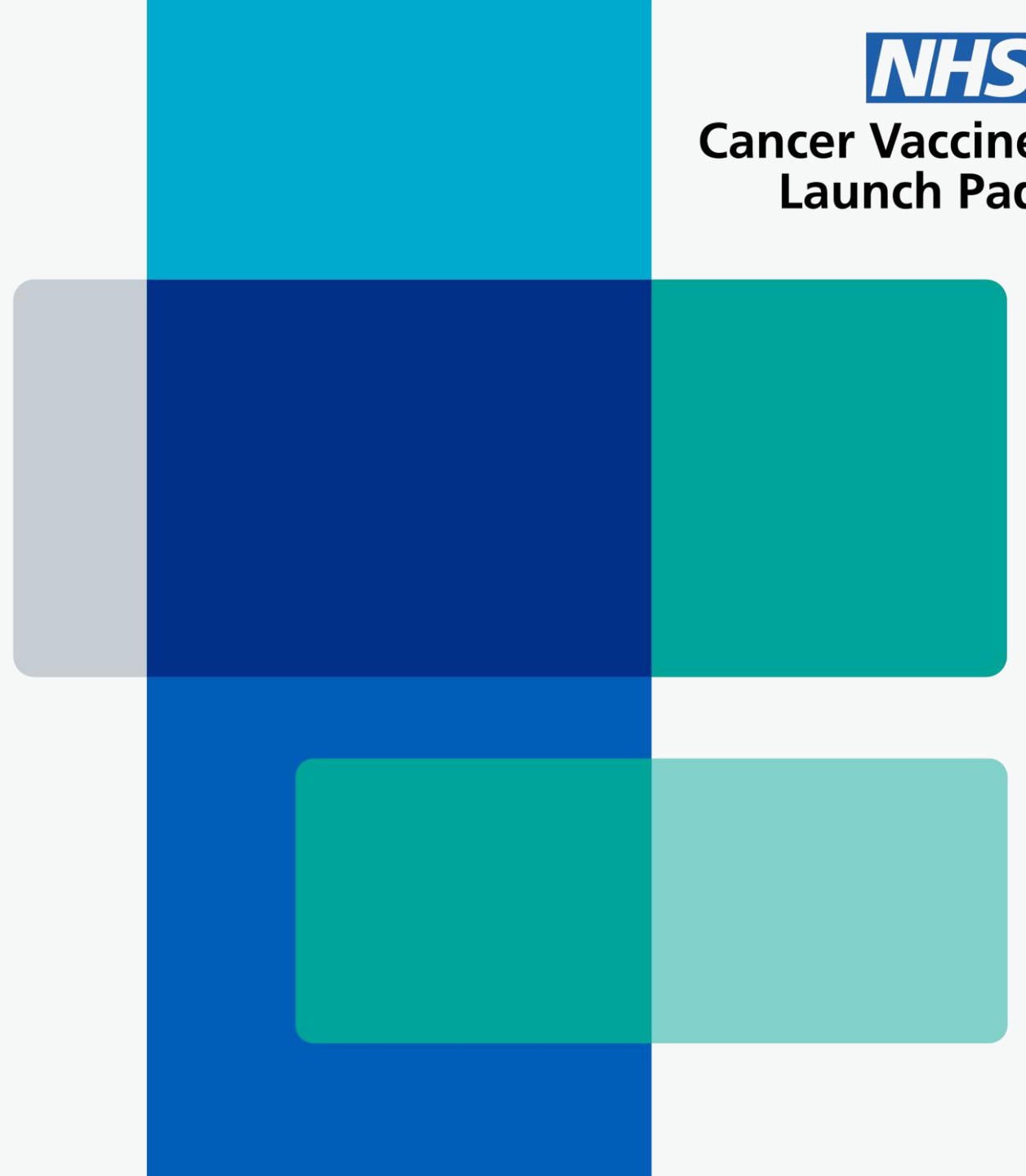


# Cancer Vaccines – now and in the future.

**Dr Dan Muller**

Cancer Vaccine Launch Pad Clinical Liaison Lead -  
Southampton Clinical Trials Unit

Honorary SpR in Medical Oncology –  
University Hospital Southampton



What is a cancer vaccine?

Brief history – how did we get to now?

How do cancer vaccines work?

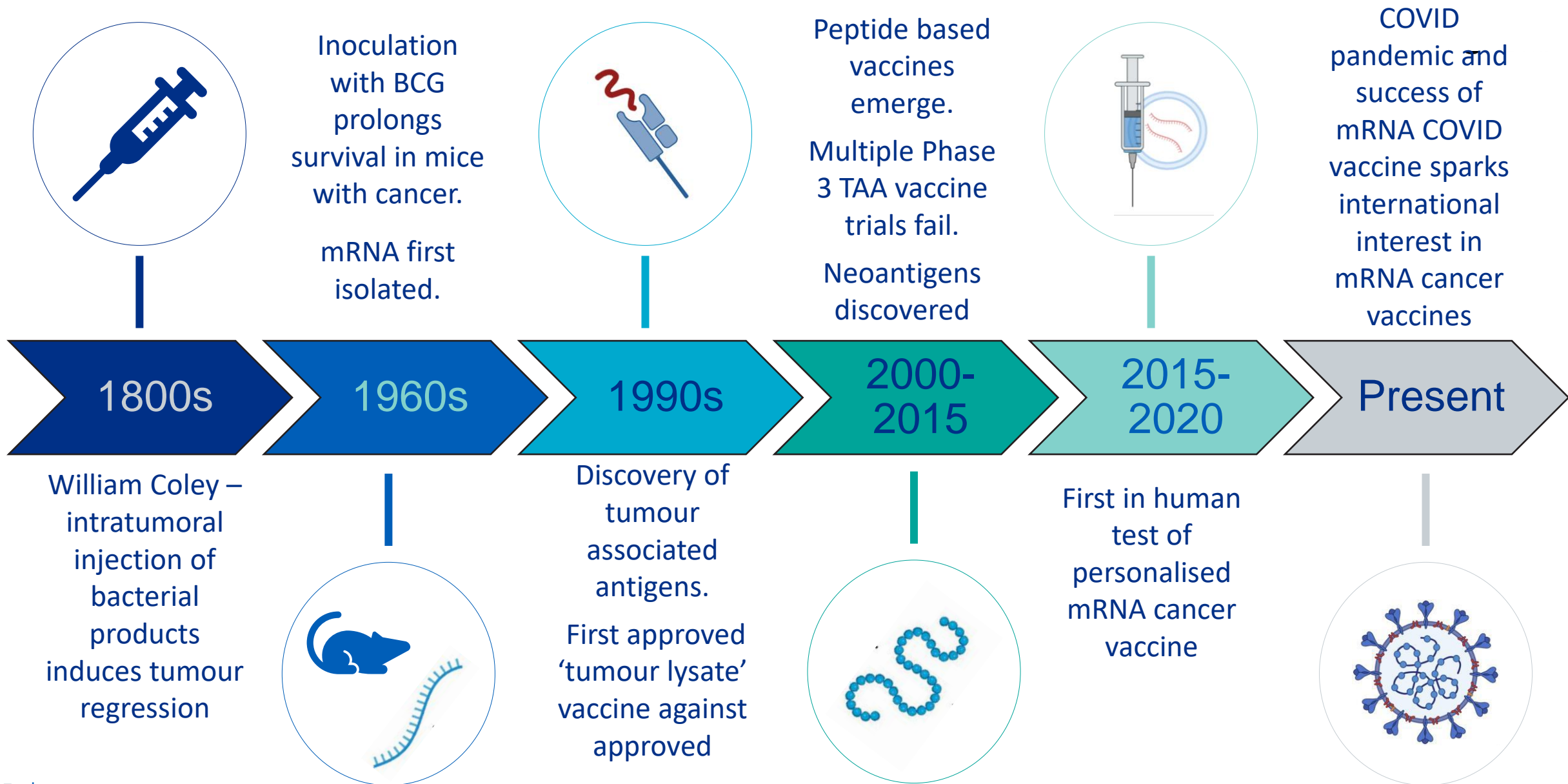
The types of cancer vaccines

mRNA vaccines

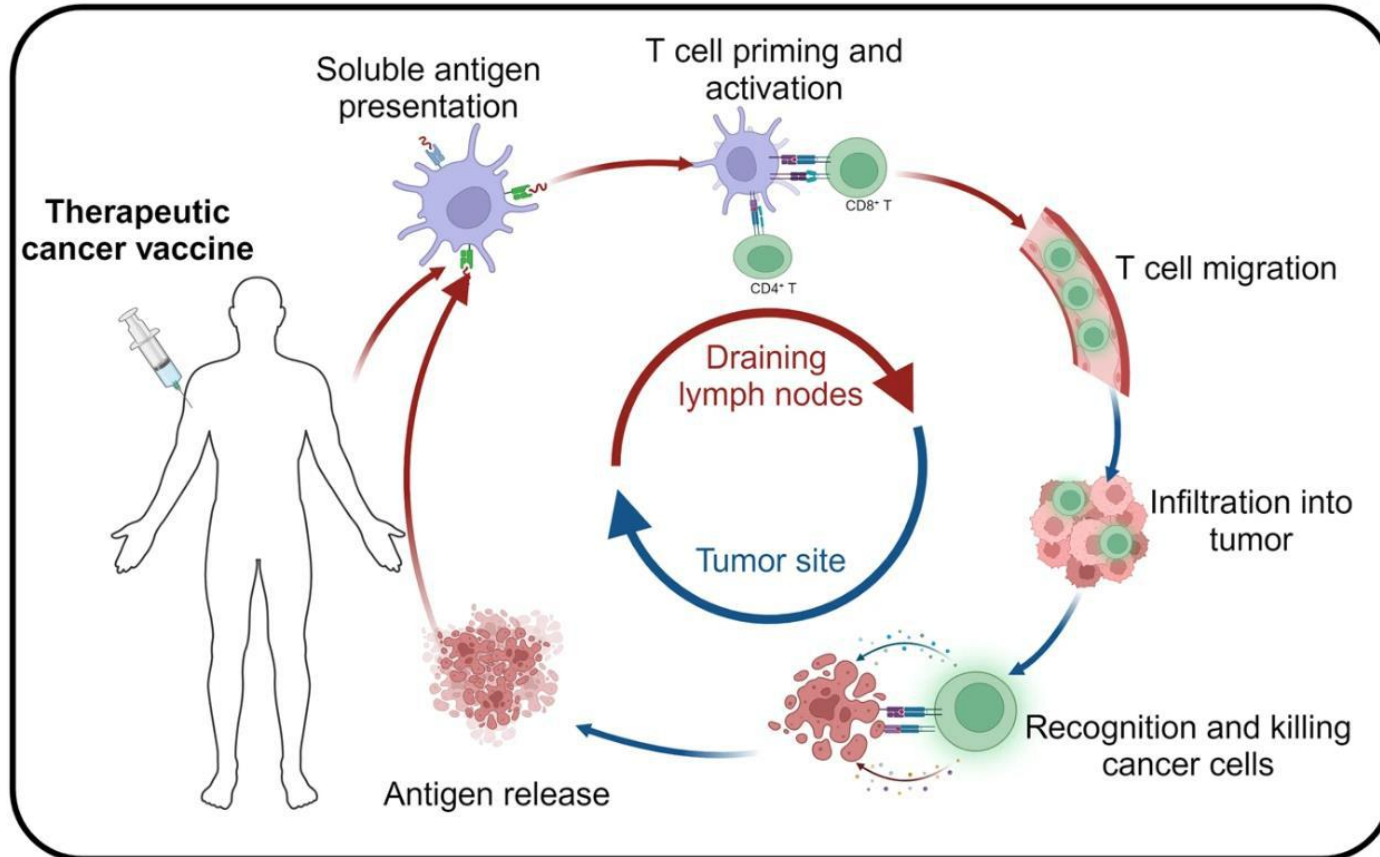
What is a cancer vaccine?

# **'Therapeutic' vs 'Preventative' Cancer Vaccine?**

# Brief History



# How do cancer vaccines work?



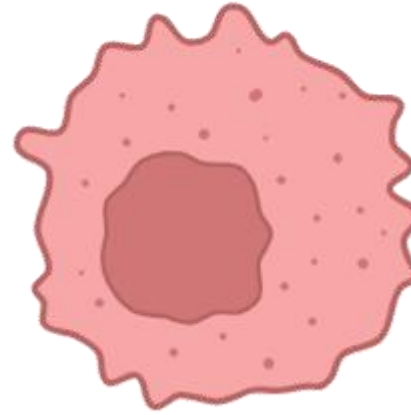
From Fan, T. *et al.* (2023) 'Therapeutic cancer vaccines: Advancements, challenges and prospects', [Therapeutic cancer vaccines: advancements, challenges and prospects | Signal Transduction and Targeted Therapy](#)

1. Inject neoantigen IV / IM
2. APCs (dendritic cells) take up neoantigen
3. Neoantigen presented on APC surface
4. T cell binding, priming and immune activation (HLA dependent)
5. T cell expansion and migration
6. T cell invasion into tumour
7. T cell mediate tumour cell death

# Neoantigen source



Tumour Lysate



Irradiated cancer cells

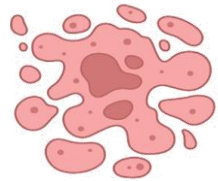


Peptide



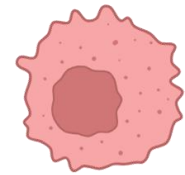
Nucleic acids

# Neoantigen source



Tumour Lysate

- Broad Antigen Spectrum
- Personalisation
- Complex Preparation
- Variable Efficacy



Irradiated cancer cells

- Antigen Diversity
- Strong immune stimulation
- Complex Preparation
- Variable Efficacy
- High cost



Peptide

- High specificity and safety
- Ease of Production
- Direct presentation on MHC
- Limited Immunogenicity
- HLA restriction
- High cost



DNA

- Broad antigen spectrum
- Personalisation
- Low cost
- Risk of integration into genome
- Risk of autoimmune reaction
- Requires intranuclear transfer



RNA

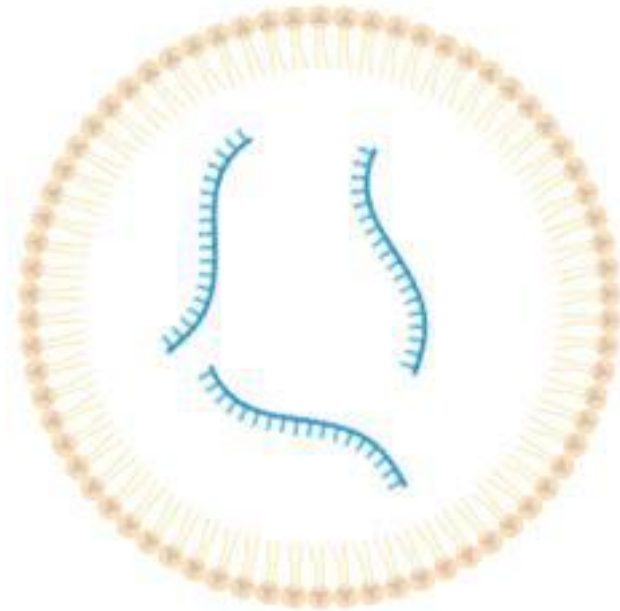
- Broad antigen spectrum
- Rapid personalisation
- Intrinsic adjuvant effects
- High immunogenicity
- Potential for inflammatory reaction
- Rapid degradation



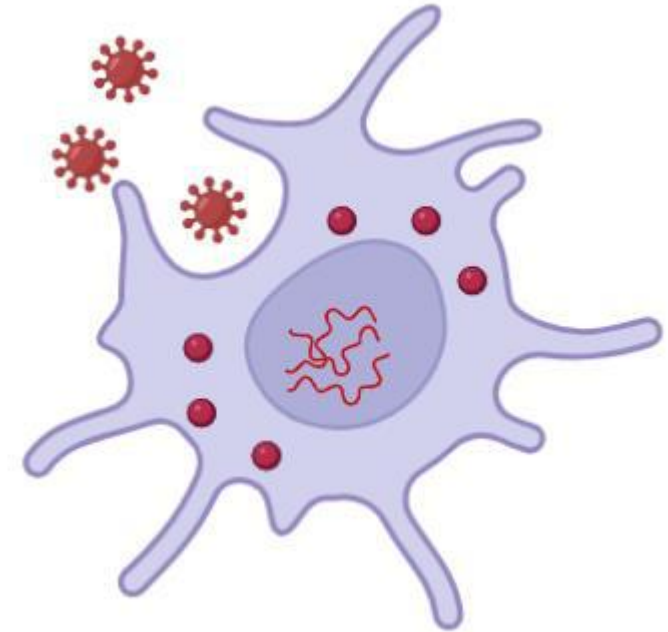
# Neoantigen delivery



Direct injection



Lipid nanoparticle



Dendritic cell transfection

What is a cancer vaccine?

Brief history – how did we get to now?

How do cancer vaccines work?

The types of cancer vaccines

mRNA vaccines

What is a cancer vaccine?

Brief history – how did we get to now?

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The types of cancer vaccines

**mRNA vaccines**



mRNA vaccines

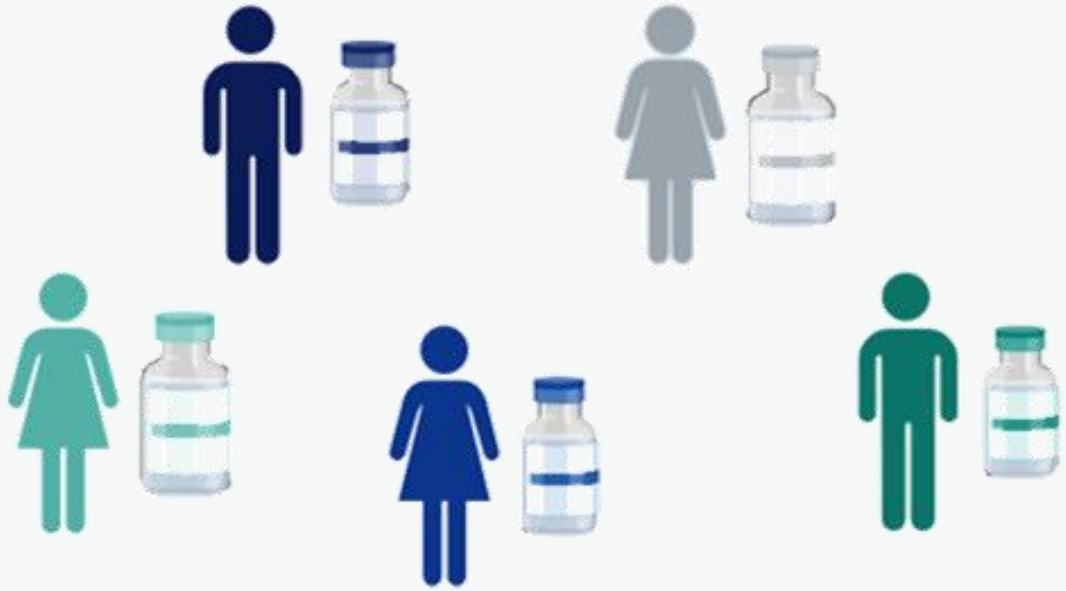
How they work

How they're made

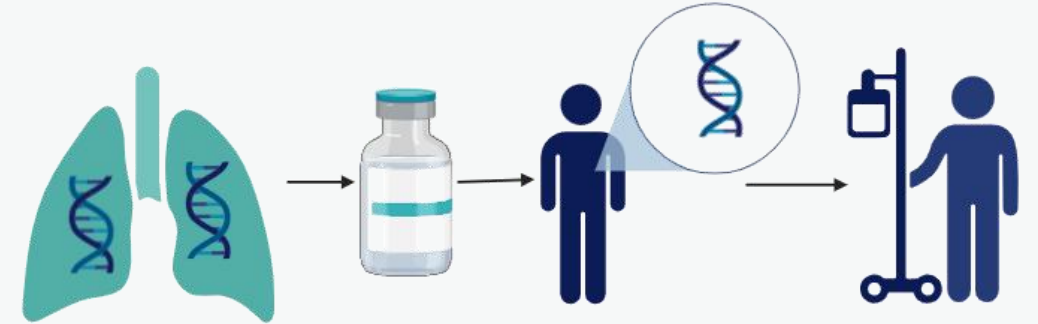
Benefits and challenges

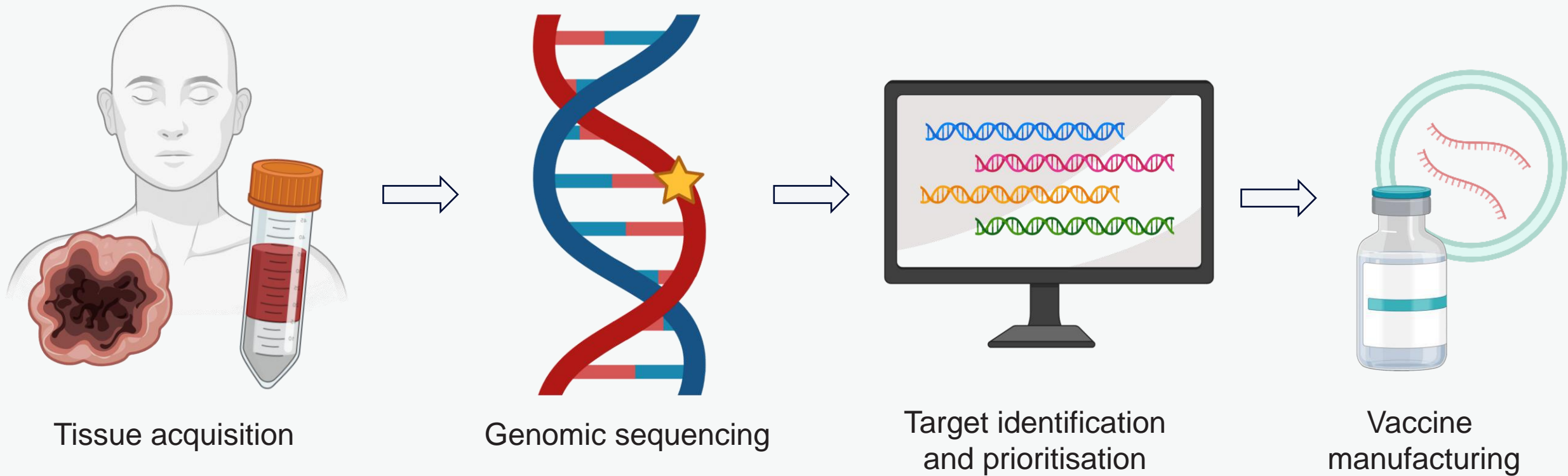
Delivery of research

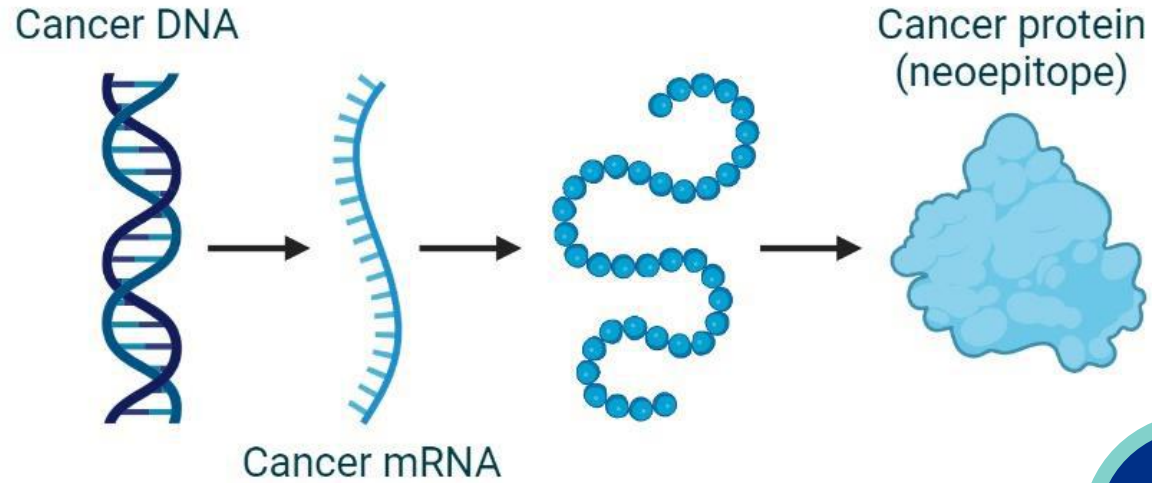
# Individualised



# Off - The - Shelf



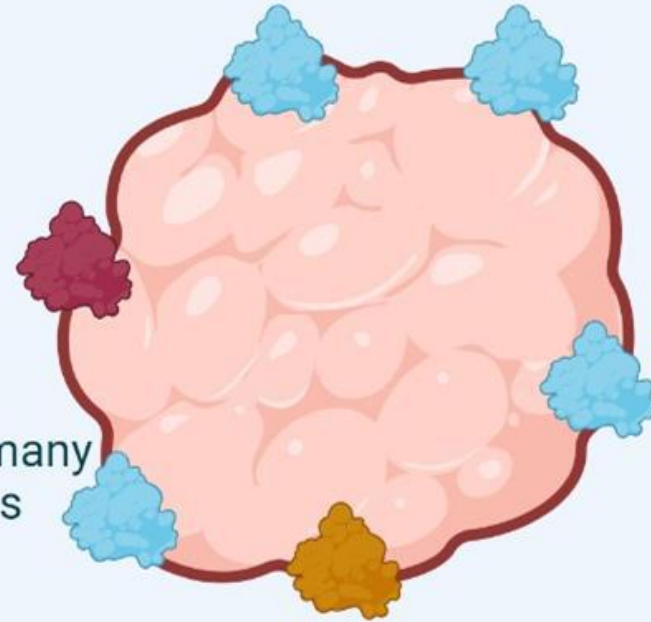




Cancer contain mutated DNA which the cells use to create cancer specific proteins (neoepitopes) – this promote cancer growth and survival

Tumours contain many different neoepitopes – some are specific to a type of cancer (e.g. bowel, lung) – neoepitopes can also be patient specific.

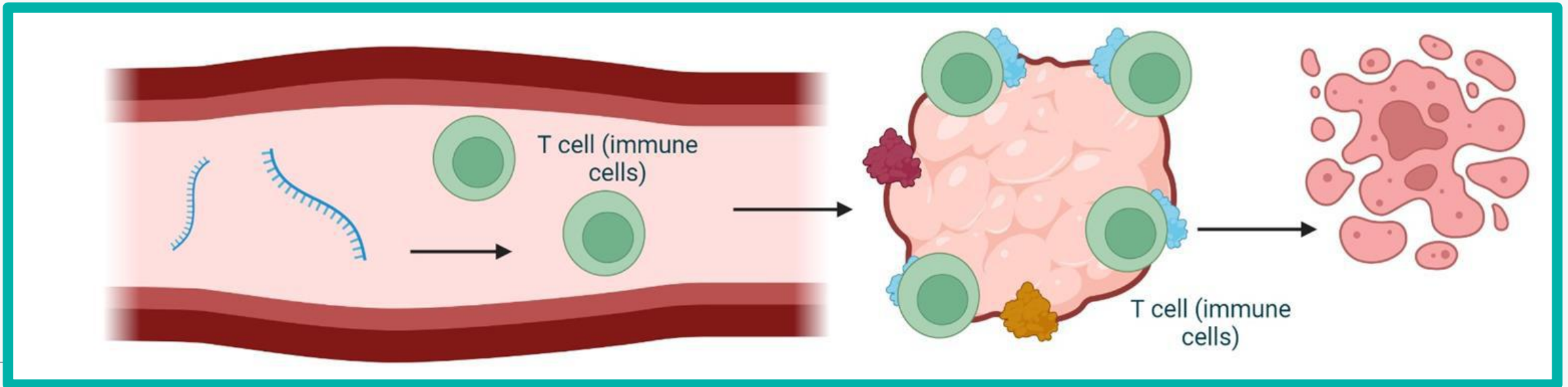
Tumour with many neoepitopes

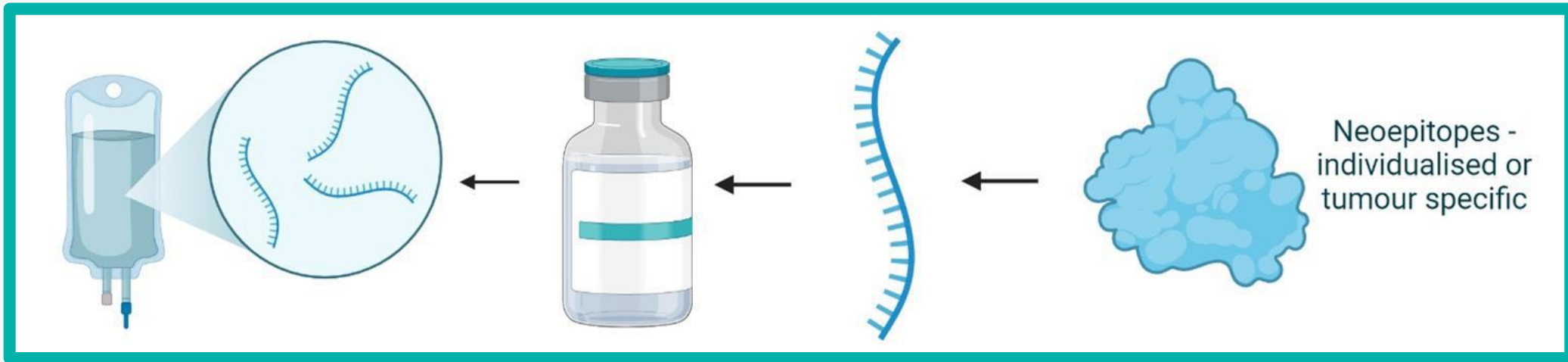






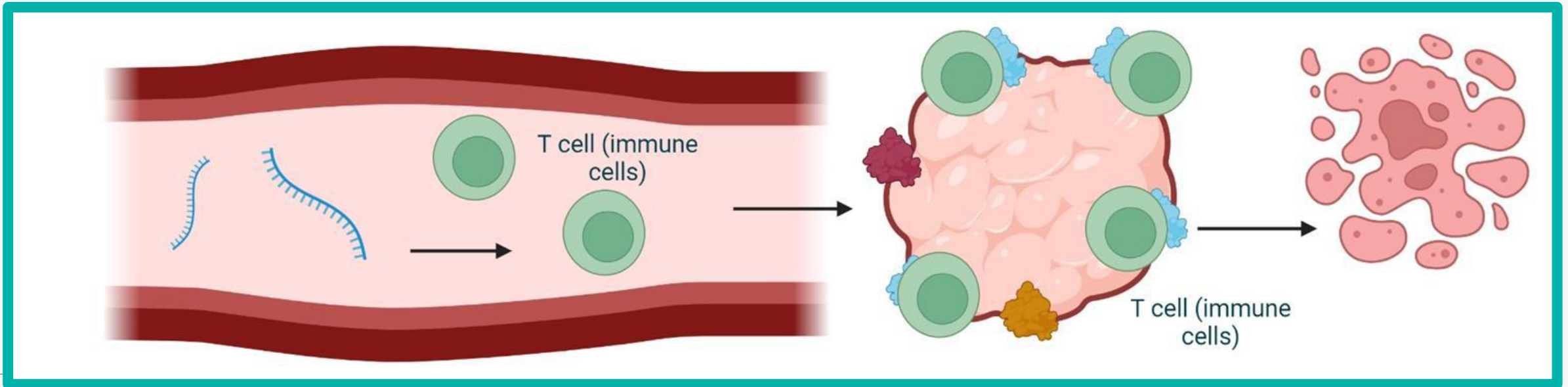
The mRNA vaccine activates the patient's immune cells to recognise and kill cancer cells



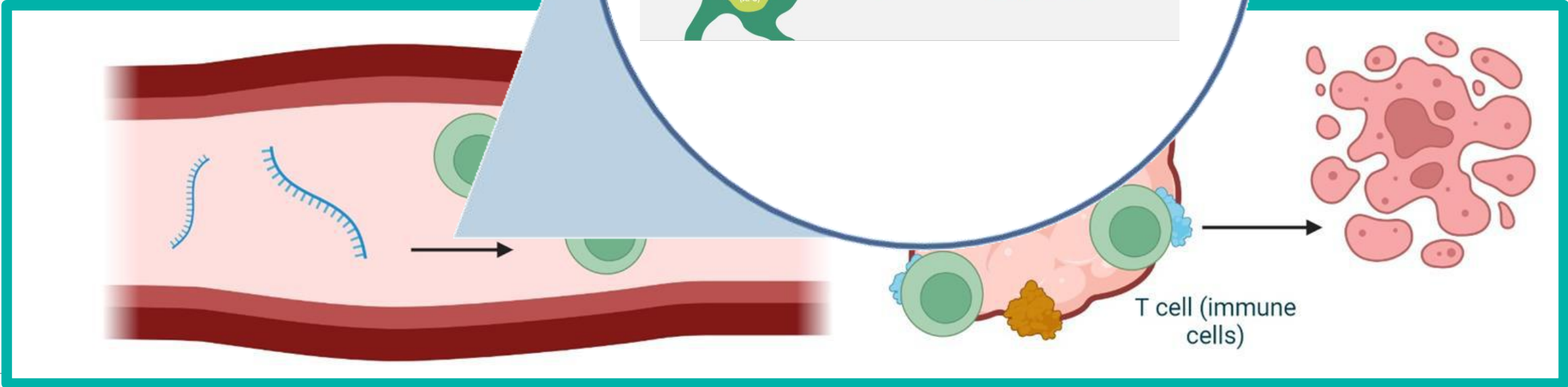
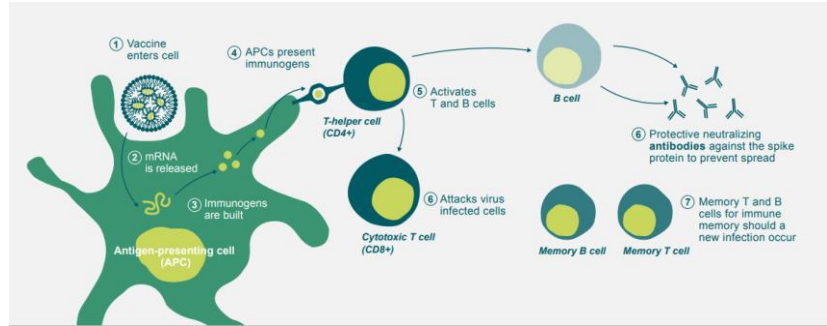


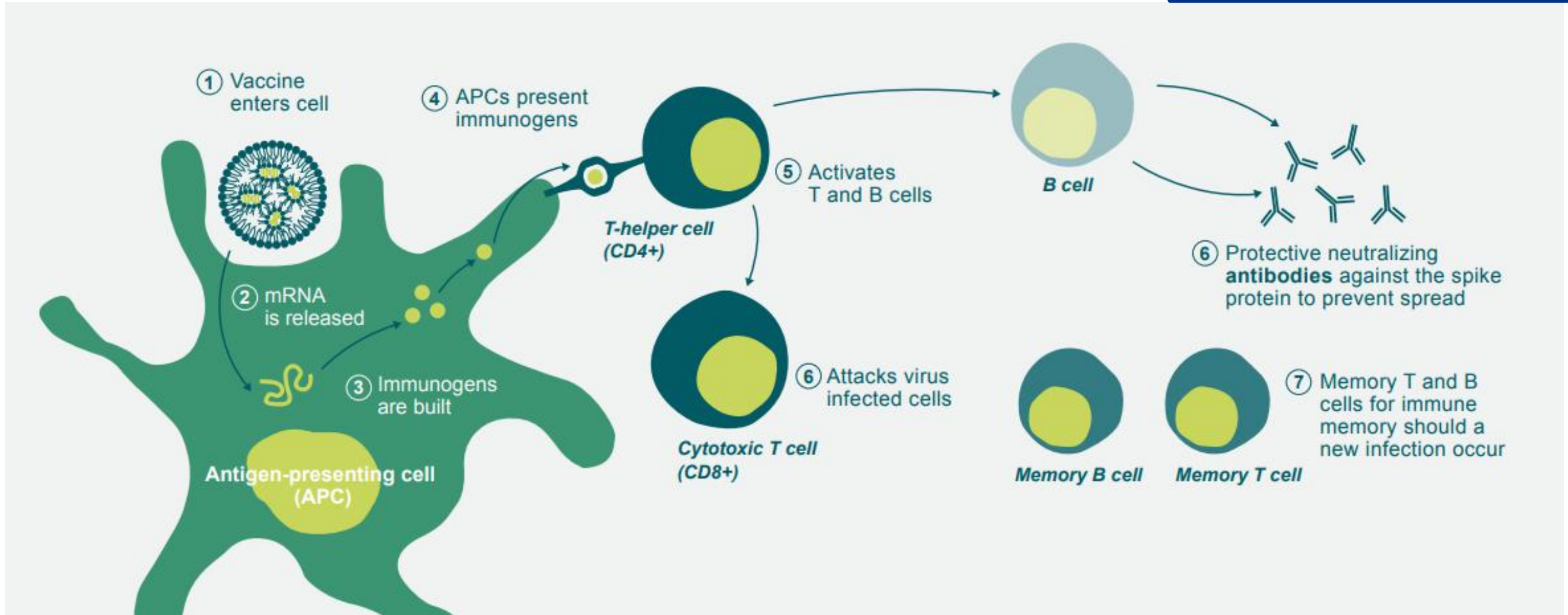
Neopeptides are 'reverse engineered' to create mRNA cancer vaccines

The mRNA vaccine activates the patient's immune cells to recognise and kill cancer cells



The mRNA vaccine activates the patient's immune cells to recognise and kill cancer cells







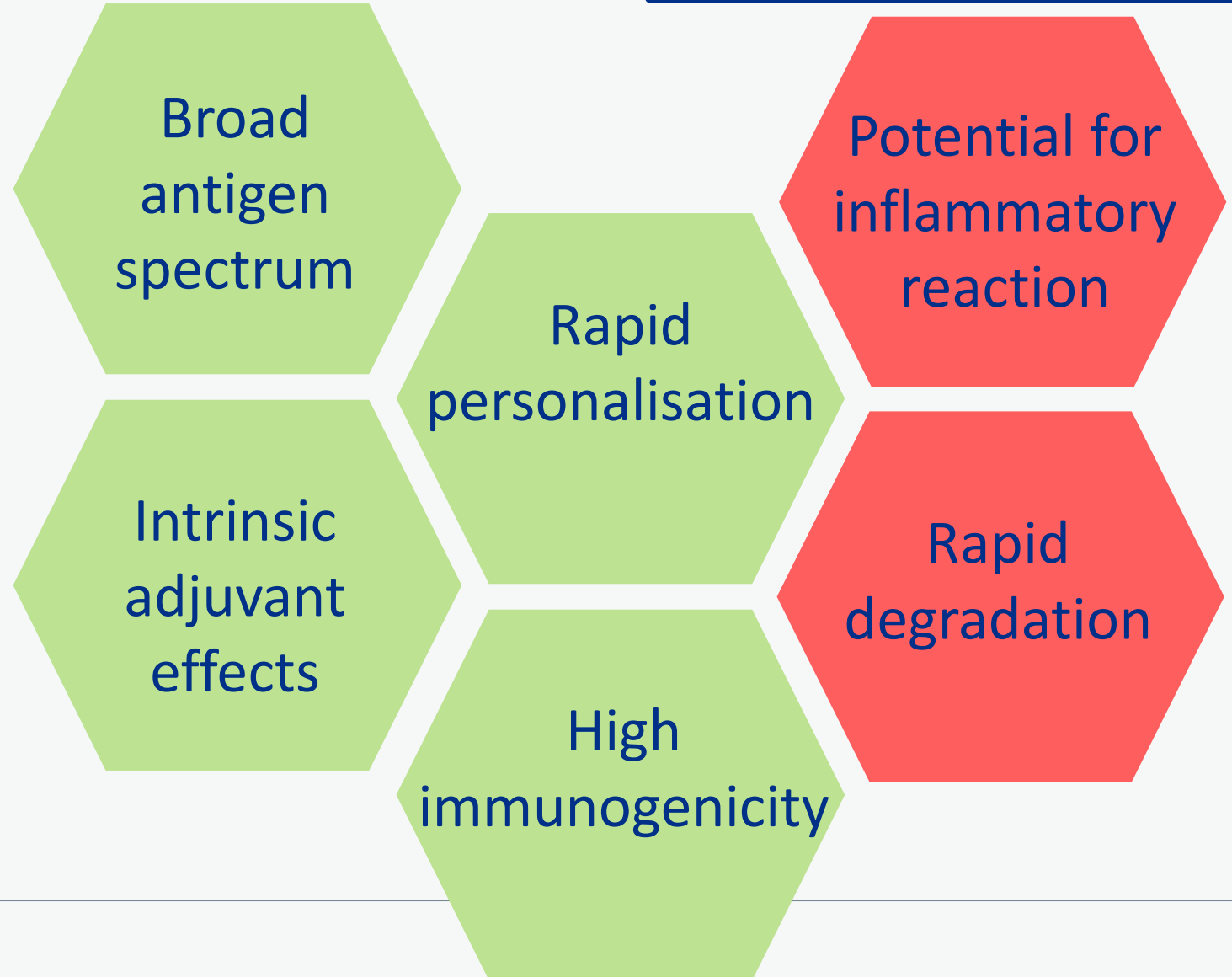
- Broad antigen spectrum
- Rapid personalisation
- Intrinsic adjuvant effects
- High immunogenicity
- Potential for inflammatory reaction
- Rapid degradation



Benefits and Challenges



# RNA

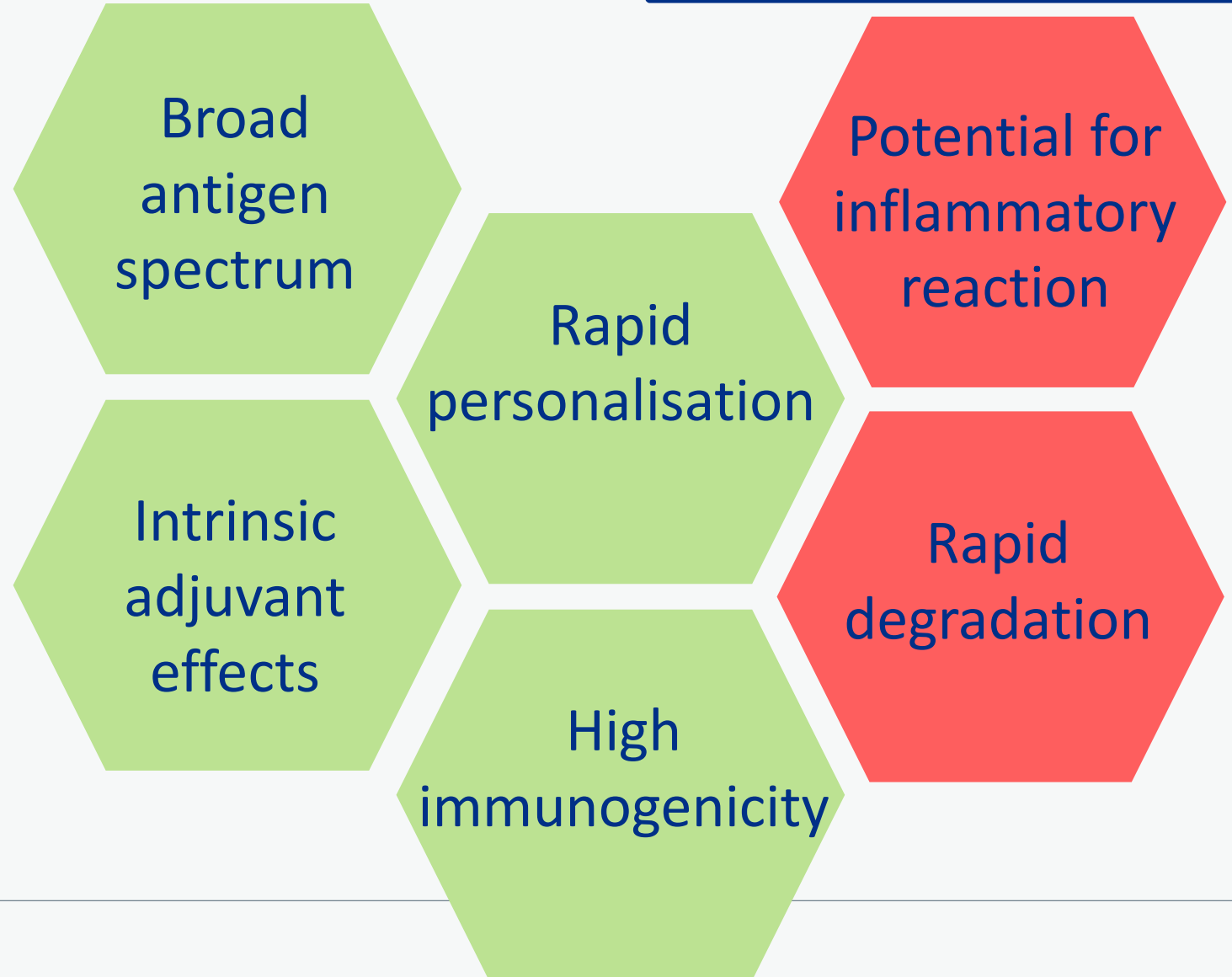




Benefits and Challenges

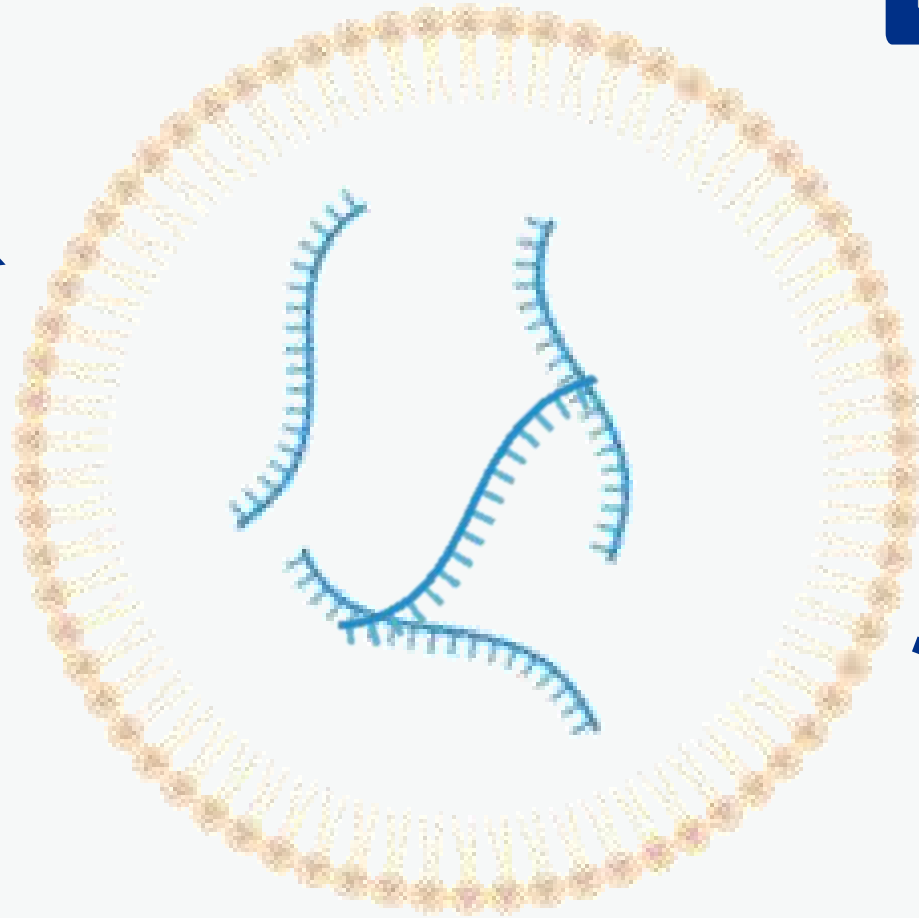


# RNA





Rapid degradation

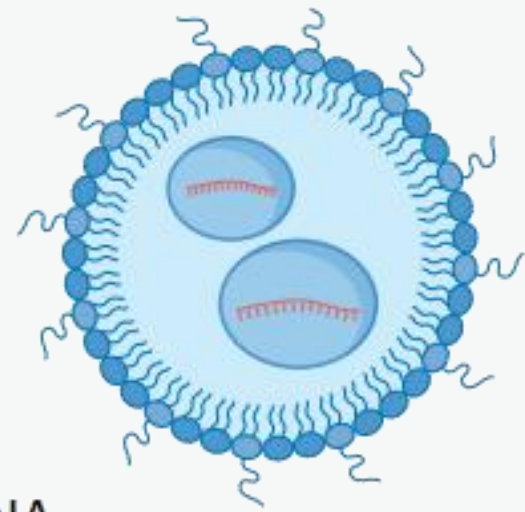


Stability

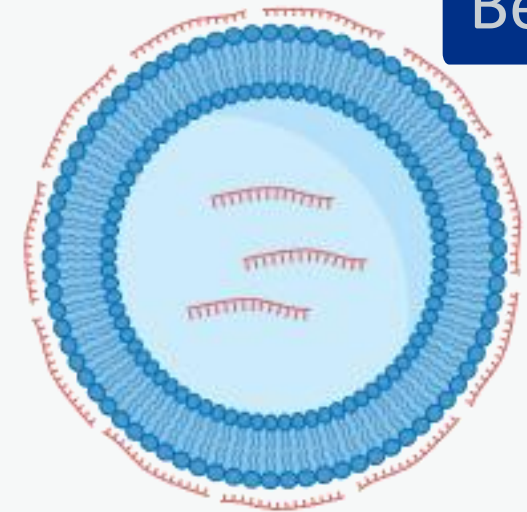
# mRNA cancer vaccines



Protamine-mRNA complex



RNA-LNP



Anionic RNA-LPX



ML RNA-LPA

Advantages			
Simplicity and Safety	Enhanced Delivery and Endosomal Release	Tissue-Specific Targeting	Increased Payload Capacity
Immunostimulatory Properties	Improved Stability	Stability and Immunostimulatory Potential	Enhanced Antitumor Activity
Cost-Effective	Scalability	Promising Clinical Results	
Disadvantages			
Lower Stability and Delivery Efficiency	Limited Targeting Specificity	Narrow Target Range	Increased Complexity and Production Cost
Limited Targeting and Uptake	Potential for Immune Response or Toxicity	Technical Complexity	Risk of Overstimulation
Variable Clinical Outcomes	Variable Efficacy for Solid Tumours	Risk of Inflammation	Limited Clinical Experience

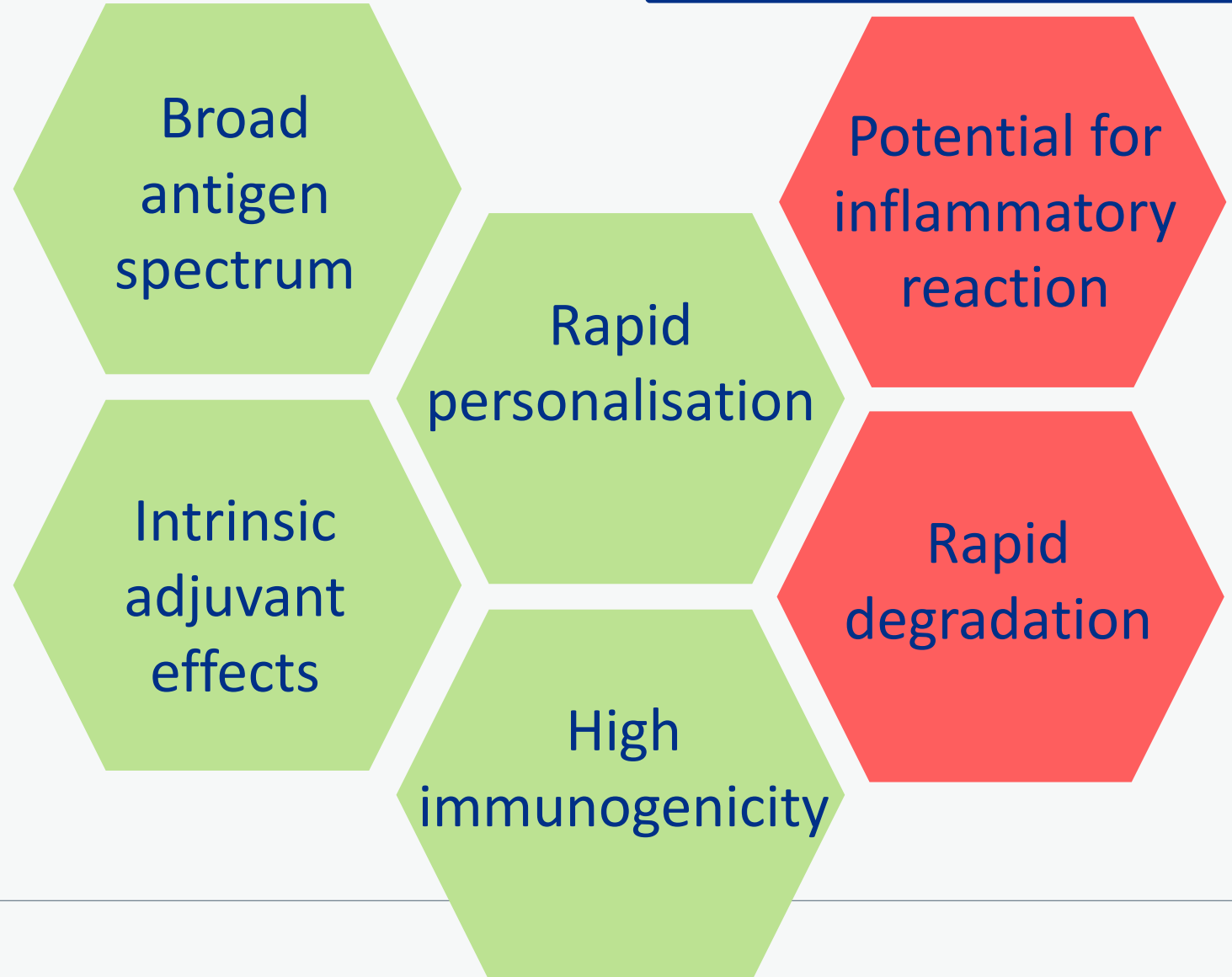
From Sayour, E.J. *et al.* (2024) 'Cancer mRNA vaccines: clinical advances and future opportunities', *Nature Reviews Clinical Oncology*, 21(7), [Cancer mRNA vaccines: clinical advances and future opportunities | Nature Reviews Clinical Oncology](#)



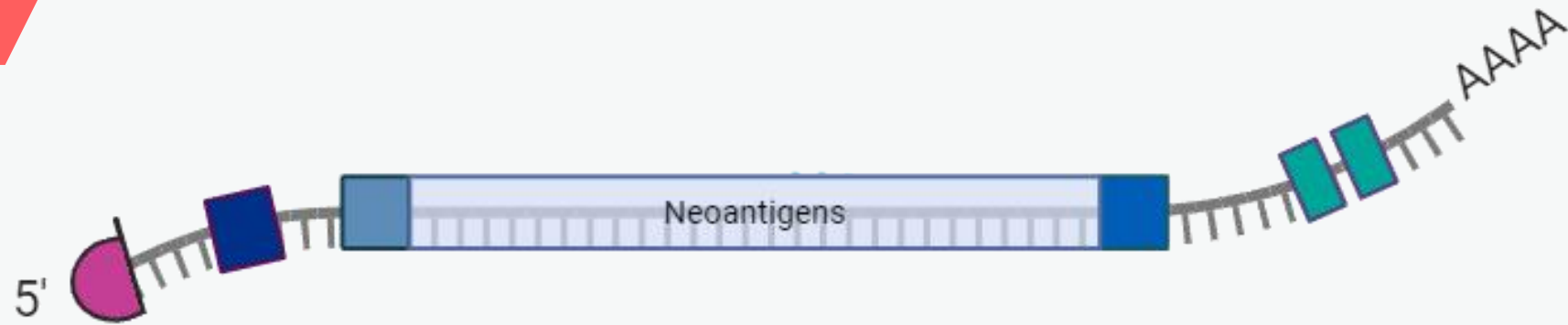
Benefits and Challenges



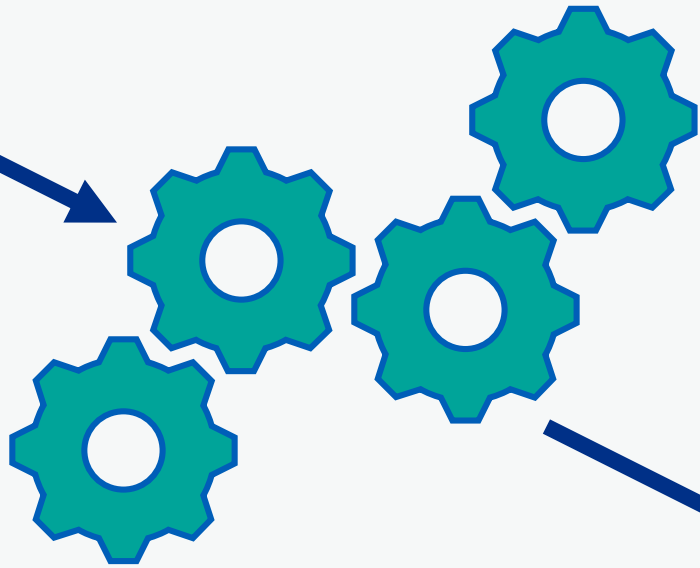
# RNA



Potential for  
inflammatory  
reaction



Potential for inflammatory reaction

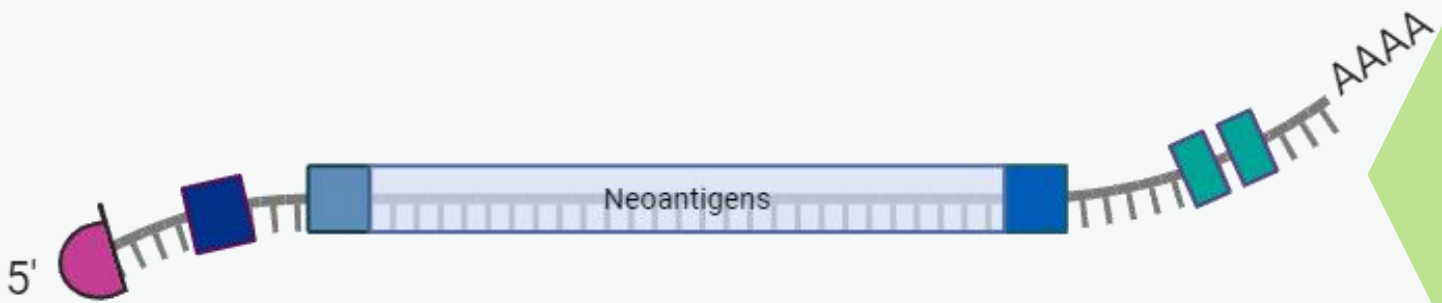


Broad antigen spectrum

Rapid personalisation

Intrinsic adjuvant effects

High immunogenicity





Benefits and Challenges

Increase transcription

Promote T cell recognition

Increase stability

Increase uptake by APCs

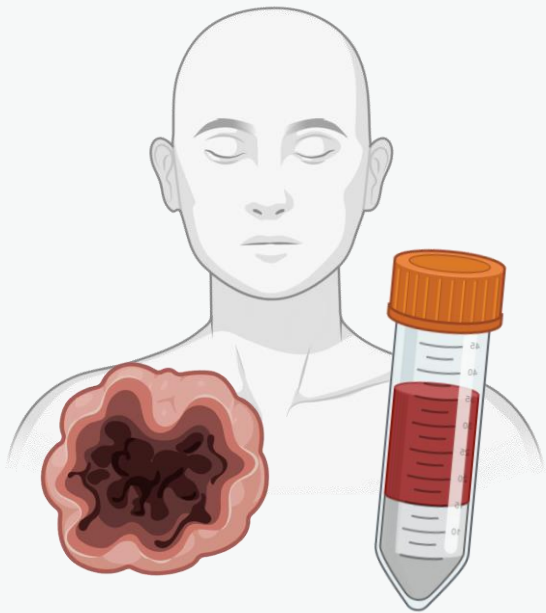
Reduce unwanted immune effects

Direct systemic and cellular localisation

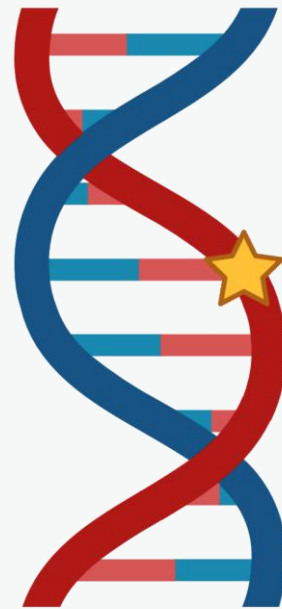
Boost immune activating cytokines

Modulate TME

Synergise with other anticancer agents (ICIs)



Tissue acquisition



Genomic sequencing



Target identification  
and prioritisation



Vaccine  
manufacturing

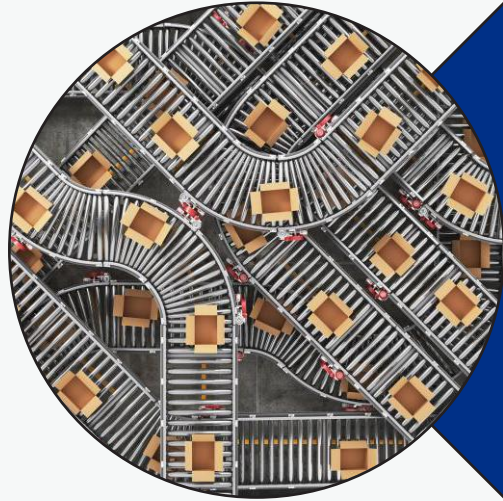


Access





Delivery of research



# Logistics



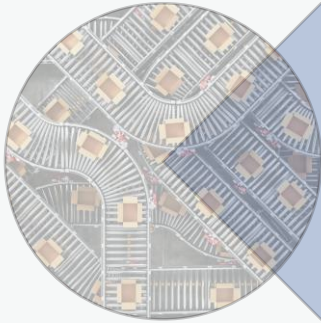
# Access



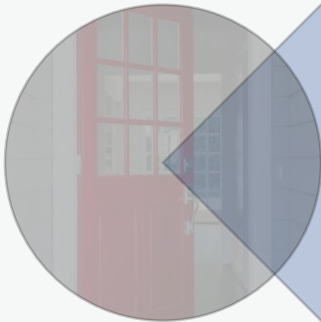
Delivery of research



Capacity



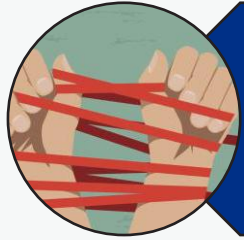
Logistics



Access



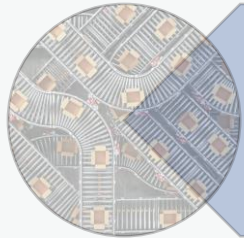
Delivery of research



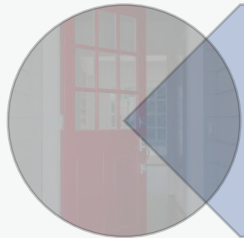
Regulation



Capacity



Logistics



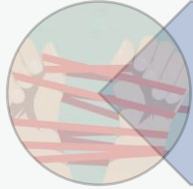
Access



Delivery of research



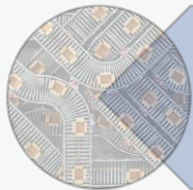
Support



Regulation



Capacity



Logistics



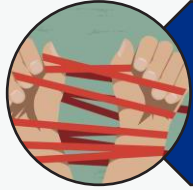
Access



Delivery of research



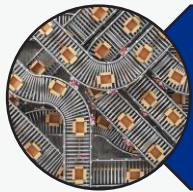
Support



Regulation



Capacity



Logistics



Access

# The NHS Cancer Vaccine Launch Pad (CVLP)

Establishing a UK Platform to Collect Tumour Samples  
and Perform DNA/RNA Sequencing for the Development  
of Personalised Cancer Vaccines

Patrick Ezeani  
Programme Support Manager  
NHS England  
National Cancer Programme

# Why are we setting up the CVLP?

# The UK: A Global Leader in New Therapies

- Vaccinology is entering a new era with the advent of mRNA vaccine technology – offering broad benefits in terms of personalisation, modularity and deployment.
- Using these recent advances to accelerate the development of personalised therapeutic cancer vaccines could drive transformative benefit across multiple cancer subtypes.
- The UK has for centuries been a leader in vaccine development, research and deployment, recently exemplified through our Covid-19 response.
- Multiple home-grown programme to develop vaccines therapies.
- Margaret Keenan, Coventry, **first in the world** to receive a COVID-19 vaccine.
- Brian Pinker, Oxford who received the **Oxford/AZ vaccine**, vaccine that saved 6.3million lives





# UK-BioNTech Strategic Partnership

- The UK Government signed an agreement with BioNTech SE to bring innovative immunotherapy research to the UK, with the potential to transform cancer patient outcomes
- The CVLP is a collaborative project including NHS England, Genomics England, the Department of Health and Social Care, the Office for Life Sciences and the National Institute of Health and Care Research (NIHR) to support delivery of shared key UK ambitions.
- The collaboration will aim to deliver 10,000 personalised therapies to UK patients by 2030
  - [Press Release: Major agreement to deliver new cancer vaccine trials - GOV.UK \(www.gov.uk\)](https://www.gov.uk/government/news/press-release-major-agreement-to-deliver-new-cancer-vaccine-trials)
  - [New partnership to boost research into vaccines for cancer - GOV.UK \(www.gov.uk\)](https://www.gov.uk/government/news/new-partnership-to-boost-research-into-vaccines-for-cancer)



# Government Strategic Partnership



NHS National Cancer Programme  
&  
NHS Genomics Medicine Service



Department  
of Health &  
Social Care



Office for  
Life Sciences



BIONTECH

# Cancer Vaccines: An Opportunity To Transform Cancer Care

- [The NHS Long Term Plan](#) aims to save thousands more lives each year by dramatically improving how we diagnose and treat cancer.
- The CVLP will support delivery the following NHS Long Term Plan ambitions:
  - We will **speed up the path from innovation to business-as-usual, spreading proven new techniques** and technologies and reducing variation.
  - Safer and **more precise treatments including advanced radiotherapy techniques and immunotherapies** will continue to support improvements in survival rates.
  - We will extend the use of molecular diagnostics and, over the next ten years, the NHS will routinely offer genomic testing to all people with cancer for whom it would be of clinical benefit and **expand participation in research.**

**NHS**

The NHS Long Term Plan



# National Cancer Vaccine Advance



## UK plan for national mRNA cancer vaccine advance

4 hours ago



By Michelle Roberts  
Digital health editor



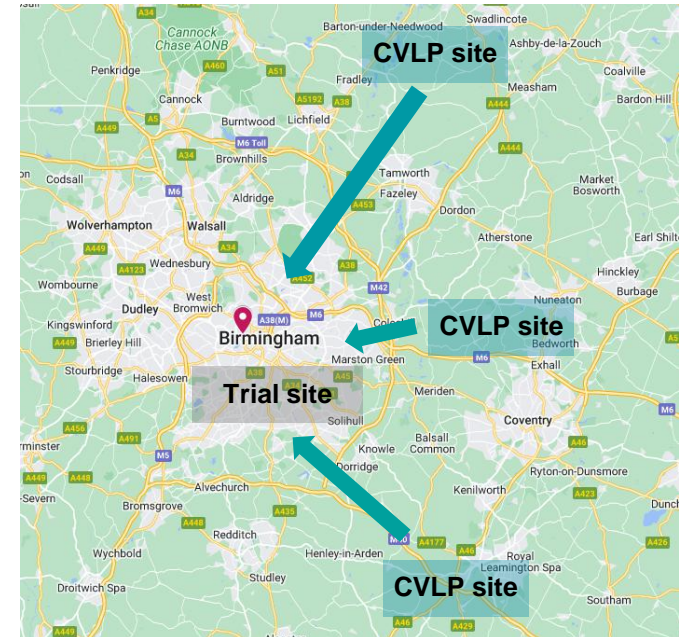
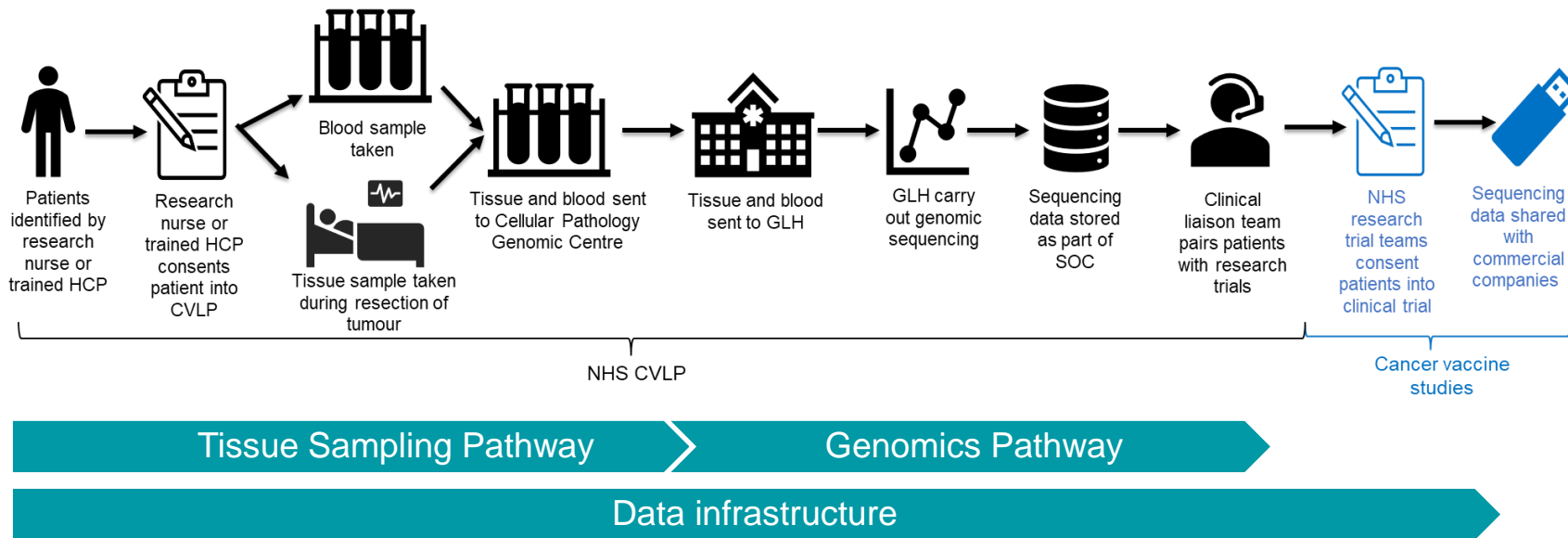
GETTY IMAGES



# Overview of the CVLP

# Overall Aims of The Cancer Vaccine Launch Pad

- Improve access for NHS patients to personalised cancer vaccine trials and reduce geographical variation.
- Speed up recruitment to personalised cancer vaccine trials so that data on their effectiveness can be obtained faster.
- Invest in pathology and genomic services to improve capacity and capability for tissue preparation and genetic sequencing within the NHS, which can be used to improve standard of care.
- Ensure the NHS is prepared to roll out personalised cancer vaccines should they prove to be effective and cost-effective.
- Encourage investment from commercial companies to carry out cancer vaccine research in the UK with NHS patients.





# The Cancer Vaccine Launch Pad Model

- The CVLP pathway is based on a defined and expanded standard of care pathway for tumour molecular analysis and sequencing. This will ensure that high quality, timely tissue samples are available for tumour characterisation and vaccine manufacturing.
- Patients will consent to be referred to a cancer vaccine trial and for surplus tissue samples, obtained through standard of care pathways, to be used to assess their eligibility for current cancer vaccine trials run by trial sponsors.
- The pathway requires collaboration between Surgeons, Pathologists, Oncologists, Clinical Nurse Specialists, and local CVLP Research Teams to run successfully.
- The establishment of the NHS CVLP will be undertaken in a phased approach to ensure alignment with the technical, quality and regulatory requirements of its commercial partners' clinical trial pipeline.
- In the first phase of the CVLP, tissue samples are sent to the commercial partner for sequencing.

# Roles in the CVLP Pathway

## CVLP site

A site that will identify eligible patients and refer them to a trial site that is delivering a cancer vaccine trial for the trial sponsor.

The local cell path department will process the tissue into FFPE tissue blocks as part of standard of care.

## Cellular Pathology Genomic Centre (CPGC)

A site set up to prepare samples for genomic testing. The CPGC will receive FFPE tissue blocks from the CVLP sites and prepare the sample for onward submission to the cancer vaccine trials.

## Trial site

A site that will be receiving CVLP referrals and delivering the cancer vaccine trial.

\*NB – standard of care treatment/ chemotherapy will still be delivered at CVLP sites.

## CVLP Clinical Liaison ([cvlp@uhs.nhs.uk](mailto:cvlp@uhs.nhs.uk))

Supports across sites in managing communications and patient journey within protocol timeframes. Works with sites to troubleshoot issues. Supports education and performance monitoring with sites.



# Advantages of the Cancer Vaccine Launch Pad

- **Increase and accelerate the rate of recruitment into clinical trials by**
  - having access to a large patient pool (from a large network of CVLP sites across England) for referral to a smaller number of nearby trial sites (in a 'hub and spoke' model).
- **Facilitate timely access to tissue samples in alignment with cancer vaccine trial and manufacturing protocols by**
  - Arranging for the selection of tumour material for molecular analysis alongside the NHS standard of care requirements including for relevant genomics analysis.
- **Improve geographic reach and diversity by**
  - Widening patient access to cutting edge cancer vaccine trials that are not available locally
- **Prepare the system for the implementation of cancer vaccine therapeutics by**
  - raising awareness amongst clinicians of this therapy type, in turn building patient awareness and engagement.

sky news

Pioneering cancer vaccine trials could start in UK by September

The prospect of a cancer vaccine takes a step forward as German pharmaceutical firm BioNTech announces a partnership with the UK government for plans to deliver personalised treatments to 10,000 patients by 2030 through a new research and development hub in Cambridge.

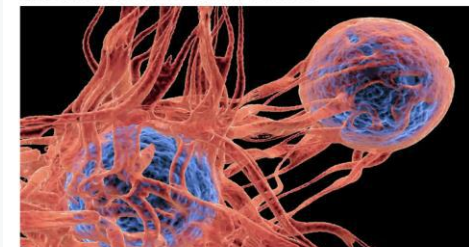
By Adam Solomons, news reporter



The Guardian  
Newspaper of the year

**'A silver lining': how Covid ushered in a vaccines golden era**

Pandemic accelerated advances in vaccine technology, opening up possibilities for combating array of diseases

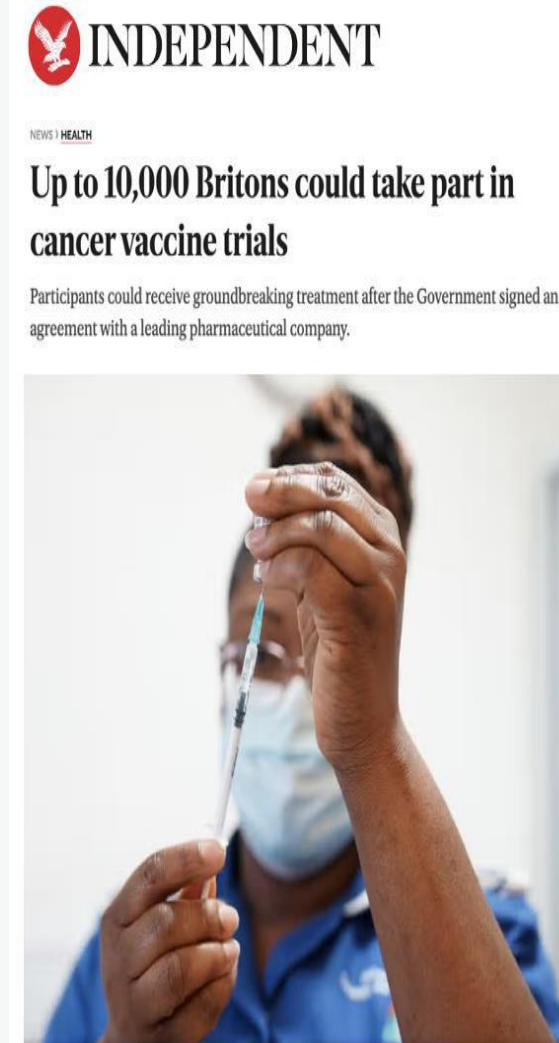




# **Impact of the Cancer Vaccine Launch Pad on Clinical Trials**

# Positive Impact on Cancer Vaccine Trials

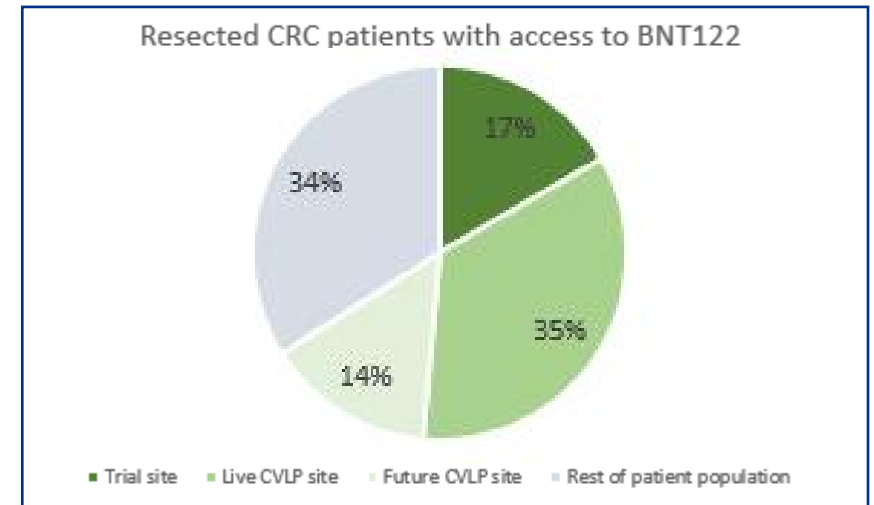
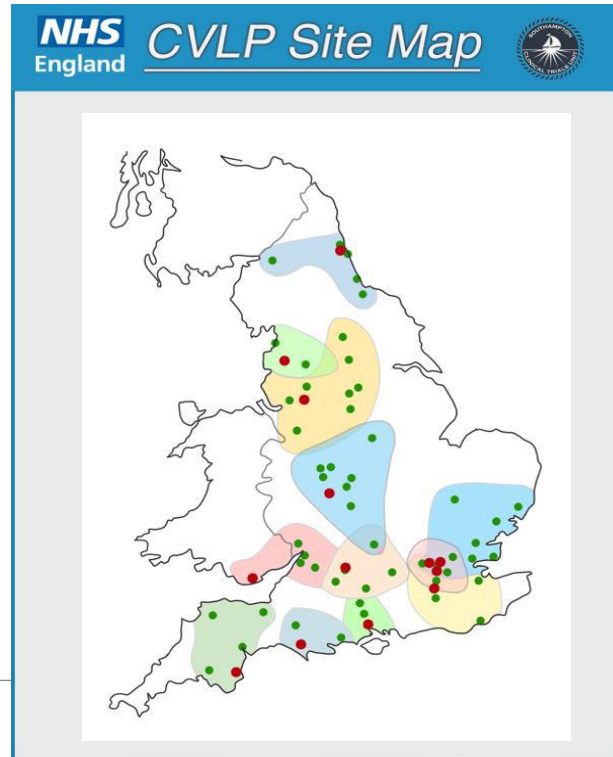
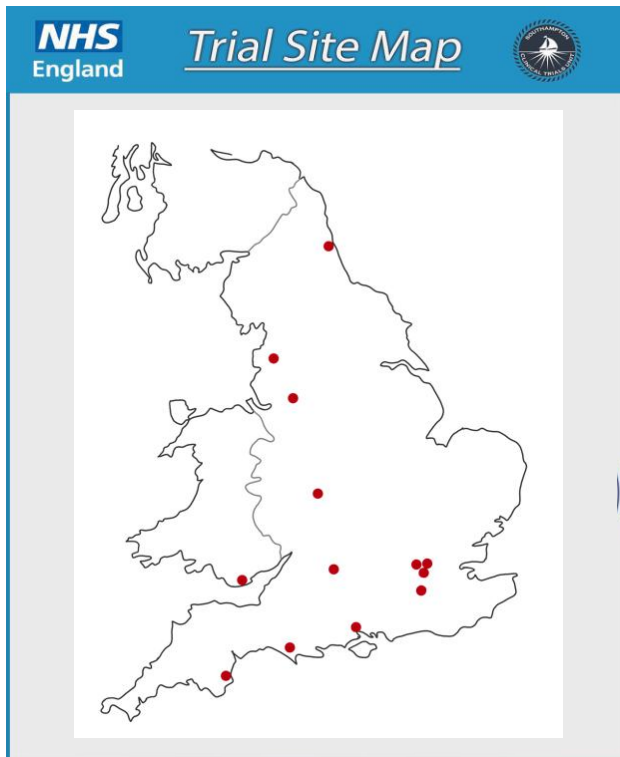
- Screening Acceleration
- Contribution to Screening
- Improved Referral and Consent Rates
- Geographic Reach and Diversity



# Improving Patient Access

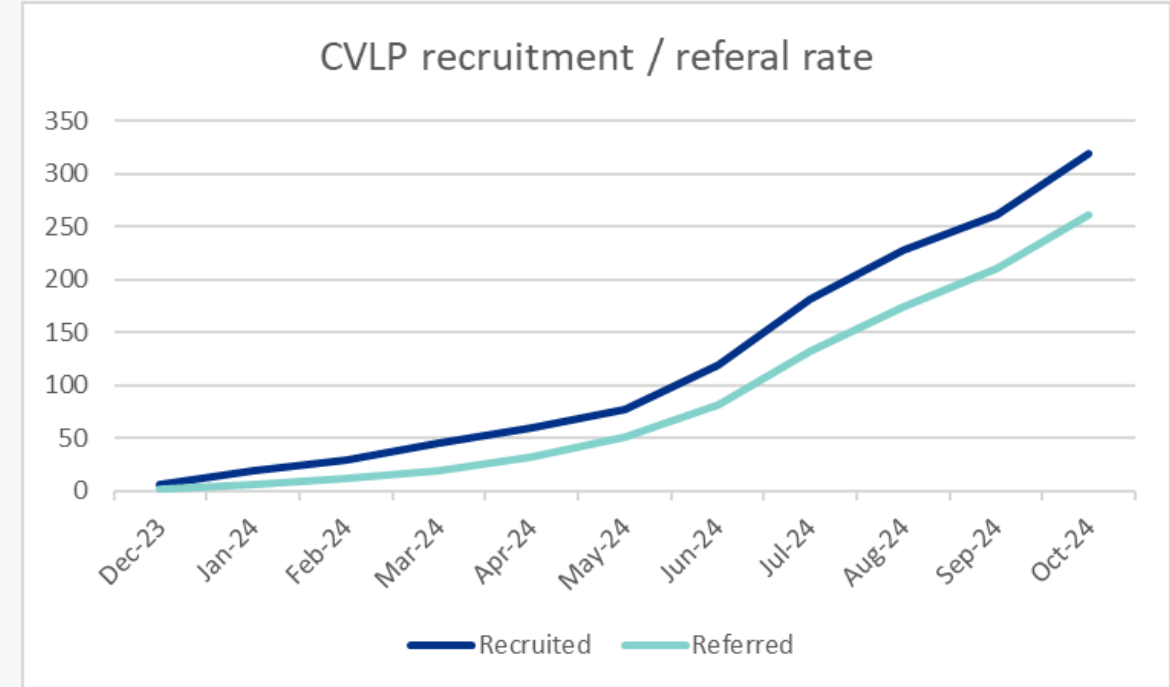
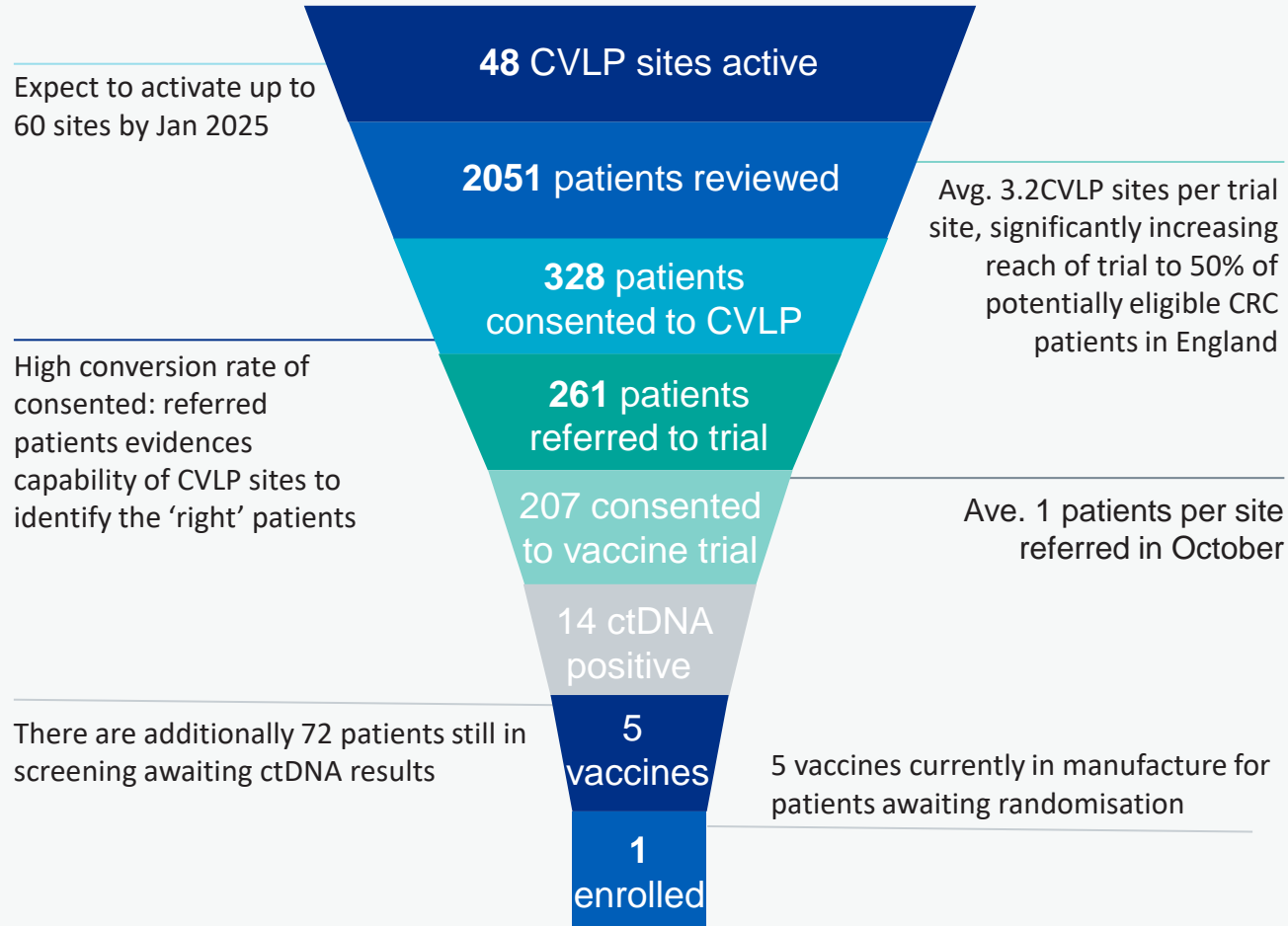
## Patient access to BNT-122 via the CVLP network

- The broad reach of the CVLP network allows for a diverse patient population in smaller hospitals to be involved in research.
- Patient can now access the BNT-122 trial from 58 different sites across the CVLP network (48 CVLP sites and 10 trial sites)
- CVLP sites are spread geographically across all regions of England.
- Travel from a CVLP site to a trial site is still a barrier to participation for some patients, which can in part be mitigated by decentralisation of trial consent and blood sampling.



Through the CVLP, patient reach has increased from 17% to **over 50%** of the resected CRC patient population in England.

# Progress update (as of 31 October 2024)



**Since March 2024 the UK has had the highest global rate of screening to the supported cancer vaccine trial.**

# Impact of the CVLP: Accelerating Trial Activity

(October 31<sup>st</sup> 2024)

The CVLP is delivering tangible benefits in accelerating recruitment to BNT122:



+



+



**73 days**

Average time from Site ID to go-live for CVLP sites – significantly faster than time to activate a new trial site

**33 days**

Average time from go-live to first referral – faster than 50% of trial sites in screening first patients

**261 patients**

Referred to the clinical trial: patients that would not otherwise have accessed the trial

**181 tissue samples**

Prepared to date by CPGCs, 97% within 5 working days

**97% acceptance rate**

of samples prepared by CPGCs – 4 samples required additional curls and slides to be prepped

The CVLP has led to the rapid increase in clinical trial activity

*“with the help of 48 CVLP sites, in a short space of time we have scaled up to screen more than 50 patients per month (a number that keeps increasing). The NHS is now screening as many patients each month as the rest of the world combined, with UK sites screening at more than 3x the global average rate and around 2x the rate of the next best country (Spain). This is unheard of in the global commercial trials world”*

BioNTech representative

**BIONTECH**





# **Beyond the Horizon: The Next Chapter in CVLP Development**



# Future Ambition of the CVLP



National platform with all suitable NHS Trusts signed up.



Multiple cancer vaccine trials covering different cancer indications run by multiple commercial companies are part of the CVLP portfolio.

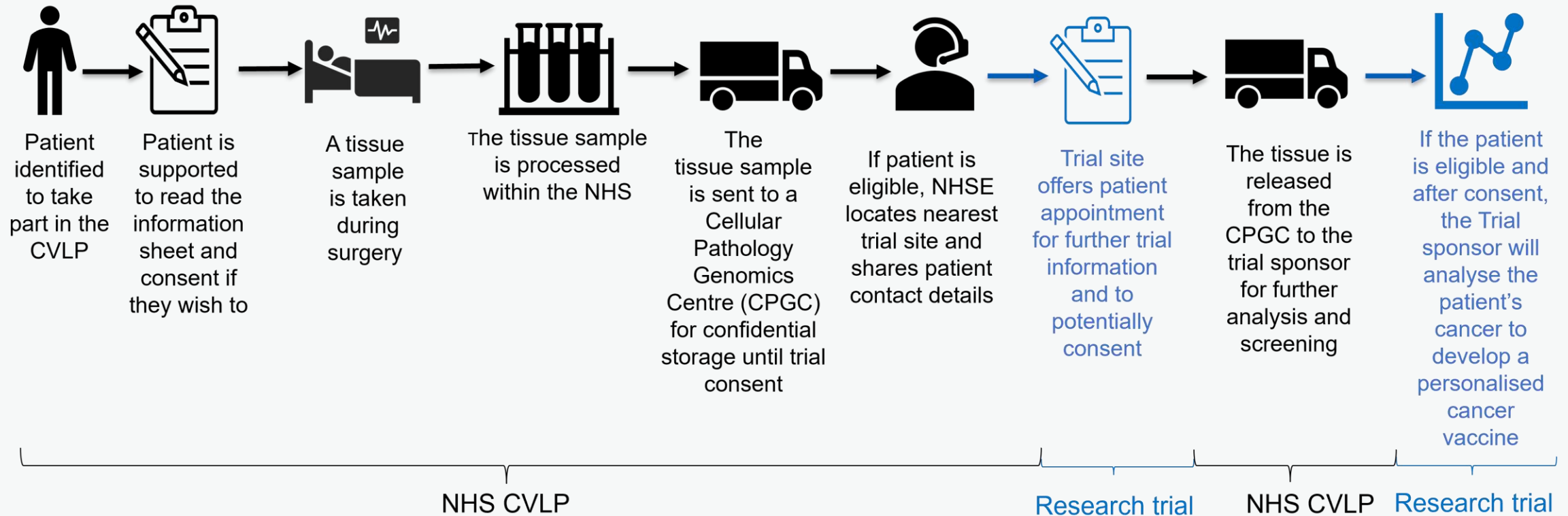


Nucleic extraction and genetic sequencing for the CVLP carried out within the NHS.



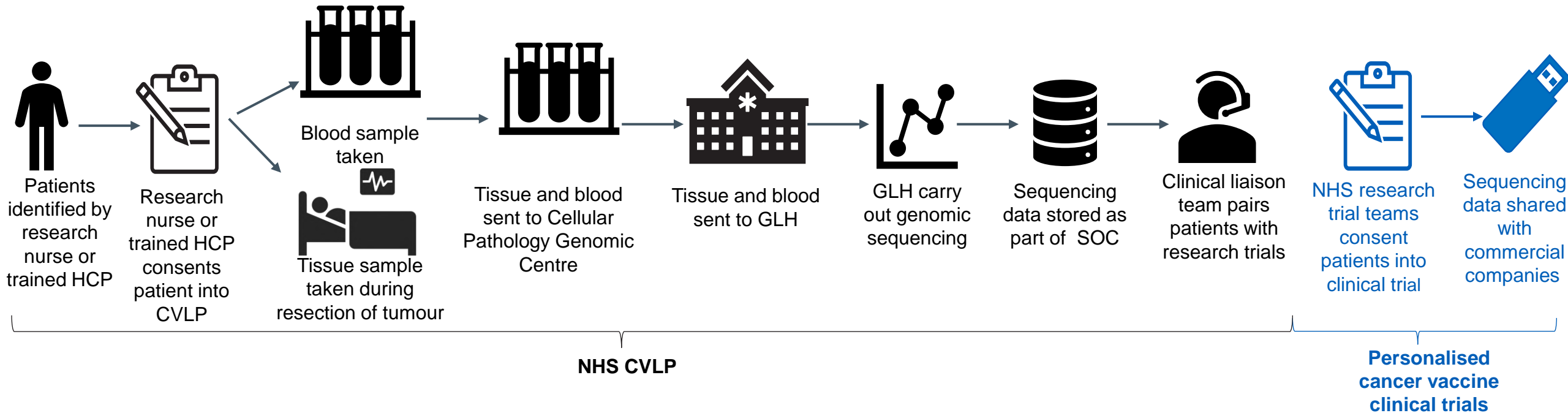
The NHS is prepared to roll-out cancer vaccines should they prove to be effective and cost-effective.

# The CVLP Pathway: Current Pathway





# Simplified Future Pathway For Fully Established CVLP



# How can you get involved in the CVLP

Associate PI Scheme



---

## Thank You



**@nhsengland**  
**@SouthamptonCTU**



**company/nhsengland**  
**company/southampton-clinical-trials-**  
**unit**



**england.nhs.uk**  
**southampton.ac.uk/ctu/cancer-**  
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