



The mRNA Case File: A Chronological Reading List in Genetic Vaccine Development

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This chronological reading list builds a strong background of primary literature in the field of nucleic acid - based vaccines. It traces the key evidence behind genetic vaccination from early DNA transfer to modern mRNA vaccine design. Together, these papers reveal how successive advances in antigen expression, immune sensing, delivery, and clinical testing built the field as it exists today.

SECTION I Early DNA Vaccine Origins & Molecular Immunology Foundations (Weeks 1–4)

1.Wolff et al., 1990 Direct DNA transfer

a.Wolff et al., 1990 — Direct gene transfer into mouse muscle in vivo, a.Science, 247(4949 Pt 1):1465–1468

This paper sets a baseline: i.m. injected DNA can express proteins in muscle cells in vivo. Very simple methods make it a good first primary article for students.

Additional reading: Liu, 2011. DNA vaccines: an historical perspective (Gene Therapy)

2.Ulmer et al., 1993 DNA immunization protects against influenza

a.Ulmer et al., 1993. Science, 259(5102):1745–1749. Heterologous protection against influenza by injection of DNA encoding a viral proteinContains basic immunogenicity and challenge experiments. Introduces the CTL Assay

Additional reading: Donnelly et al., 1997. DNA vaccines: progress and challenges

3.Wang et al., 1993 DNA Vaccination against HIV

a.Wang et al., 1993. PNAS, 90(9):4156–4160. Gene inoculation generates immune responses against human immunodeficiency virus type 1

An early demonstration that DNA vaccines work for non-influenza antigens, with accessible techniques including plasmid injection, ELISA, western blot, and lymphocyte proliferation assays.

Additional reading: Liu, 2003. DNA vaccines: a review

4.Tang et al., 1992 Gene gun delivery of DNA

a.Tang et al., 1992 .Nature 356, 152–154 (1992). Genetic immunization is a simple method for eliciting an immune response.

Introduces gene gun DNA delivery — simple concept, minimal complex methods. Shows that delivery method matters.

Additional reading: Ulmer & Donnelly, 1998. DNA delivery systems





SECTION II Early mRNA Vaccine Foundations (Weeks 5–7)

5. Martinon et al., 1993 mRNA in liposomes induces CTLs

a. Martinon et al., 1993. Eur J Immunol. 1993 Jul;23(7):1719-22. Induction of virus-specific cytotoxic T lymphocytes in vivo by liposome-entrapped mRNA. First mRNA vaccine demonstration.

Additional reading: Pardi et al., 2018. mRNA vaccines: a new era in vaccinology

6. Hoerr et al., 2000 Unmodified mRNA induces T and B cell responses

a. Hoerr et al., 2000. 1. Eur J Immunol. 2000 Jan;30(1):1-7. In vivo application of RNA leads to induction of specific cytotoxic T lymphocytes and antibodies. Expands biological readouts and delivery approaches.

Additional reading: Weissman & Karikó, 2015 — Overview of mRNA therapeutic development

7. Petsch et al., 2012 Protective efficacy of in vitro transcribed mRNA vaccines against influenza in mice

a. Petsch et al., 2012. Nat Biotechnol. 2012 Dec;30(12):1210-6. Protective efficacy of in vitro synthesized, specific mRNA vaccines against influenza A virus infection

Optimized mRNA synthesis and antigen expression. Introduces more modern formulation but still avoids advanced ionizable lipid chemistry. Acts as a mid-semester difficulty bump.

Additional reading: Kramps & Elbers, 2017. mRNA vaccine technology (Curr Opin Immunology)

SECTION III Innate Immune Sensing, Modified Nucleosides, & Delivery Innovations (Weeks 8–11)

8. Karikó et al., 2005 Pseudouridine reduces innate sensing

a. Karikó K et al. (2005). Immunity. 23(2):165-75. Suppression of RNA recognition by Toll-like receptors: the impact of nucleoside modification and the evolutionary origin of RNA.

Foundational molecular immunology and nucleoside chemistry that makes RNA vaccinations a leading model.

Additional reading: Kawai & Akira, 2010 — Overview of innate immune sensing pathways (TLRs, RLRs)

9. Karikó et al., 2008 Incorporation of pseudouridine into mRNA yields superior translation and reduced immune activation

a. Karikó et al., 2008. Mol Ther. 2008 Nov;16(11):1833-40. Incorporation of pseudouridine into mRNA yields superior nonimmunogenic vector with increased translational capacity and biological stability.

Builds directly on the 2005 paper with more mechanistic detail. Demonstrates improved translation, cytokine reduction, and increased protein expression. Adds depth.

Additional reading: Mauger et al., 2019 — RNA structure and translation efficiency

10. Hassett et al., 2019 Optimization of lipid nanoparticles for RNA delivery

a. Hassett et al., 2019. Mol Ther Nucleic Acids. 2019 Apr 15;15:1-11. Optimization of Lipid Nanoparticles for Intramuscular Administration of mRNA Vaccines

Provides a pre-COVID view of LNP optimization. Introduces controlled variation of ionizable lipids, PEG-lipids, etc. Ideal preparation for the clinical-era work.

Additional reading: Hou et al., 2021 — Lipid nanoparticles for mRNA delivery (Nat Rev Mater)





SECTION IV COVID-19 Era Design, Immunogenicity, and Clinical Outcomes (Weeks 12–15)

11.Laczkó et al., 2020 Cell and Antibody responses

a.Laczkó et al., 2020. Immunity. 2020 Oct 13;53(4):724-732.e7. A Single Immunization with Nucleoside-Modified mRNA Vaccines Elicits Strong Cellular and Humoral Immune Responses against SARS-CoV-2 in Mice.

12.Corbett et al., 2020 Moderna antigen design study

a.Corbett et al., 2020 . Nature 586, 567–571 (2020). SARS-CoV-2 mRNA vaccine design enabled by prototype pathogen preparedness.

Prototype pathogen preparedness, spike modification rationale.

Additional reading: Graham, 2020 — Review on the prototype pathogen preparedness program

& Saunders et al., 2020 — “COVID preclinical vaccine design” summary commentary

13.Walsh et al., 2020 Pfizer–BioNTech Phase

a.Walsh et al., 2020. N Engl J Med. 2020 Dec 17. Safety and Immunogenicity of Two RNA-Based Covid-19 Vaccine Candidates.

Early human data with dose finding

Additional reading: Corey et al., 2020 — “Rapid COVID-19 vaccine development” (NEJM editorial)

14.Vogel et al., 2021 Vaccine protects rhesus macaques

a.Vogel et al., 2021. Nature 592, 283–289 (2021). BNT162b vaccines protect rhesus macaques from SARS-CoV-2. Core preclinical study explaining why BioNTech selected BNT162b2 over BNT162b1.

Deep insight into antigen selection, immune profiling, and comparative immunology.

Excellent precursor to clinical trials (Baden).

Additional reading: Sahin & Türeci, 2021 — Commentary on BioNTech vaccine design

15.Baden et al., 2021 — Moderna Phase 3

a.Baden et al., 2021. N Engl J Med. 2021 Feb 4. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine.384(5):403-416

Additional reading: McGill et al., 2021 — Vaccine efficacy review commentary

& Polack et al., 2020 (Pfizer Phase III)