Moderna's latent & public health vaccines: EBV vaccines (mRNA-1189 & mRNA-1195)

Last program update: May 4, 2022

Modality	Program	ID #	Preclinical development	Phase 1	Phase 2	Phase 3	Commercial	Moderna rights
Latent vaccines	CMV vaccine	mRNA-1647						Worldwide
	EBV vaccine *(to prevent infectious mononucleosis)*	**mRNA-1189**						Worldwide
	EBV vaccine *(to prevent EBV sequelae)*	**mRNA-1195**						Worldwide
Prophylactic vaccines	HSV vaccine	mRNA-1608						Worldwide
	VZV vaccine	mRNA-1468						Worldwide
	HIV vaccines	mRNA-1644						Worldwide ***IAVI/others*** *funded*
		mRNA-1574						Worldwide ***BMGF/NIAID/ others*** *funded*
Public health vaccines	Zika vaccine	mRNA-1893						Worldwide ***BARDA*** *funded*
	Nipah vaccine	mRNA-1215	Open IND					Worldwide ***NIH*** *funded*

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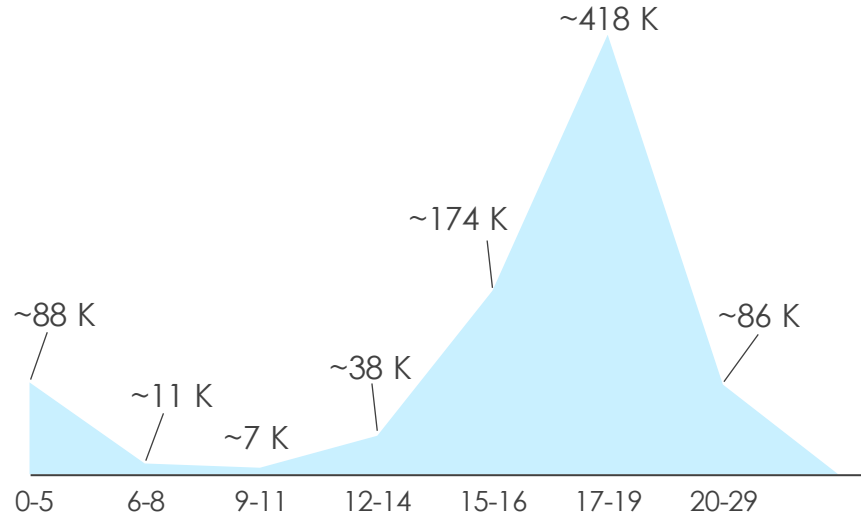
Epstein-Barr virus (EBV) is a major cause of infectious mononucleosis (IM)

- EBV is spread through bodily fluids (e.g., saliva) and **contracted primarily by young children and adolescents**

- **EBV is a major cause of infectious mononucleosis (IM) in the U.S.**, accounting for over 90% of the ~1+ million cases annually[1]
  - IM symptoms includes sore throat, lymphadenopathy, fever, body aches, fatigue and splenic rupture (rare complication)

U.S. Estimated Infectious Mononucleosis
Cases By Age Group (<30 years old) Per Year[2]



Modelling and not actual surveillance; Based on published study that observed Danish population, <30 years old, from 2006-2011

(1) Dunmire, Samanatha et al. *Curr Top Microbiol Immunol* (2015), https://doi.org/10.1007/978-3-319-22822-8_9
(2) Rostgaard, Klaus et al. *Plos One* (2019), https://doi.org/10.1371/journal.pone.0226436

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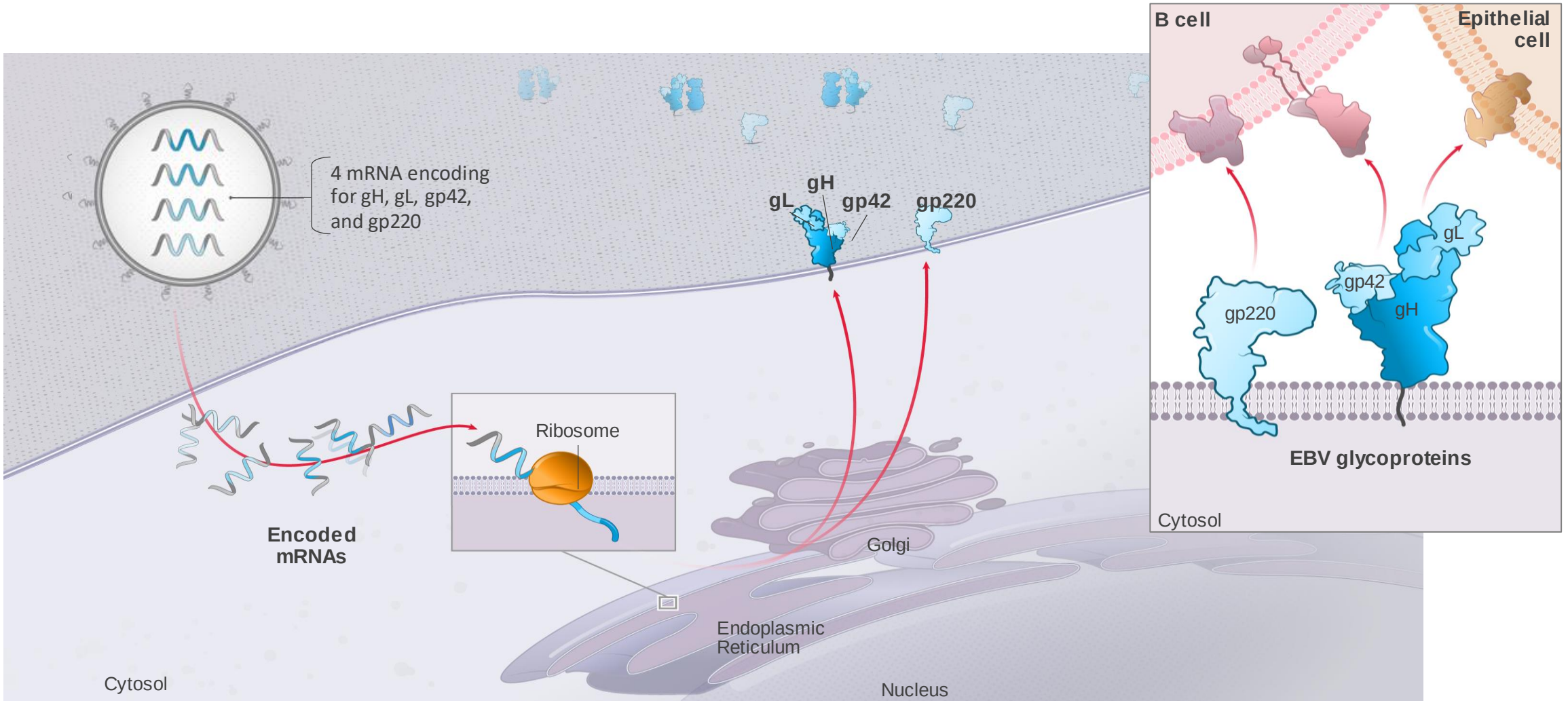
EBV vaccine (mRNA-1189) encodes for four antigens



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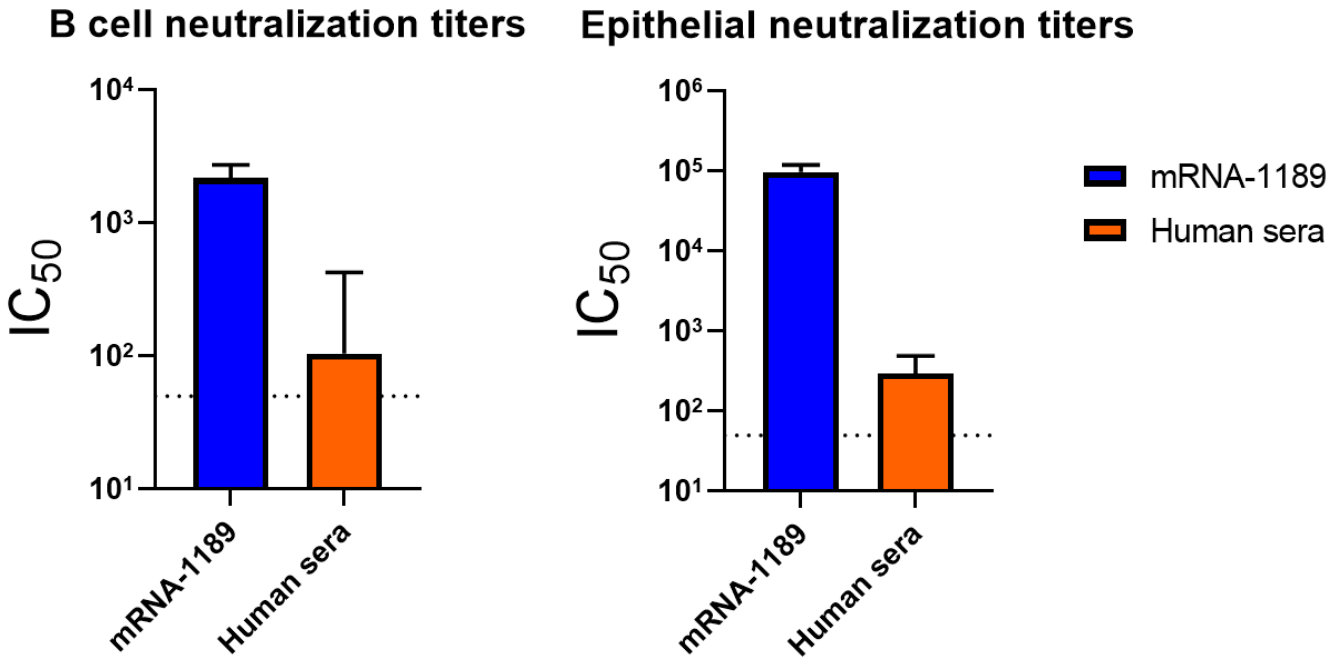
mRNA-1189 induces a robust immune response in preclinical animal studies



Results shown here represent eight animals per group and demonstrate high levels of neutralizing antibodies against B and epithelial cells, and at levels significantly higher than those observed in naturally-infected human sera

Naïve Balb/c mice were given two doses of a vaccine comprised of EBV antigens approximately three weeks apart. Neutralizing antibodies against B cell or epithelial cell infection were measured two weeks after the second dose using GFP-labeled virus. Neutralizing antibodies in a set of eight convalescent human sera were measured for comparison.
Dotted lines represent lower limit of detection.

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EBV vaccine (mRNA-1189) Phase 1 trial ongoing with the aim to reduce the rate of IM

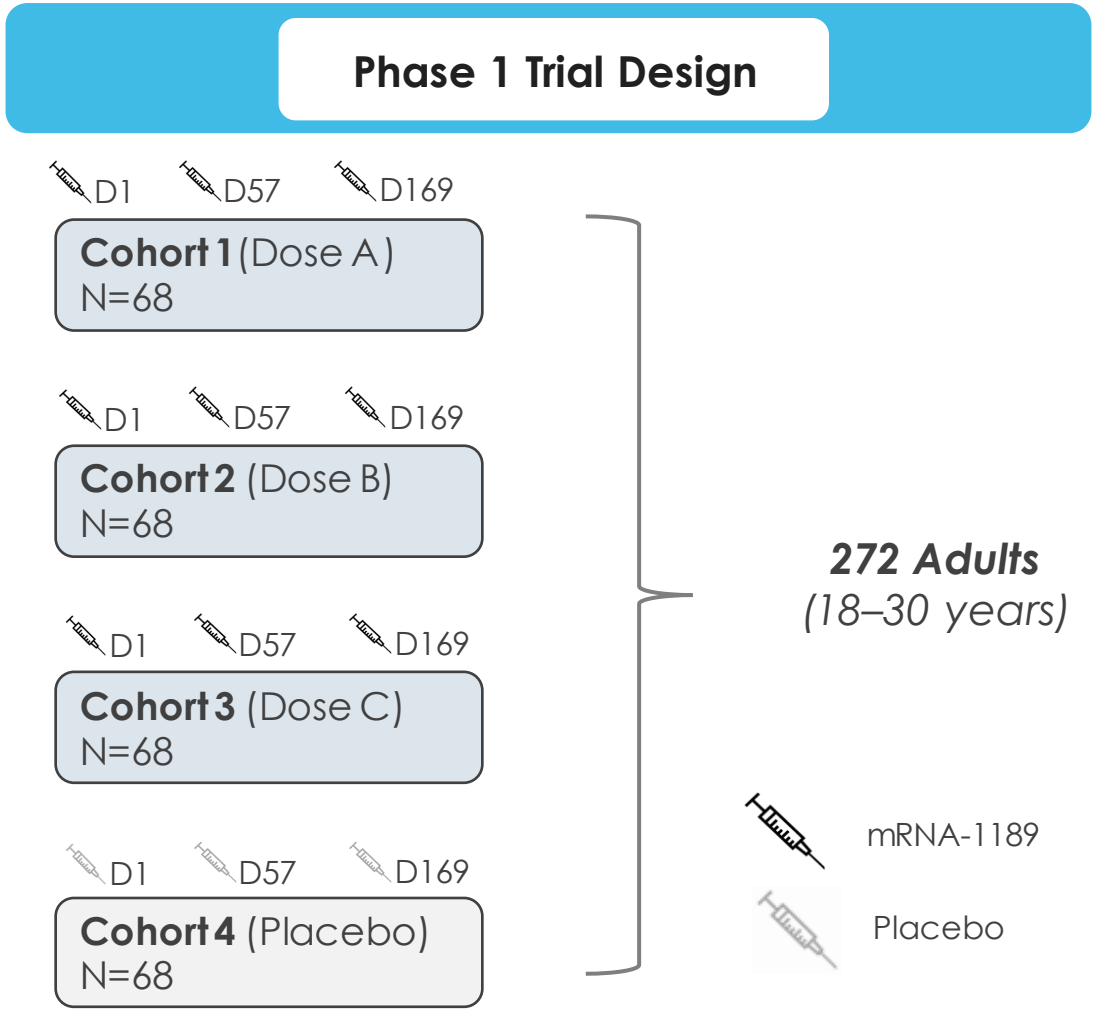
- Evaluating safety and reactogenicity of 3 different dose levels of an EBV vaccine

Outcome measures

- Safety and immunogenicity

Trial progress

- Enrollment started in December 2021
- Expansion phase ongoing



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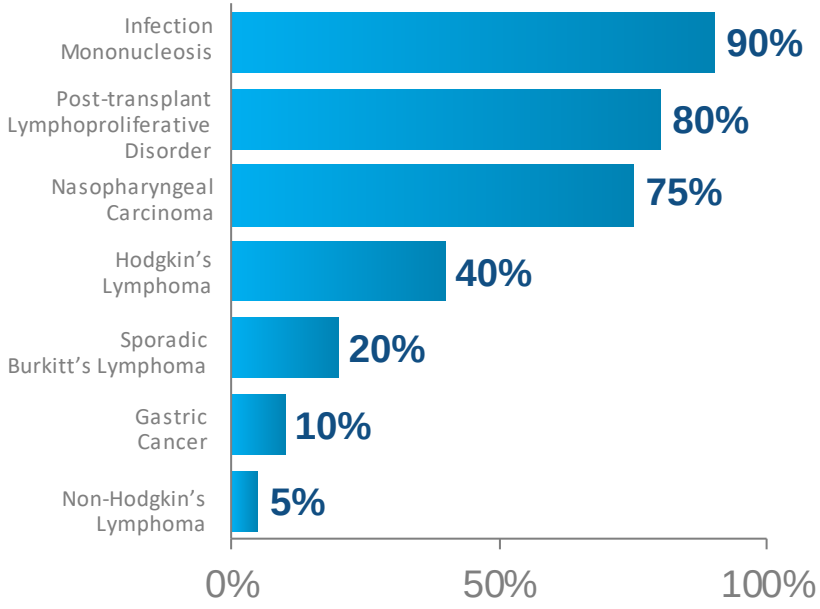
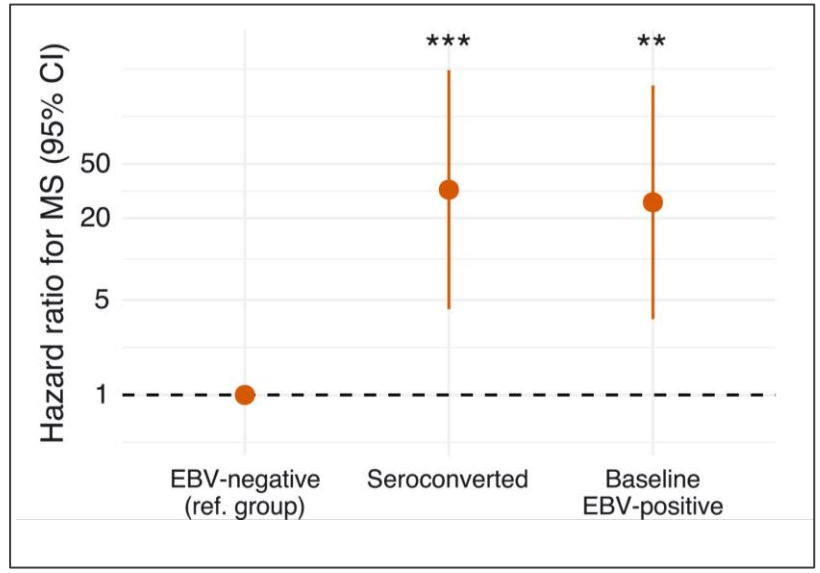
EBV also has significant long-term impacts

- **Lifetime associated risks include:**
  - Associated with certain lymphoproliferative disorders
  - Higher risk of developing cancers and autoimmune diseases
  - Increased risk of developing multiple sclerosis by ~32 fold
- **~90% EBV prevalence** in the U.S.

Association of Epstein-Barr Virus by Indication in the United States



Hazard ratio for MS in those who are EBV seropositive



Risk ratio for MS according to EBV status. Sample includes 955 incident MS cases among active-duty military personnel and 1,566 controls matched for demographics; three serum samples were collected before date of MS

Gequelin, Lucian, et al. *Rev Bras Hematol Hemoter* (2011), https://doi.org/10.5581/1516-8484.20110103
Bjornevik, Khetil et al, Science (2022), https://www.science.org/doi/10.1126/science.abj8222

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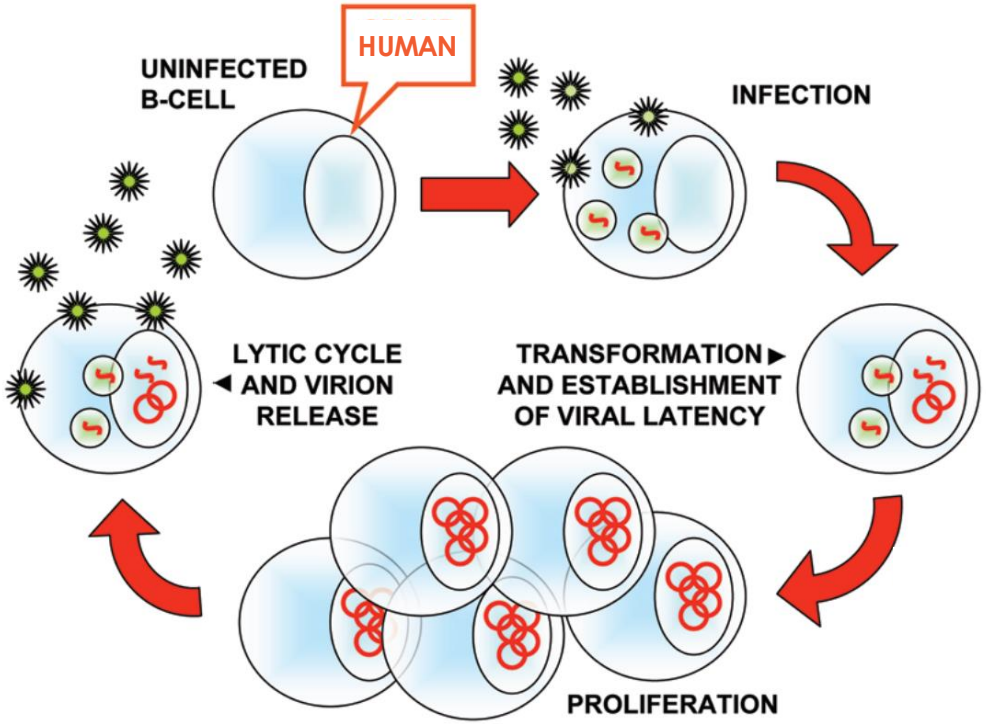
We are developing an EBV vaccine (mRNA-1195) against long-term EBV sequelae

EBV Vaccine (mRNA-1195)

- To prevent longer term sequelae of EBV infection
- Encodes for additional latent antigens
- Indications
  - Post-transplant lymphoproliferative disease (80% of PTLD cases can be attributed to EBV)
  - Multiple sclerosis
- In preclinical development



Gequelin, Lucian, et al. *Rev Bras Hematol Hemoter* (2011), https://doi.org/10.5581/1516-8484.20110103
Godshalk, Sirie et al. *Cell Cycle* (2008), https://doi.org/10.4161/cc.7.22.7120

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