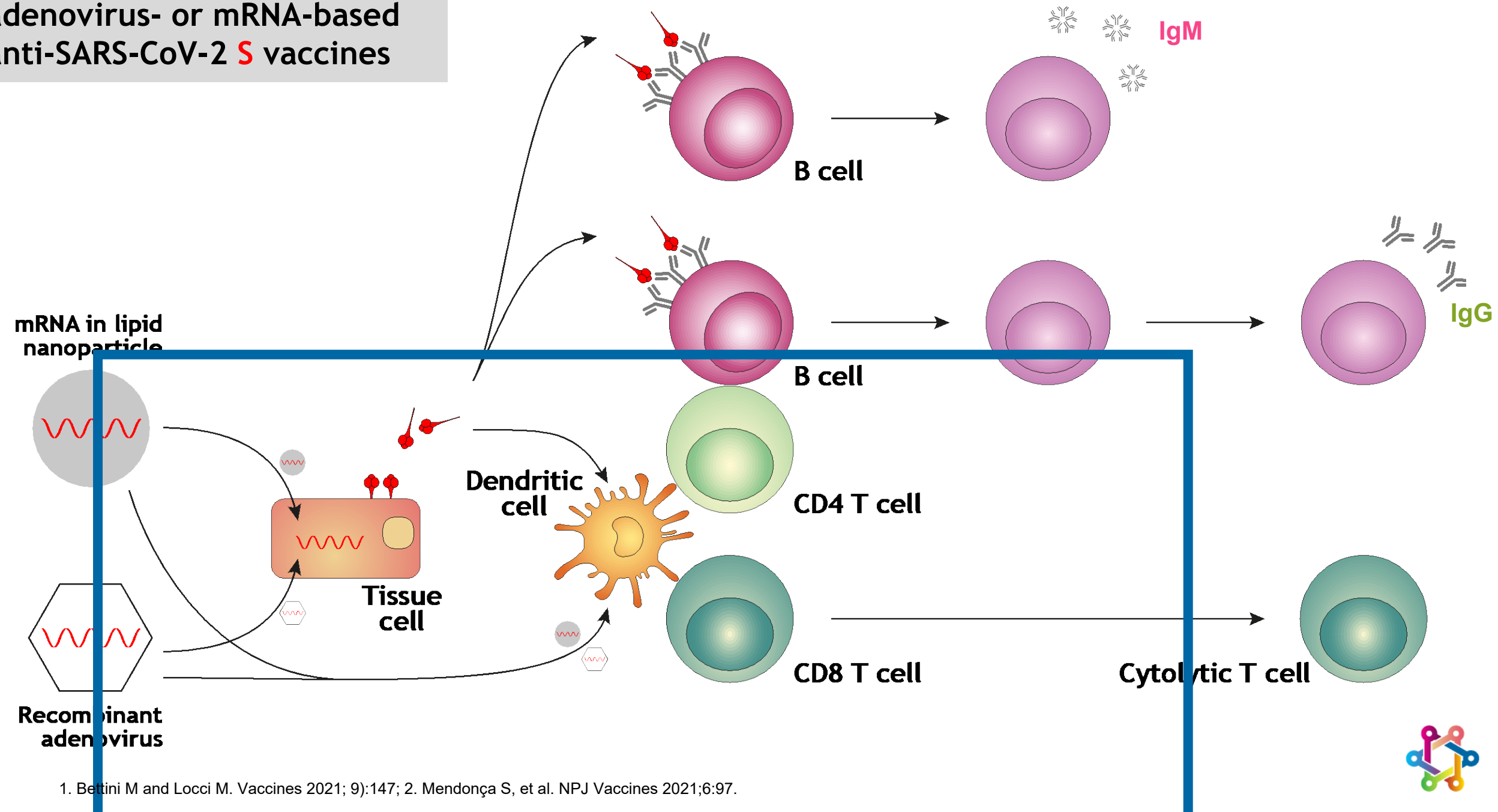

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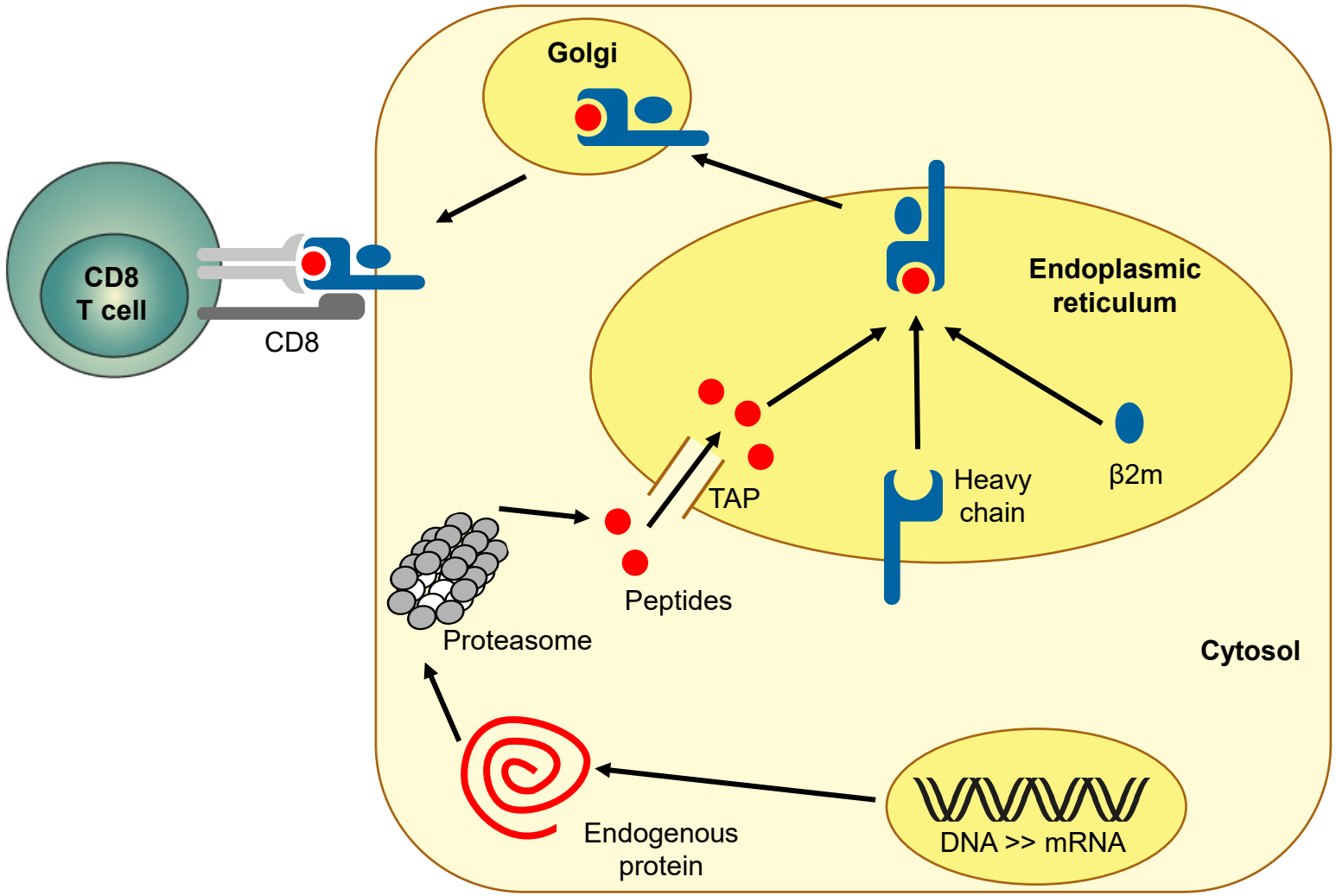
Canonical HLA class I antigen processing pathway

- Proteins are degraded by the proteasome
- Next, the resultant peptides are translocated by TAP into the ER lumen and loaded onto HLA class I molecules
- The peptide–HLA class I complexes are then released from the ER and transported via the Golgi to the plasma membrane
- The antigenic peptide is presented to CD8+ T cells



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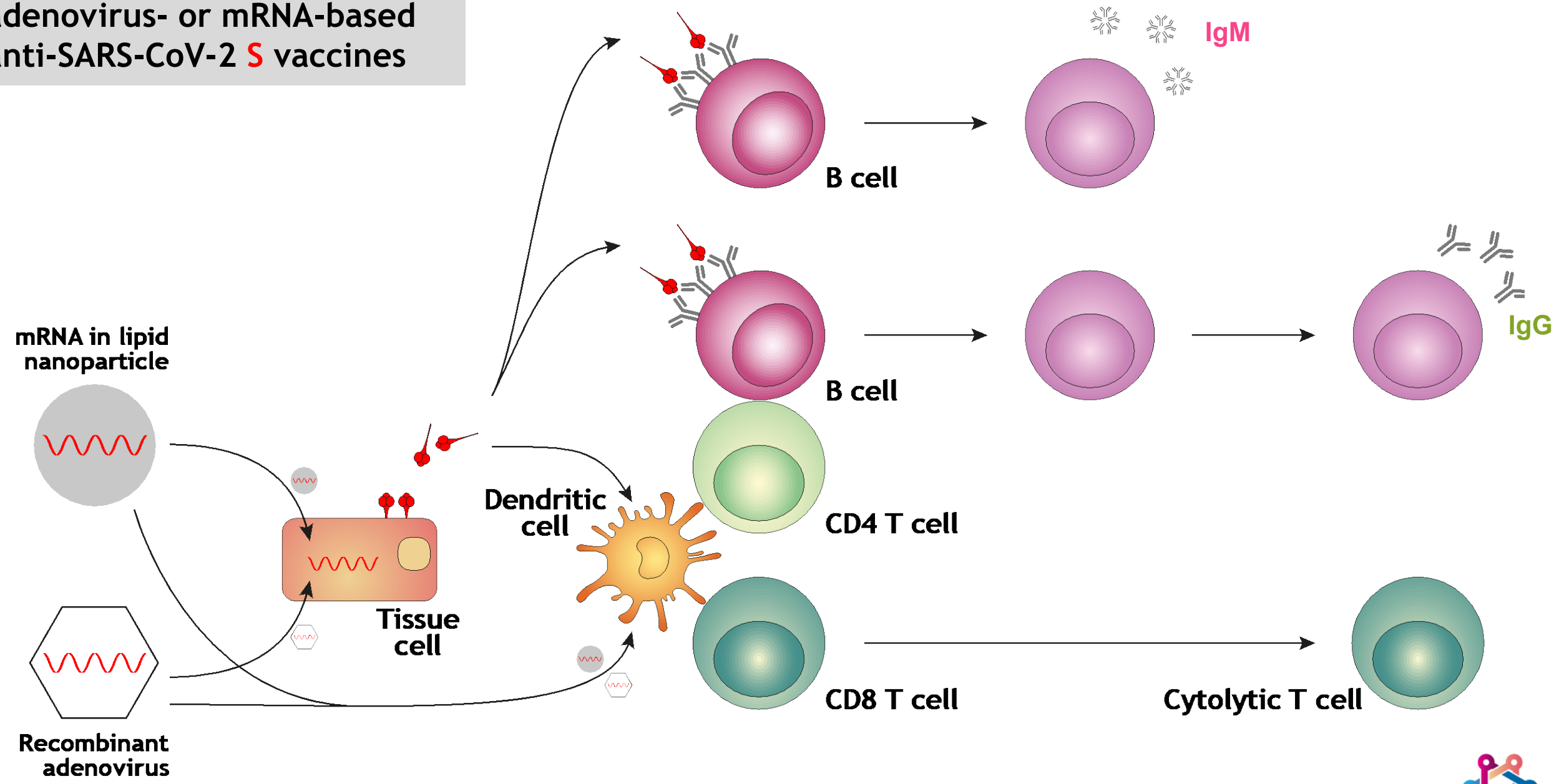

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- Adaptive immune response to these vaccines
- **Towards better vaccines?**

Towards better vaccines?

- Broader immunity, i.e. not limited to the S protein
- Stimulate the production of IgA, to protect nasopharyngeal mucosae
- Longer immunity and protection
- Better protection against variants