# CANCER VACCINES: LESSONS FROM INFECTIOUS DISEASE IMMUNOLOGY

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**ABSTRACT**

The development of cancer vaccines marks a promising frontier in immuno-oncology, one built on decades of progress in infectious disease immunology. Shared principles from infectious disease vaccination such as antigen presentation, dendritic cell activation, and the generation of durable T-cell memory continue to inform cancer vaccine development. Drawing on core concepts such as immunological memory, antigen presentation, T-cell priming, and adjuvant selection, this literature review explores how successful infectious disease vaccines have inspired both prophylactic (e.g., Gardasil-9) and therapeutic (e.g., Sipuleucel-T) cancer vaccines. However, cancer presents unique challenges: tumours often express self-antigens, evolve rapidly, and create immunosuppressive microenvironments that blunt vaccine efficacy. The recent success of COVID-19 messenger ribonucleic acid (mRNA) vaccines has catalysed interest in personalised mRNA-based cancer vaccines targeting tumour-specific neoantigens. This highlights the interdisciplinary nature of cancer immunotherapy, merging genomics, bioinformatics, and immunology to tailor interventions to the individual tumour profile. This review examines the intersections between infectious disease immunology and cancer immunotherapy, demonstrating how the understanding of pathogen-specific immunity informs vaccine-based strategies against cancer. By tracing the immunological and translational connections between infectious diseases and immuno-oncology, this literature review situates cancer vaccines within the broader theme of interconnectedness not only between diseases, but also across scientific disciplines.

## INTRODUCTION

Cancer remains a leading global health challenge, responsible for an estimated 10 million deaths (1 in 6 deaths) in 2020 (WHO, 2025). It is also one of the most prevalent chronic diseases worldwide, with approximately 19.3 million new cases reported annually and a projected rise to nearly 30 million by 2040 (Sung et al., 2021). Despite substantial improvements in early detection and therapy, the five-year survival rate for many cancers, such as pancreatic and lung cancer, remains below 20%, underscoring the urgent need for more effective interventions (Siegel et al., 2024).

Treatment strategies for cancer are multifaceted, encompassing surgery, chemotherapy (use of chemical drugs to kill fast growing cells in the body), and radiotherapy (use of high energy radiation to kill cancer cells). These treatments often lack specificity and can have severe side effects (Baskar et al., 2012). Over the past two decades, immunotherapy (use of biologics to harness the power of the immune system to kill cancer cells) has transformed the field of oncology, demonstrating the potential of mobilising immunity against tumours (Zhang and Zhang, 2020). Well-known examples include immune checkpoint inhibitors and Chimeric Antigen Receptor (CAR)-T cells, a patient's own T cells that have been genetically engineered to express a CAR, allowing them to better recognise and destroy cancer cells (Mateusz Kciuk et al., 2023). However, one area of immunotherapy that remains underdeveloped is cancer vaccination. Vaccine strategies originated as a method of infectious disease treatment, where they have been successful. However, these strategies have had limited success in oncology (Fan et al., 2023).

Cancer vaccines can be broadly divided into two categories: prophylactic vaccines, which aim to prevent cancer from developing in the first place, and therapeutic vaccines, which aim to stimulate the immune system to attack established tumours (Lei et al., 2025). Prophylactic vaccines have already shown striking success in virus-associated cancers: the hepatitis B virus (HBV) vaccine reduces the risk of hepatocellular carcinoma, and the human papillomavirus (HPV) vaccine prevents cervical and other anogenital cancers (Schiller and Lowy, 2018). These landmark achievements provide evidence that vaccination can be a powerful tool in oncology. However, extending these successes to therapeutic vaccines that target non-viral cancers has proven far more challenging (Fan et al., 2023).

At the heart of this difficulty lies the biology of cancer. Unlike pathogens, tumours arise from the body's own cells, displaying only subtle molecular differences, which make it harder for the immune system to detect. Yet, there are several parallels between infection and malignancy (uncontrolled division of cancer cells): both rely on antigen recognition, T-cell activation, and durable immune memory. Borrowing immunological tools and principles from infectious disease vaccinology (including antigen design, adjuvants, and immune memory) could inform the next generation of cancer vaccines, helping overcome obstacles such as tumour antigen variability and immune evasion (Fan et al., 2023).

By comparing the principles of successful infectious disease vaccines with the unique challenges posed by cancer, this review explores how decades of vaccine research can inform the design of innovative therapies. Framing cancer within this wider

immunological landscape highlights an interconnectedness that crosses disease boundaries; the same immune strategies that protect us from viruses and bacteria could, with careful adaptation, be harnessed to combat malignancy.

## SIMILARITIES BETWEEN INFECTIOUS DISEASE AND CANCER IMMUNOLOGY

Despite their differences, infectious diseases and cancer share fundamental immunological principles. Both require recognition of abnormal molecular patterns and targeted immune activation (Liu and Zeng, 2012).

A central similarity lies in antigen presentation and T-cell activation. Pathogen-derived antigens (molecular fragments that signal the presence of infection) are processed by antigen-presenting cells (immune cells that capture and display antigens). These processed antigens are then displayed on the major histocompatibility complex (MHC: a molecular display platform that helps the immune system recognise what belongs to the body and what does not). This in turn activates $CD4^+$ helper T cells, which coordinate immune responses and $CD8^+$ cytotoxic T cells, which kill infected or abnormal cells. Tumour antigens are presented in a similar way, though cancers often evade detection by downregulating MHC or inducing tolerance (Schumacher and Schreiber, 2015).

Another crucial lesson learnt from infectious disease immunology comes from the role of adjuvants, which are substances that enhance the effect of another drug and boost the immune response. Infectious disease vaccines use adjuvants such as aluminium salts or toll-like receptor ligands to stimulate the innate immune system and enhance responses (Lavelle and McEntee, 2024). Cancer vaccines similarly require strong adjuvants to overcome immune tolerance and boost responses to tumour antigens (Temizoz et al., 2016). Recent advances, such as STING agonists (compounds that activate the Stimulator of Interferon Genes pathway, a crucial part of innate immune response) and CpG oligonucleotides (synthetic DNA molecules with unmethylated cytosine-guanine, mimicking bacterial and viral DNA, hence activating the immune response), illustrate how tools originally studied in infectious disease immunology are being repurposed for oncology (Kranz et al., 2016; Corrales et al., 2016).

Finally, both fields are exploring innovative vaccine platforms. While traditional peptide vaccines have limited potency, viral vectors enhance antigen delivery and immunogenicity (Mellman et al., 2011). The rapid success of messenger ribonucleic acid (mRNA) vaccines against SARS-CoV-2 has reinvigorated cancer vaccine research, with personalised mRNA platforms encoding tumour neoantigens under clinical investigation (Sahin and Türeci, 2018).

Together, these parallels highlight how infectious disease vaccinology provides not only a conceptual framework but also practical tools for advancing cancer immunotherapy.

## UNIQUE CHALLENGES IN CANCER

Despite shared mechanisms, several unique obstacles have hindered the development of effective cancer vaccines.

Self-antigen tolerance and central deletion pose a fundamental barrier. As most tumour-associated antigens are derived from normal self-proteins, T cells recognising them with high affinity are often deleted during thymic development (the process by which the thymus gland, a primary immune organ, matures and produces a diverse pool of T cells). This process, called central deletion, prevents autoimmunity. As a result, cancer vaccines must work with a T-cell repertoire that is relatively tolerant to tumour antigens (Rosenberg and Restifo, 2015). This contrasts sharply with infectious disease vaccines, which benefit from a naïve immune system capable of generating strong responses to non-self antigens.

Tumour heterogeneity and mutational burden complicate vaccine design. Cancers often accumulate numerous mutations, creating a highly diverse set of antigens both within a single tumour and between patients. While this diversity produces potential neoantigens, only a subset are immunogenic or presented on MHC molecules (McGranahan et al., 2016). This means that ‘one-size-fits-all’ vaccines are unlikely to succeed, requiring personalised approaches. Additionally, unlike infectious diseases, cancer prevention cannot benefit from herd immunity, as tumours arise independently in each patient. This necessitates optimising individualised vaccine responses (Finn, 2018).

The immunosuppressive tumour microenvironment is a major barrier to vaccine efficacy. Tumours actively recruit regulatory T cells and myeloid-derived suppressor cells. They also secrete inhibitory signalling proteins called cytokines such as Transforming growth factor-beta (TGF-β) and interleukin-10 (IL-10), which dampen anti-tumour immune responses (Binnewies et al., 2018). In addition, immune checkpoint molecules like Program death-ligand 1 (PD-L1) expressed on tumour or stromal cells can inactivate cytotoxic T lymphocytes, counteracting vaccine-induced immunity. Finally, tumours employ a range of immune evasion strategies that differ from pathogens such as downregulating antigen presentation, upregulating inhibitory ligands, and even inducing metabolic conditions (e.g., hypoxia, nutrient depletion) that impair T-cell function (Joyce and Fearon, 2015).

These challenges explain why progress in therapeutic cancer vaccination has been slower than in infectious disease vaccinology, highlighting the need for innovative, cancer-specific strategies.

## TRANSLATIONAL SUCCESS STORIES

Despite the barriers faced by therapeutic cancer vaccines, several notable successes demonstrate that vaccination can meaningfully contribute to cancer prevention and treatment.

The most striking achievements come from prophylactic vaccines against virus-driven cancers (Gupta et al., 2023). The hepatitis B virus (HBV) vaccine has substantially reduced the global incidence of hepatocellular carcinoma in vaccinated populations, especially in endemic regions such as East Asia (Chang et al., 2009). Similarly, the human papillomavirus (HPV) vaccine has been transformative in reducing precancerous cervical lesions and is expected to drastically lower cervical cancer incidence worldwide (Schiller and Lowy, 2014). These successes show that vaccines can protect against malignancies when a viral oncoprotein acts as the initiating carcinogen (Enokida et al., 2021).

Progress in therapeutic vaccines has been slower, but landmark examples exist. The most prominent is Sipuleucel-T (brand name: Provenge®), the first US Food and Drug Administration approved therapeutic cancer vaccine, licensed in 2010 for metastatic castration-resistant prostate cancer. This personalised cell-based vaccine involves ex vivo activation of a patient's antigen presenting cells with a fusion protein (Prostatic Acid Phosphatase [PAP] and Granulocyte-Macrophage Colony-Stimulating Factor [GM-CSF]), followed by reinfusion to stimulate an anti-tumour immune response. Although its survival benefit was modest (median - 4.1 month improvement), Sipuleucel-T validated the principle that immune activation via vaccination can extend survival in late-stage cancer (Kantoff et al., 2010).

Another promising direction comes from mRNA vaccines, which have gained popularity following the success of COVID-19 vaccines. Companies such as BioNTech and Moderna are now testing personalised mRNA vaccines encoding patient-specific tumour neoantigens in melanoma and other cancers. Early clinical trials have shown encouraging immune responses and signals of improved progression-free survival (Lorentzen et al., 2022). These findings suggest that the flexibility and rapid manufacturing of mRNA platforms could overcome the hurdle of tumour heterogeneity, allowing highly personalised vaccine strategies.

Other notable examples of translational success stories include peptide-based vaccines combined with checkpoint blockade and dendritic cell vaccines, which are both under investigation across multiple tumour types (Mellman et al., 2011). Collectively, these translational milestones show that therapeutic cancer vaccines are transitioning from conceptual to clinical reality.

## PUBLIC HEALTH AND COMMUNICATION ASPECTS

Beyond laboratory and clinical innovation, the success of cancer vaccines will depend heavily on public trust, effective communication, and equitable access. Translating scientific breakthroughs into public health impact requires navigating societal perceptions, health policy, and global disparities.

Public perception of vaccines has historically shaped their success. The rollout of the HPV vaccine illustrates this challenge; early adoption faced resistance due to misinformation, perceived moral implications, and safety concerns (Gamble et al., 2009). However, reframing the narrative around cancer prevention rather than infection substantially improved acceptance, especially when supported by school-based immunisation programmes (Bruni et al., 2016). This lesson highlights the importance of framing cancer vaccines as lifesaving, evidence-based interventions rather than experimental treatments.

The COVID-19 pandemic profoundly altered public discourse around vaccination. The rapid deployment of mRNA vaccines showcased the potential of this technology while also revealing public anxieties about scientific speed and trust in institutions (Ball, 2020). Importantly, the pandemic demonstrated that widespread confidence can be achieved through transparent communication and clear evidence of efficacy. For cancer vaccines, leveraging this increased familiarity with mRNA technology could foster acceptance, but only if communication remains clear, accessible, and grounded in data (Dolgin, 2021).

At the same time, inequities in vaccine access remain a major concern. Global distribution of COVID-19 vaccines was starkly unequal, with low and middle-income countries receiving doses years later than high-income nations (Tatar et al., 2021). A similar pattern could emerge for cancer vaccines if they rely on expensive production pipelines. Prophylactic vaccines like HBV and HPV demonstrate that equitable implementation is achievable and can have profound public health impact in low-resource settings, especially when supported by strong health infrastructure (Chang et al., 2009; Bruni et al., 2016).

Finally, public messaging for therapeutic cancer vaccines must distinguish them from traditional prophylactic vaccines. Whereas infectious disease vaccines prevent transmission, cancer vaccines aim to treat or prevent recurrence at an individual level. Managing these expectations is essential to avoid misunderstanding or misplaced scepticism (Finn, 2018). By maintaining scientific transparency, prioritising affordability, and investing in community-based education, cancer vaccine developers can build the trust necessary for long-term success.

## CONCLUSION

The development of cancer vaccines represents both a scientific and conceptual bridge between oncology and infectious disease immunology. While progress has been slower than in traditional vaccinology, the similarities between the two fields offer valuable lessons. Decades of research into antigen design, immune activation, and vaccine delivery have provided a strong foundation on which cancer immunologists can build.

However, the challenges unique to cancer (self-tolerance, tumour heterogeneity, and an immunosuppressive microenvironment) demand innovative approaches that extend beyond existing models. The success of mRNA vaccines during the COVID-19 pandemic has reignited hope, proving that rapid, adaptable vaccine technologies are possible when research, policy, and public engagement align.

Moving forward, the future of cancer vaccines will rely on interconnectedness at every level: between innate and adaptive immunity, between laboratory science and clinical practice, and between researchers and the public. Collaboration across disciplines will be essential in overcoming biological and societal barriers alike.

Ultimately, by reimagining the immune system not only as a defence against infection but as a therapeutic partner in the fight against cancer, we stand at the threshold of a new era in medicine, one where lessons from infectious disease immunology pave the way toward truly personalised and preventive cancer care.

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