WA Health Translation Network

COVID-19 Research Collaboration

Minutes

Monday 10 August 2020, 3.00pm – 4.00pm

Via Zoom

https://www.wahtn.org/wa-covid-19-research-coordination/

1. Welcome and update

Gary Geelhoed gave a brief introduction and overview of current status in Western Australia and reminded members that the WAHTN can share and promote current research in the WAHTN newsletter and/or the WAHTN COVID-19 dedicated website.

The ANPC featured prominently in the Weekend Australian (8 - 9 August). The Centre's research aimed to find a "metabolic signature" for the virus that would show what the abnormal biochemical effects of being COVID-19 positive are on a patient.

Minutes

The Minutes from this meeting and all previous meetings are circulated as quickly as possible and uploaded to the WAHTN COVID-19 website.

2. Funding

Darren Gibson advised that the first tranche of funding ($6million) from the WA Future Health Research and Innovation Fund will be allocated to research and innovation projects related to COVID-19. The WA Department of Health are hoping to have clarity on how the funding will be dispensed in due course.

A review of the COVID-19 Project Grants is underway to ascertain if the projects are still applicable with the current COVID-19 research requirements. Some funding may be re-purposed for other studies and projects.

3. Updates from Key Areas

Responding to the need for solutions against pandemics (Glen Travers and Roger New)

Glen Travers (Executive Chairman) and Roger New (Chief Scientific Officer and Executive Director) from Vaxine presented at the meeting. A summary of the presentation is as follows:

- The team developed the first point of care testing for Heliobacter phlori.
- The initial research was conducted on MERS-CoV and published: *Antibody-medicated protection against MERS-CoV in the murine model*.
- Vaxine have developed platform technologies supporting 4 major projects:
    1. Oral vaccine (immunity in mucosa).
    2. Nasal vaccine (first line of defence, for all ages).
    3. Diagnostic Aptamers (point of care, rapid, antibody and virus).

4. Therapeutic Aptamers (treatment to block the attachment of the virus and clear virus from the lungs).

The intention of the presentation was to connect with colleagues in Western Australia and look at opportunities for collaboration.

Roger New advised that his PowerPoint presentation will be distributed with the Minutes from the meeting.

It was noted that conversations have commenced at the Telethon Kids Institute with regards to immune compromised cancer patients. Stephen Stick and Glen Travers agreed to progress these discussions.

COVID-19 Research Response (CRR) (Toby Richards)
The successful CRR framework has shown that WA is able to run a clinical trial across the public hospital system and hopefully the private health system (with Joondalup Private Hospital agreement currently in discussions).

The CRR expertise is focusing on supporting the Immunity Collaboration group.

CIVIC (Chris Reid)
The CIVIC activities are continuing, including the mental health project. The survey responses are providing a good indication and sense of the COVID-19 impact across the mental health sector.

Companies are actively participating in the CIVIC and DETECT FIFO programs.

Rio Tinto has developed a returning to work in the city project, as well as a new initiative which focuses on working in remote areas and the opportunities for early detection.

A new CIVIC project has been funded with Aged Care providers, focusing on prevention activities. Further information on this will be provided.

Mental Health (Sean Hood)
The mental health group have been contributing to the surveys which are feeding into the CIVIC surveys. The survey has pivoted to be re-branded focusing on mental health care workers in Western Australia. The ethics for this project is currently in progress.

Sean Hood informed members that the mental health group unanimously decided not to submit an application for the MRFF mental health systems opportunity. However, Sean has subsequently been asked to review the projects.

COVID-19 Immunity Collaboration (Dominic Mallon)
The COVID-19 Immunity Collaboration is making progress to look at patients with confirmed SARS CoV-2 and their close contacts.

Currently adjusting protocols to allow the collaboration to work from the Clinical Trials Unit located at the Harry Perkins Institute South building. In kind support has been received from the CRR and ANPC.

Application has been submitted to MRFF, in collaboration with the Kirby Institute (Sydney), Peter Doherty Institute (Melbourne) and the University of Adelaide for Immunity work.

4. Next Meeting

The next meeting will be scheduled in one month, Monday 14 September, 3.00pm – 4.00pm.

Platform Technologies Supporting Four Different Projects

Vaccines

Nasal – first line of defence, for all ages

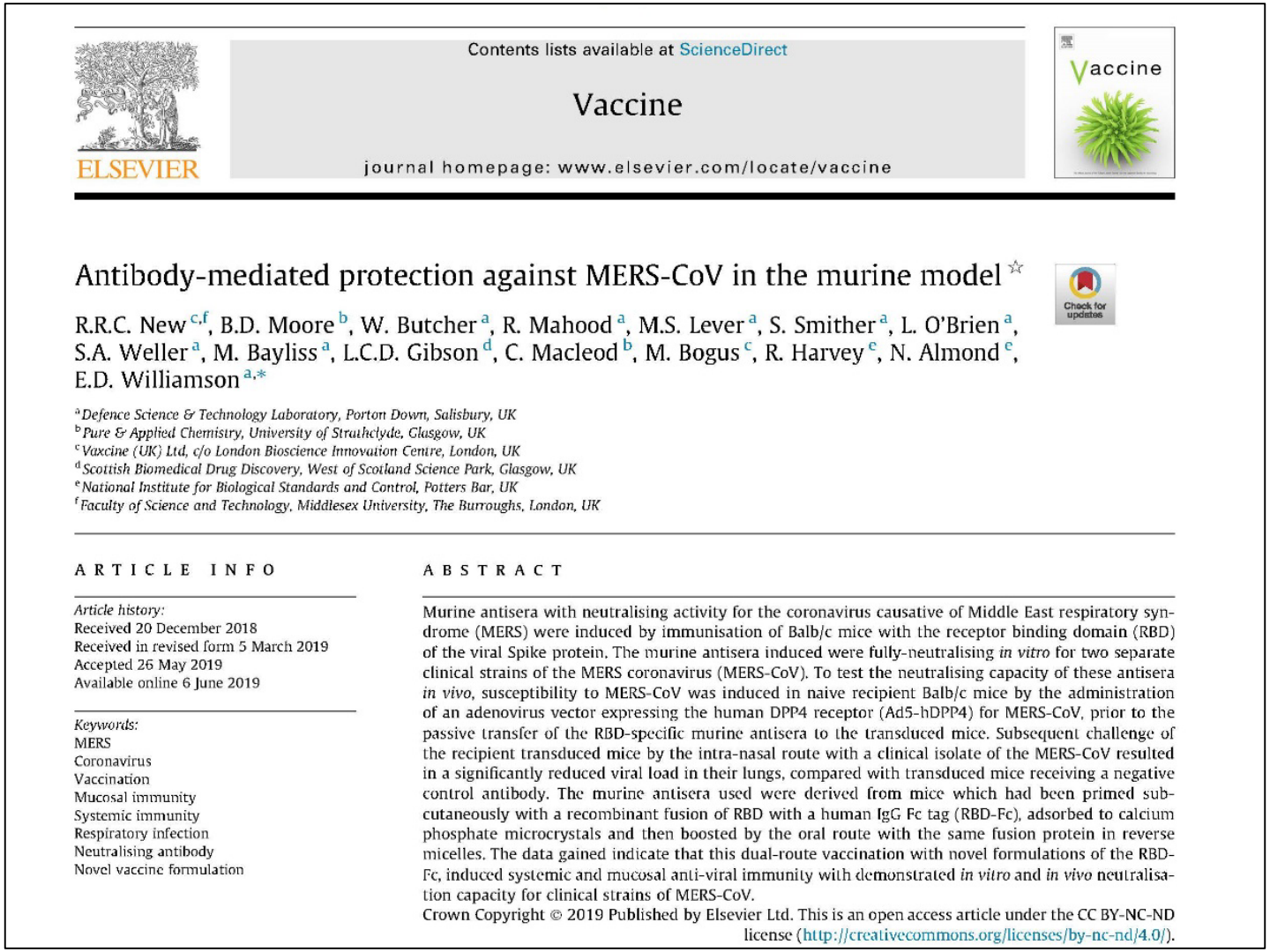
Oral – immunity in mucosa

Aptamers

Diagnostic – point of care, rapid, antibody and virus

Therapeutic – clear virus from the lungs

Oral Vaccine – Previous Experience with Coronavirus



Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Antibody-mediated protection against MERS-CoV in the murine model ☆

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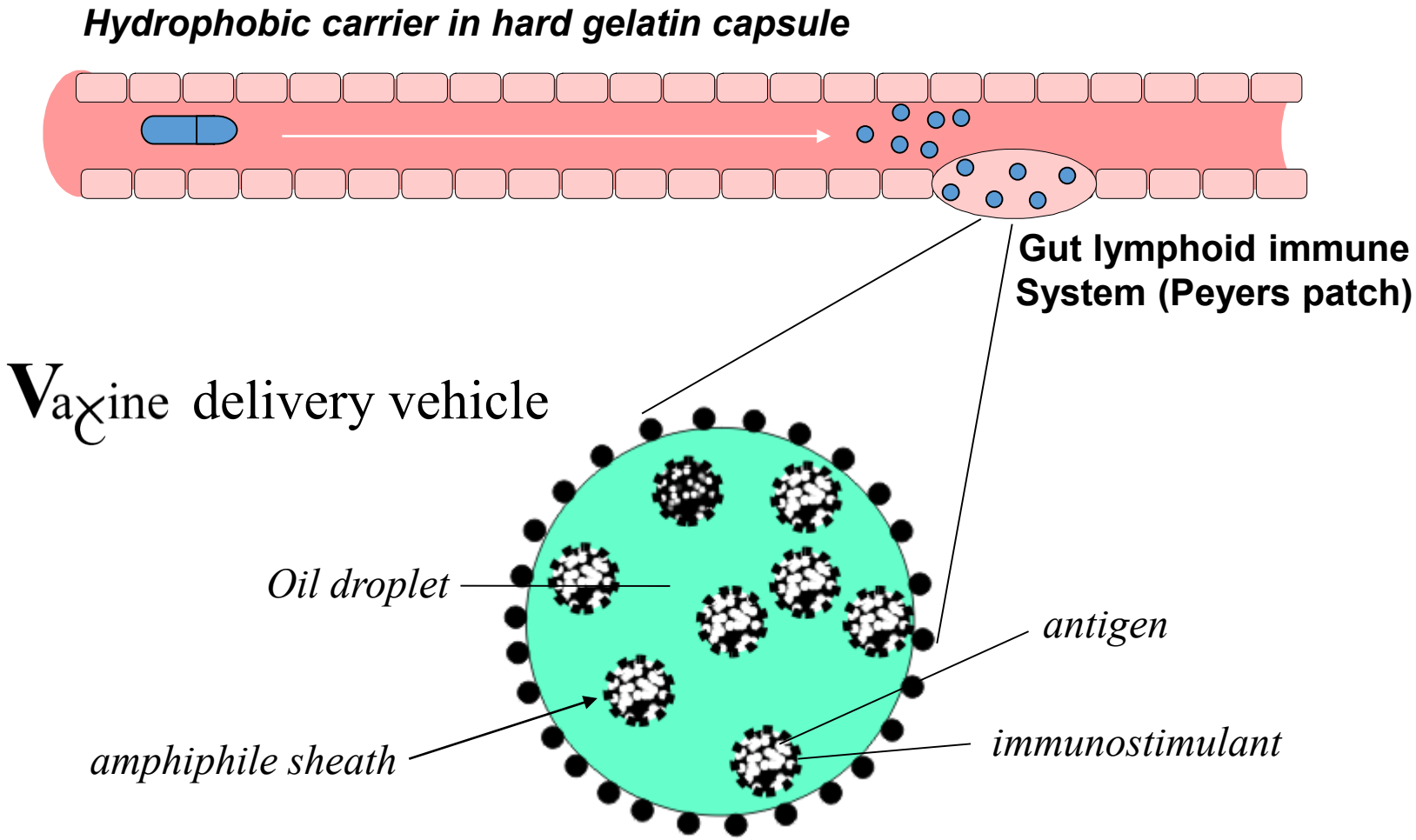
Novel vaccine formulation

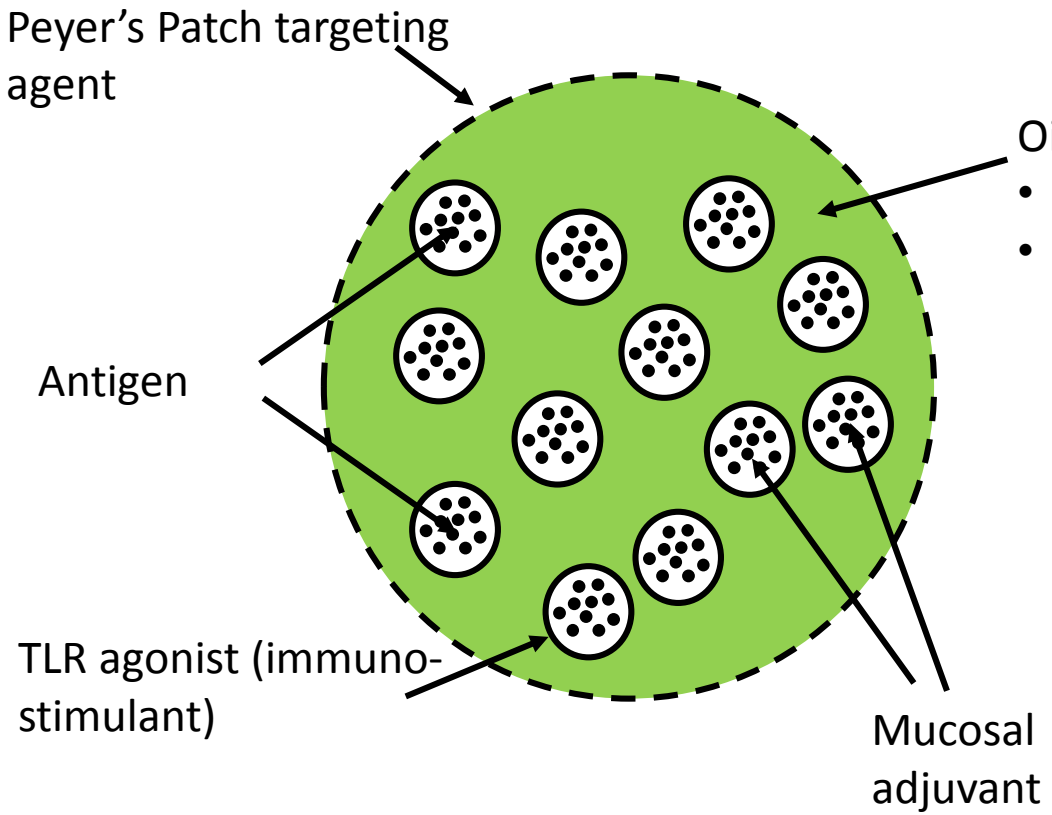
ABSTRACT

Murine antisera with neutralising activity for the coronavirus causative of Middle East respiratory syndrome (MERS) were induced by immunisation of Balb/c mice with the receptor binding domain (RBD) of the viral Spike protein. The murine antisera induced were fully-neutralising *in vitro* for two separate clinical strains of the MERS coronavirus (MERS-CoV). To test the neutralising capacity of these antisera *in vivo*, susceptibility to MERS-CoV was induced in naive recipient Balb/c mice by the administration of an adenovirus vector expressing the human DPP4 receptor (Ad5-hDPP4) for MERS-CoV, prior to the passive transfer of the RBD-specific murine antisera to the transduced mice. Subsequent challenge of the recipient transduced mice by the intra-nasal route with a clinical isolate of the MERS-CoV resulted in a significantly reduced viral load in their lungs, compared with transduced mice receiving a negative control antibody. The murine antisera used were derived from mice which had been primed subcutaneously with a recombinant fusion of RBD with a human IgG Fc tag (RBD-Fc), adsorbed to calcium phosphate microcrystals and then boosted by the oral route with the same fusion protein in reverse micelles. The data gained indicate that this dual-route vaccination with novel formulations of the RBD-Fc, induced systemic and mucosal anti-viral immunity with demonstrated *in vitro* and *in vivo* neutralisation capacity for clinical strains of MERS-CoV.

Vaxine Technology Achieving Oral Immunisation



Combine Immunological Expertise with Formulation Know-how To create Designer Vaccines



Oil phase:

- Mineral oil (stimulates macrophages)
- GRAS immunopotentiators:
  - *Enhance ab response, IL-6 ↑*
  - *Improve ag presentation, Th1 ↑*
  - *Strengthen homing, T cell memory ↑*

Vaxine

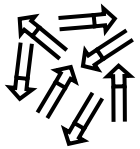
Vaxcine Competitive Advantages

	Vaxcine	Micro-particles	Viruses & VLPs	Bacteria	Metal Particles
Examples			Vaxart*	Prokarium*	Immunitor*
All antigens possible?	Yes	Yes	No, only protein	Yes, in theory	Not all
High efficiency of incorporation?	Yes	No	Yes	Yes	Yes
Flexibility in choice of immuno-modulator?	Yes	Yes	No	No	No
Reproducibility of manufacture?	Yes	No	n.d.	n.d.	n.d.
Patent position?	Yes	No	n.d.	n.d.	Limited
Easy to register?	Yes	Yes	Not if live	Not if live	Yes

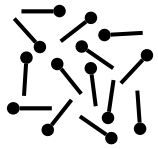
** based on information in the public domain*

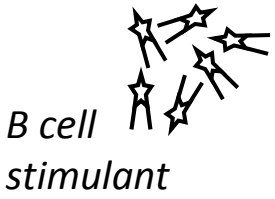
Vaxcine

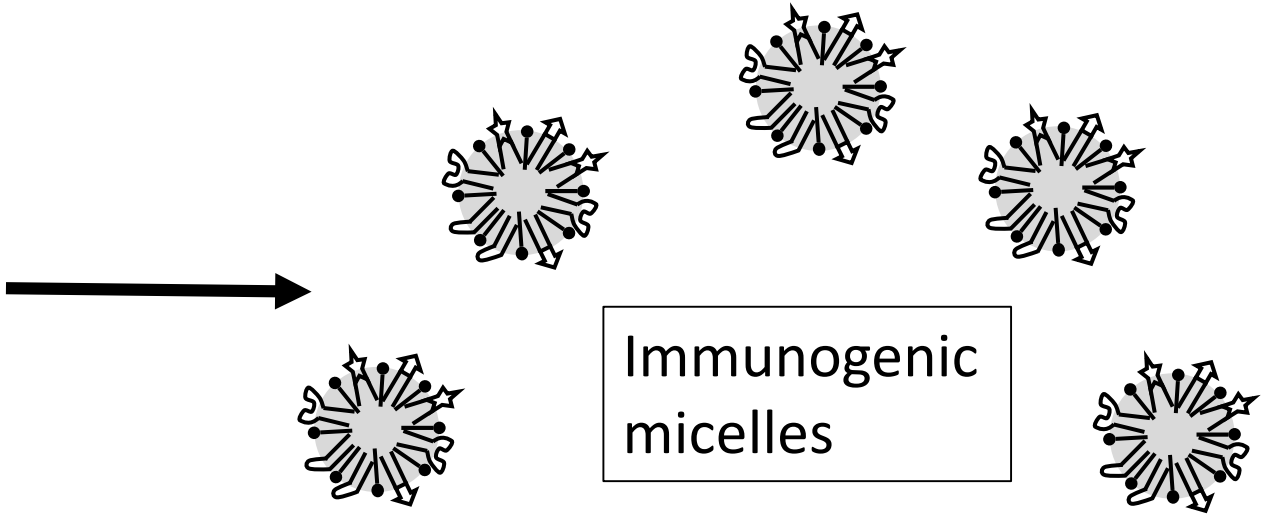
Nasal Vaccine – Easy to Manufacture



Ingredients







Immunogenic micelles

Clear colourless solution

Pre-filled applicator

Vaxine

Patient-friendly Administration

Painless

Non-invasive

Suitable for all ages

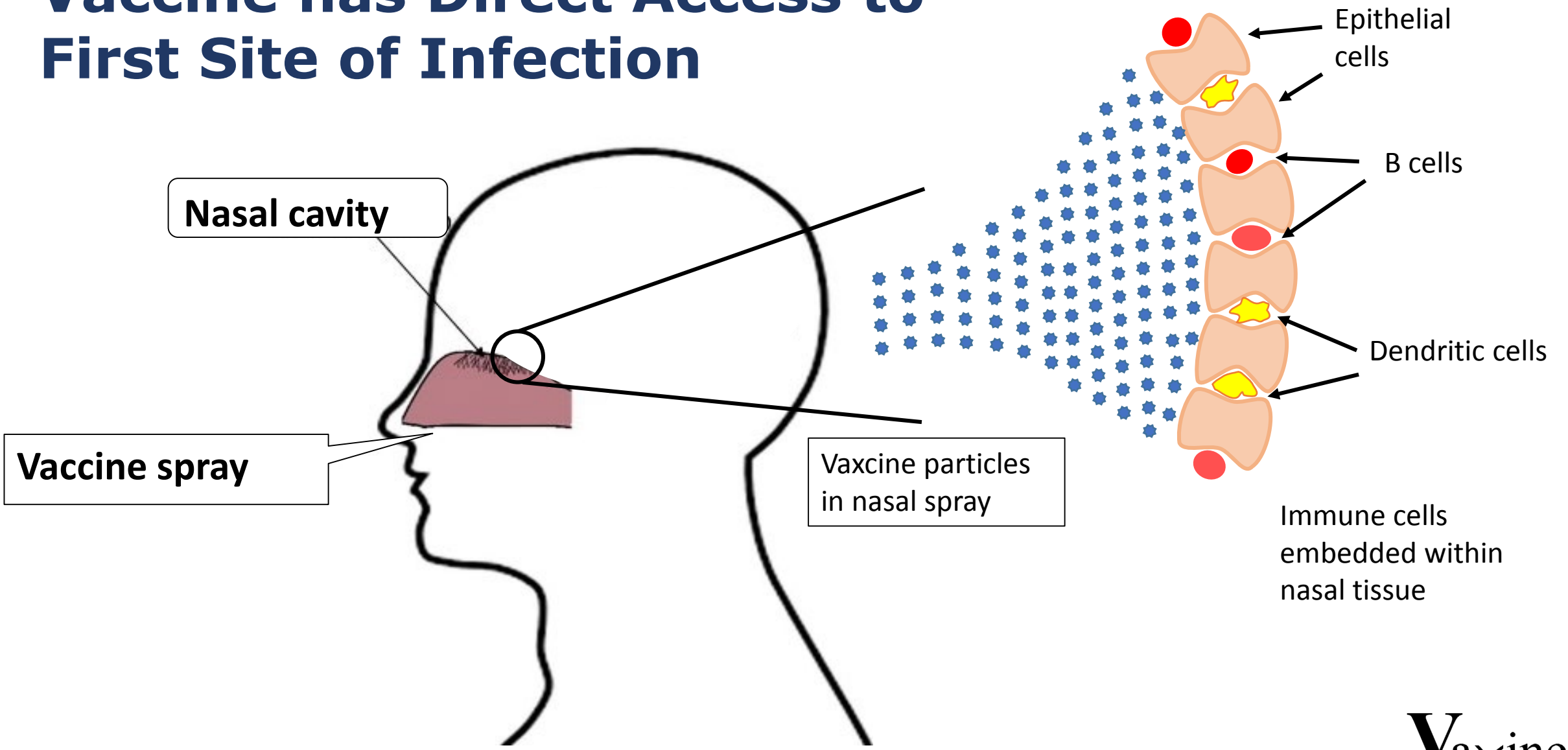
No hazardous waste

Generates immunity where needed

Proof-of-Concept in Universal ‘flu vaccine

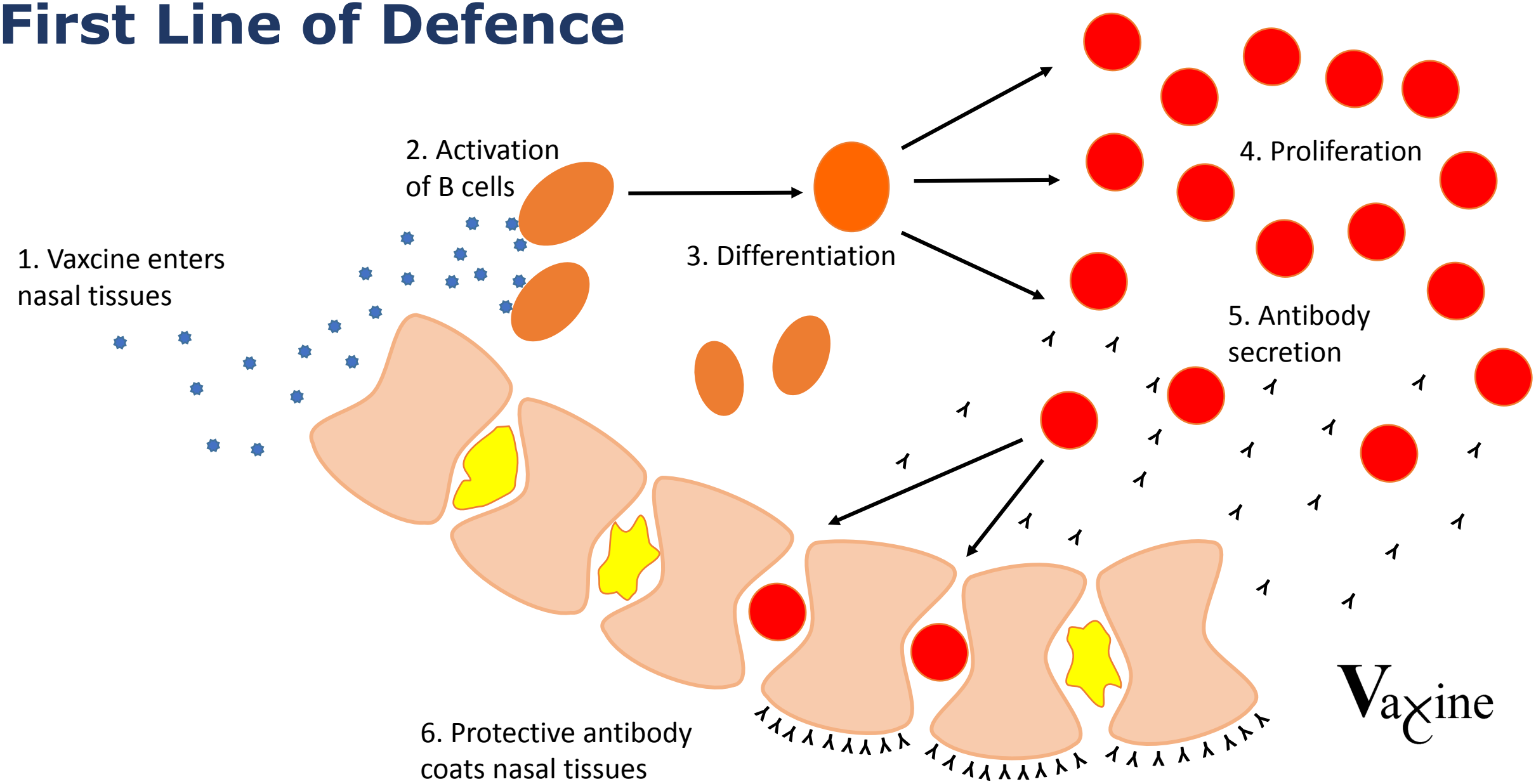
Vaxine

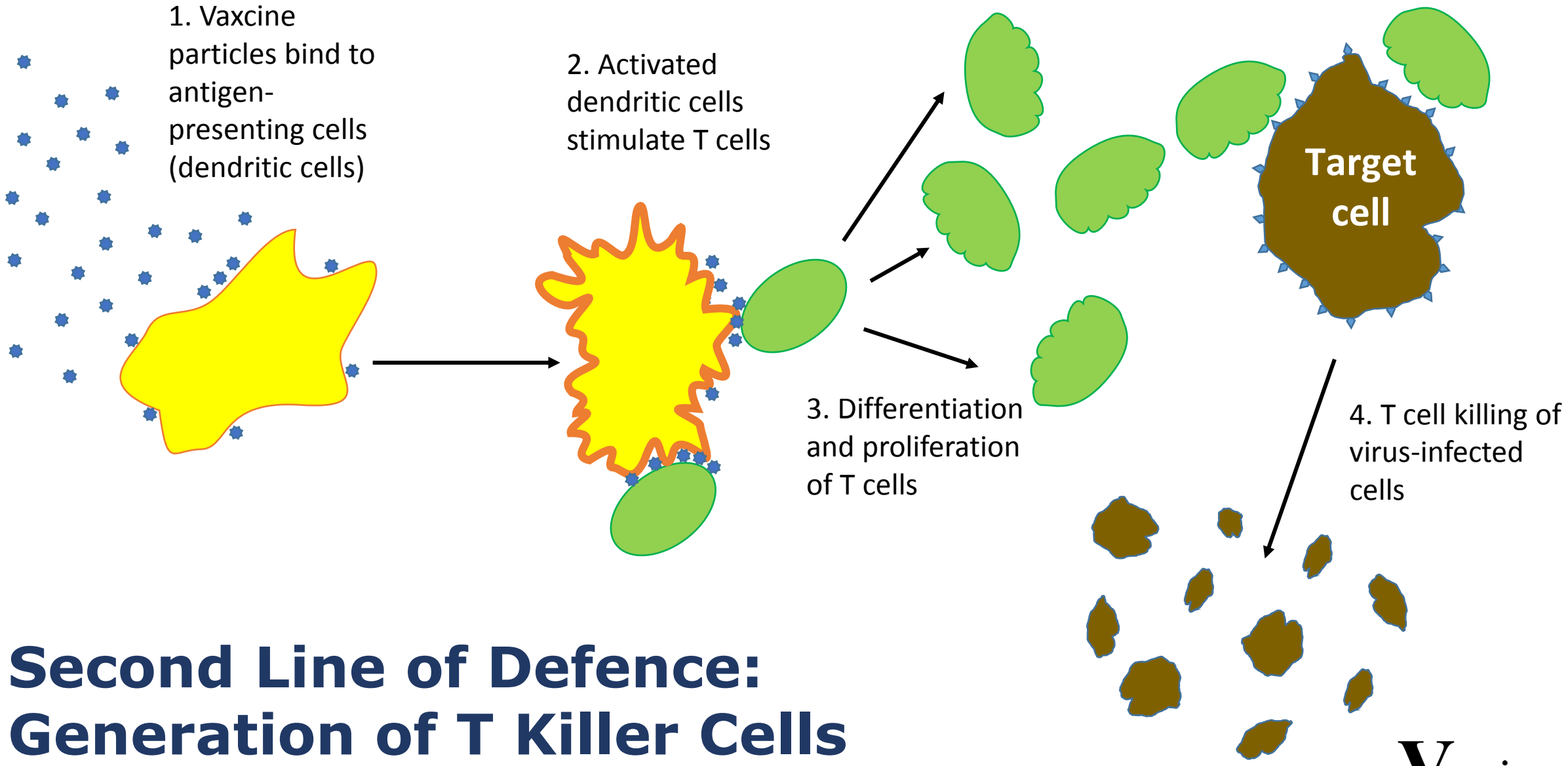
Vaccine has Direct Access to First Site of Infection



Vaxine

Vaccine Generates Antibody as First Line of Defence

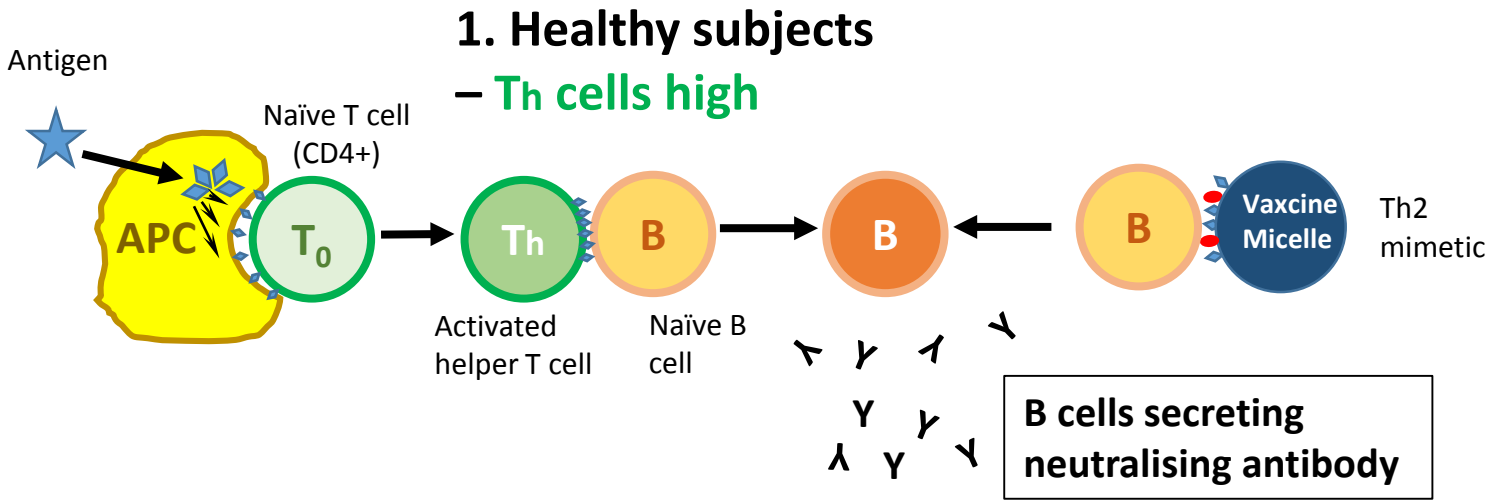




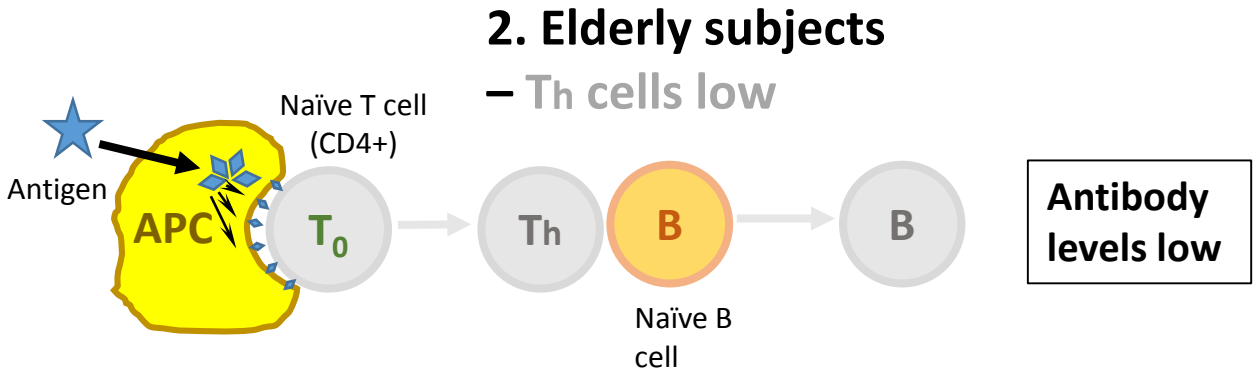
Second Line of Defence: Generation of T Killer Cells

Vaxine

Efficacy in Elderly or Immuno-compromised Subjects



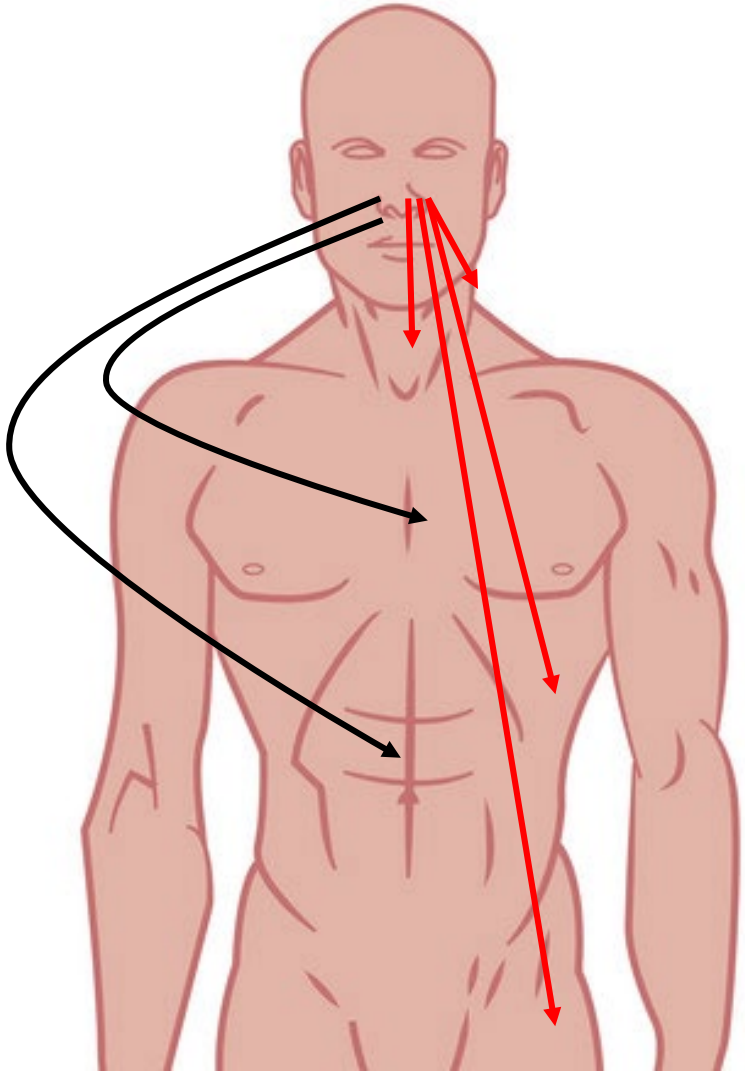
3. Vaxcine solution bypasses T helper cells, so good immunity in elderly subjects



Vaxine

Strong Immunity Generated Throughout the Whole Body

Mucosal immunity spreads from nasal passages to lung and intestine

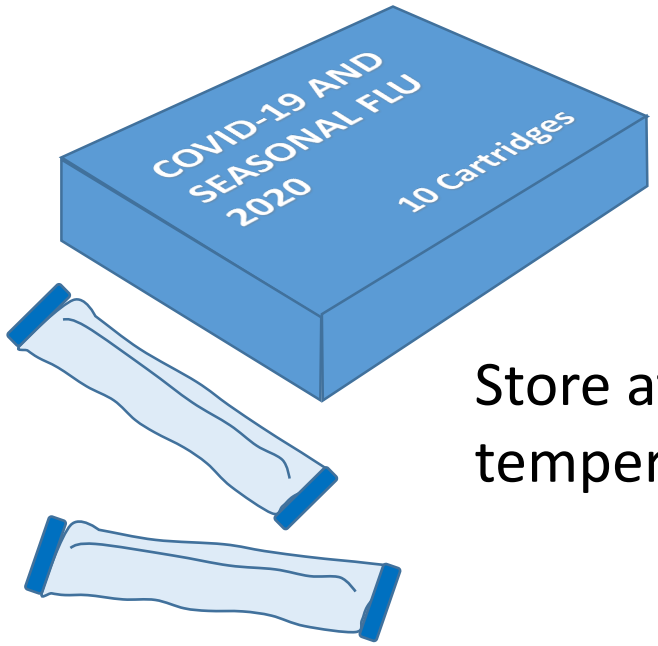


Antigen passes into draining lymph nodes and generates systemic immunity in the bloodstream

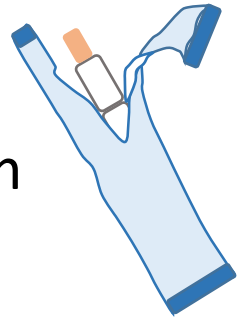
Vaxine

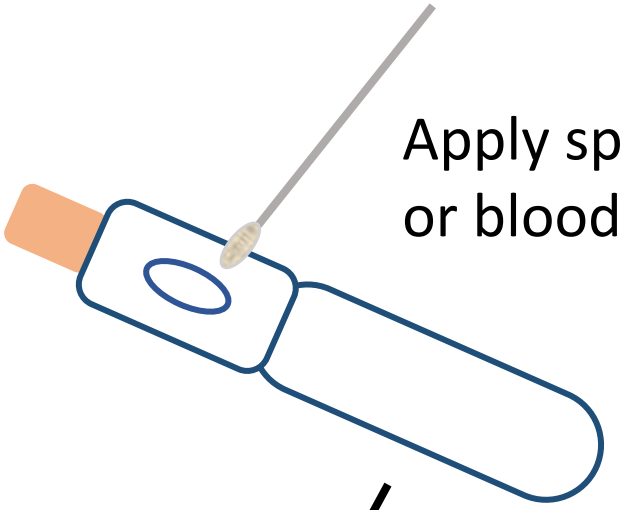
Point-of-care Test:
5 minutes to Diagnosis

Vaxine



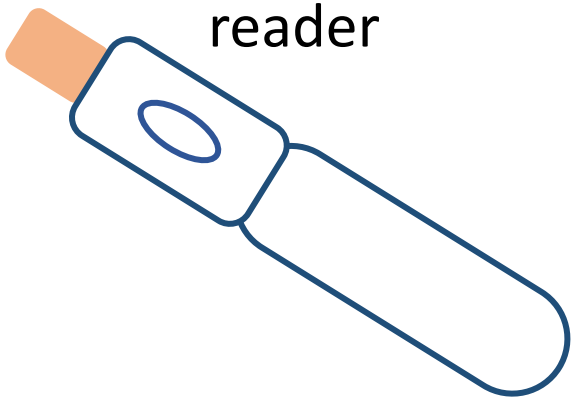
Store at room temperature

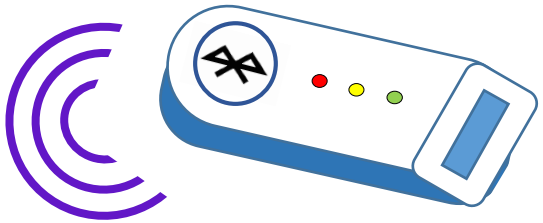




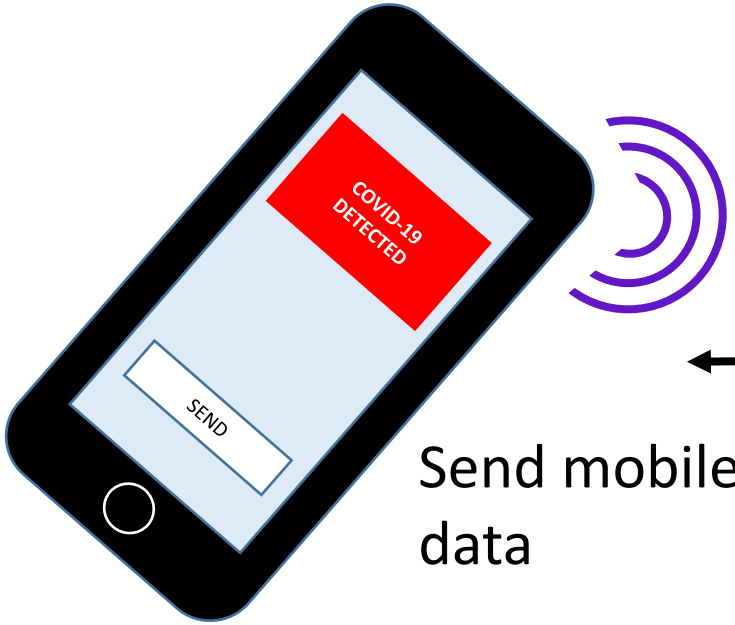
Apply sputum or blood

Insert into reader





View result



Send mobile data

Samples Applied On-the-spot

Vaxine

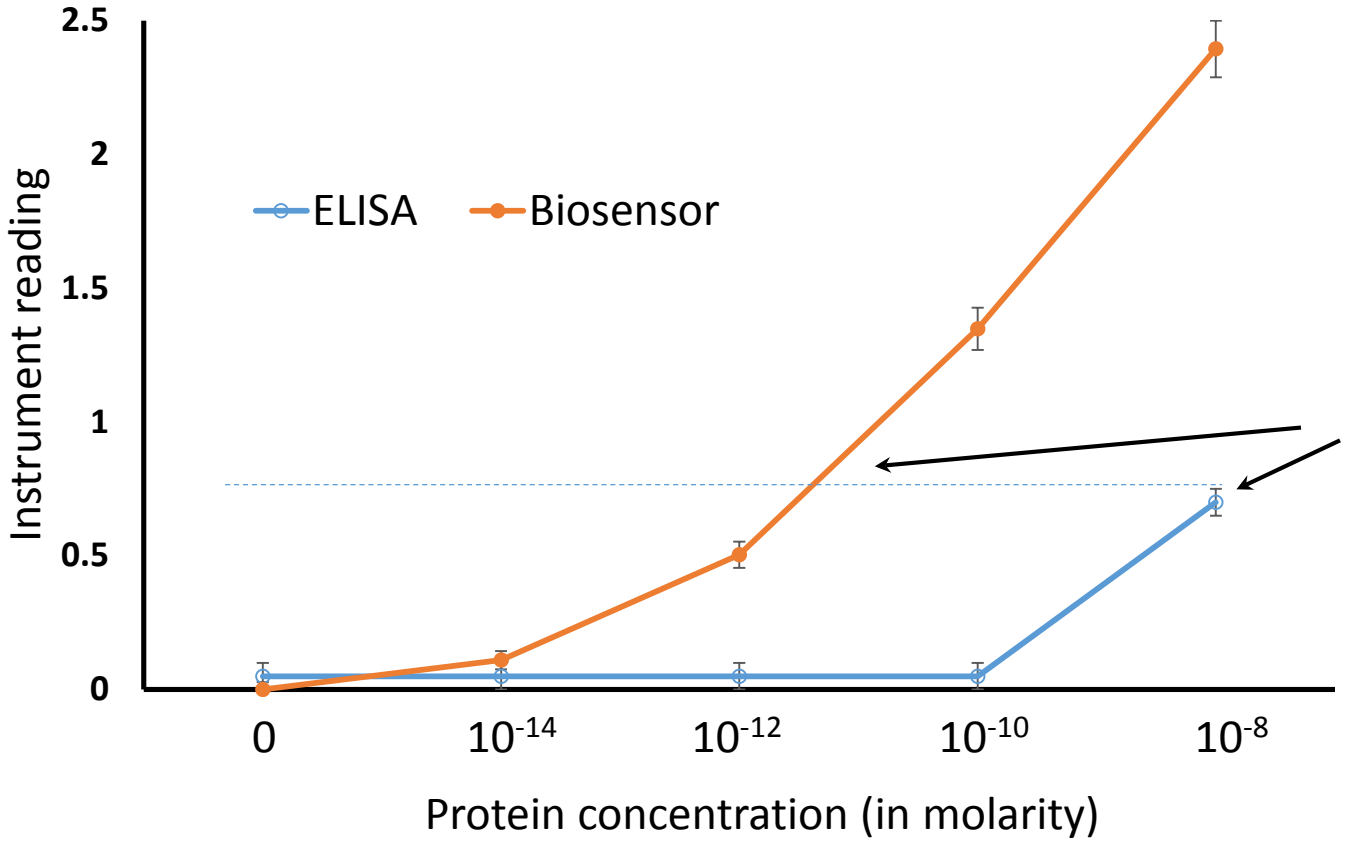
Sputum/saliva

Finger-prick whole blood

Biosensor probe

Biosensor Much More Sensitive than Traditional Techniques

Vaxine

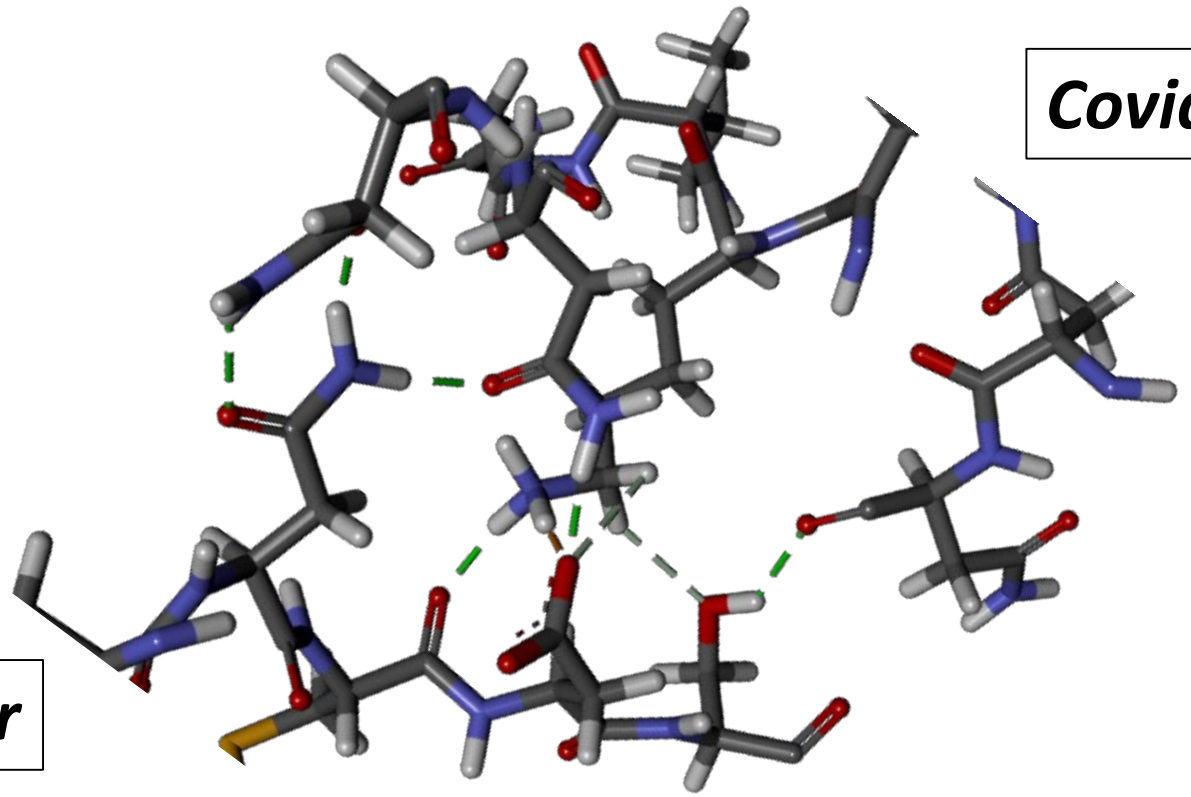


biosensor can detect proteins at 1000-fold lower concentration than ELISA

Middlesex University

Wang *et al* (2017) *Biosensors and Bioelectronics* **92**:482-488

Biosensor Probe has Peptide Aptamer Attached

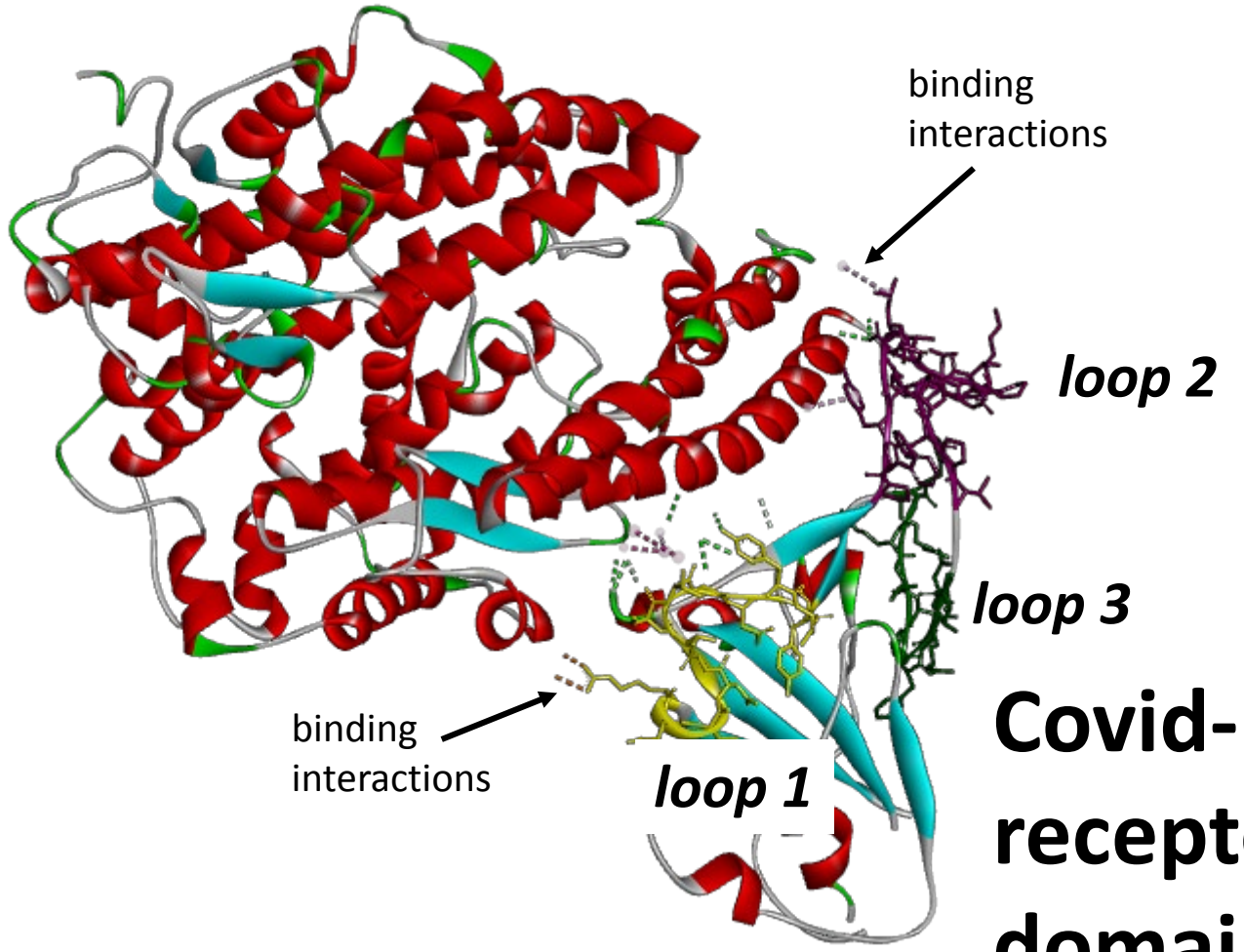


Aptamers designed using algorithms derived from data-mining of protein-protein interactions, to maximise multicentre interactions

Vaxine

Coronavirus binds to the ACE-2 Cell Receptor via Three Peptide Loops

ACE-2 receptor



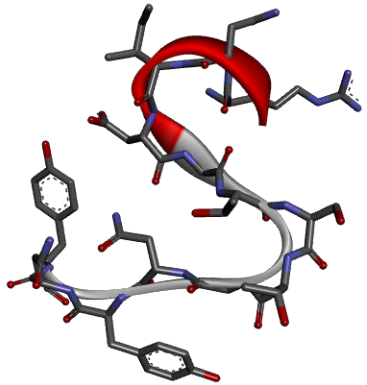
Covid-19 receptor-binding domain

Vaxine

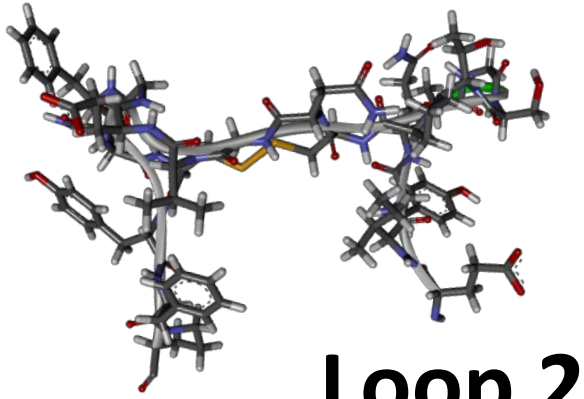
Vaxine

Specific Aptamers are Designed to Bind to Each Loop

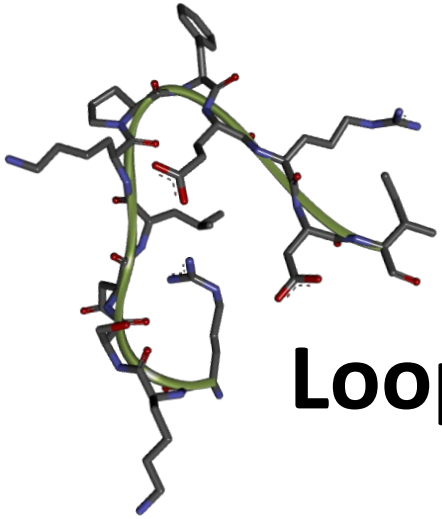
Vaxine



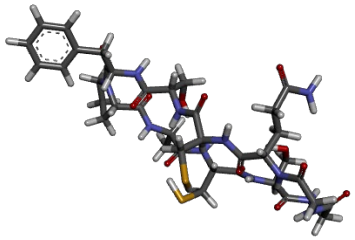
Loop 1



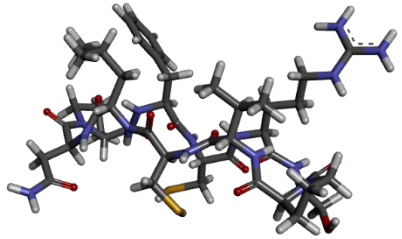
Loop 2



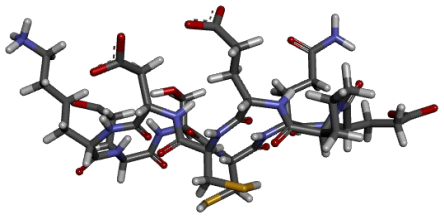
Loop 3



Aptamer 1



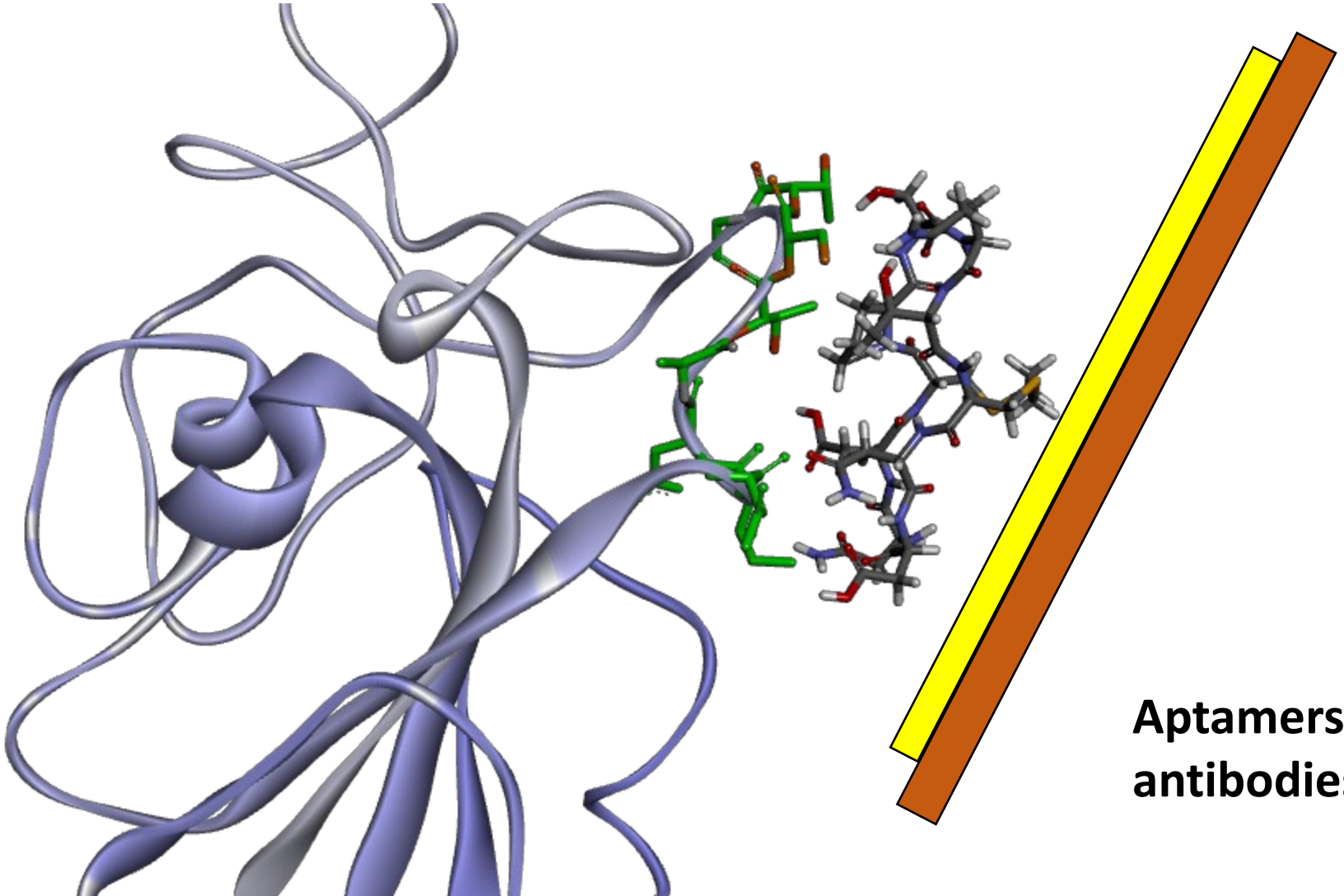
Aptamer 2



Aptamer 3

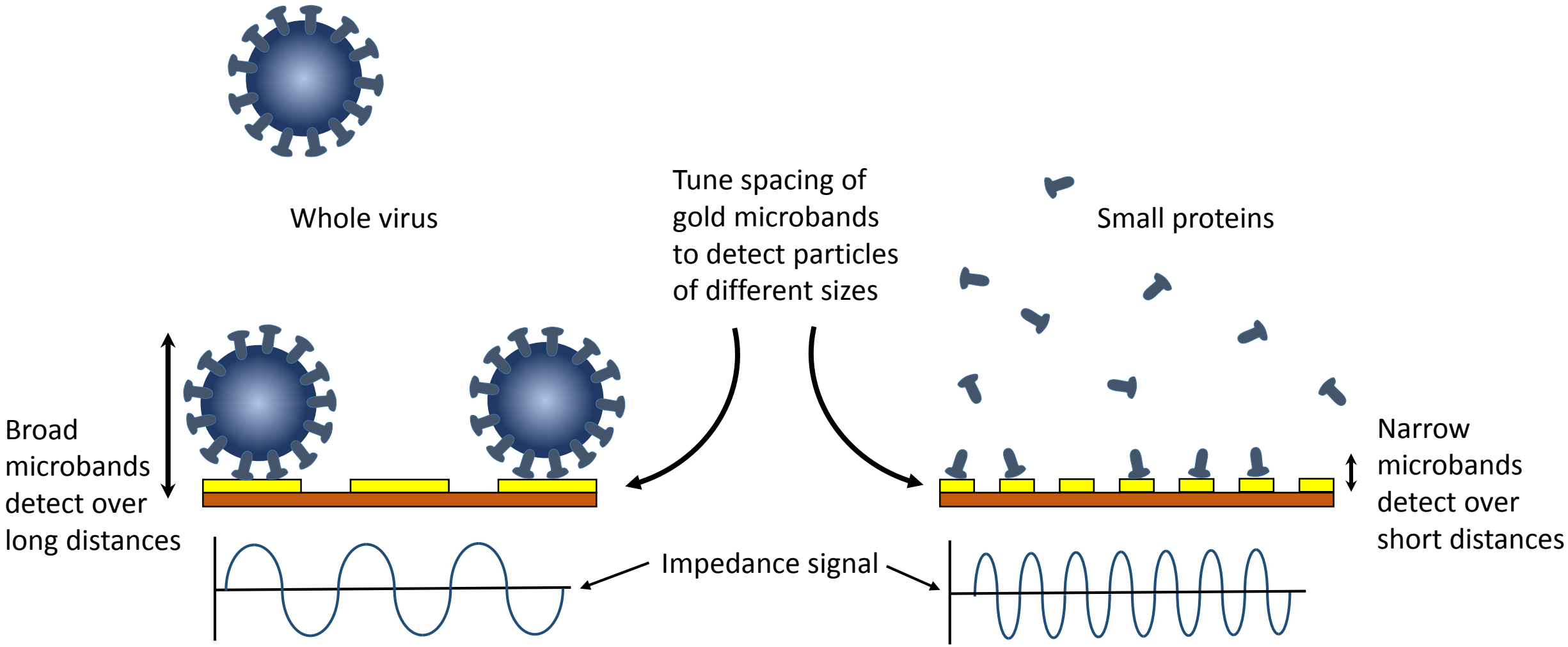
Specific Aptamers Attached to Sensor Allows Virus to Bind Selectively

Vaxine



Aptamers more sensitive than antibodies, and more stable

Device Can Distinguish Between Virus and Protein



Multiple Analytes will be Detected Simultaneously

Vaxine

Covid-19
- ✓ Virus
- ✓ N-protein
- ✓ Antibody

MERS coronavirus
- ✓ Virus
- ✓ N-protein
- ✓ Antibody

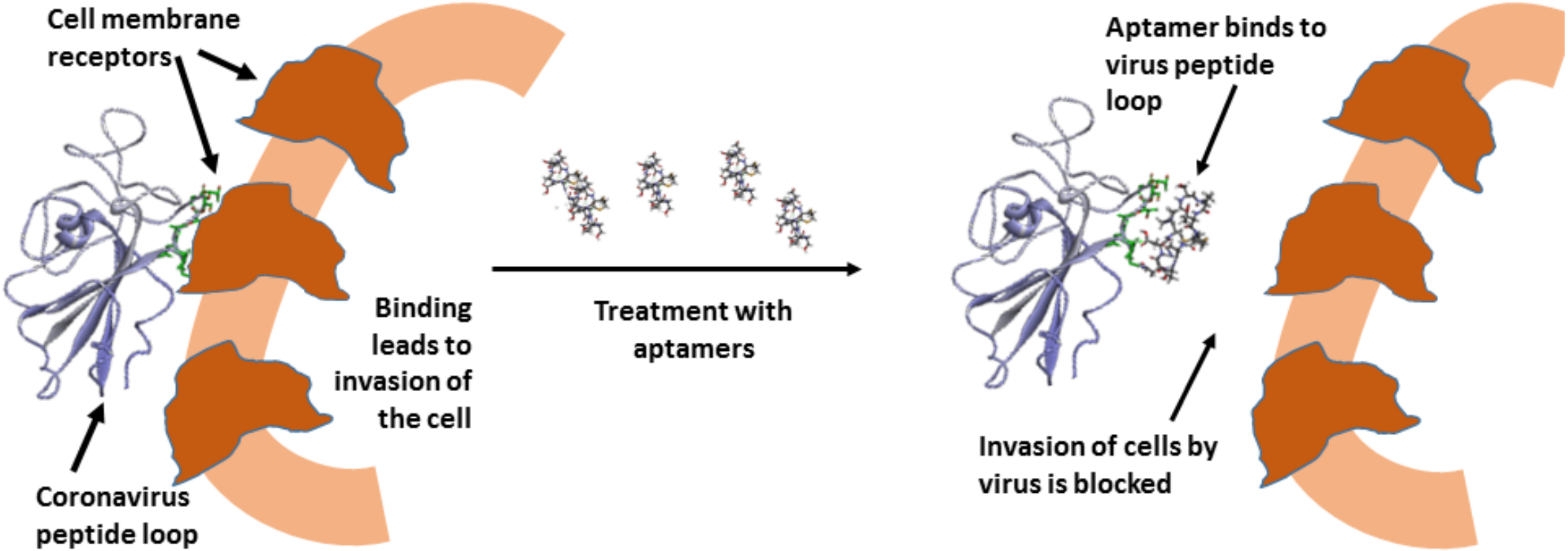
SARS coronavirus
- ✓ Virus
- ✓ N-protein
- ✓ Antibody

Seasonal ‘flu
- ✓ Virus
- ✓ N-protein
- ✓ Antibody

Swine ‘flu
- ✓ Virus
- ✓ N-protein
- ✓ Antibody

Bird ‘flu
- ✓ Virus
- ✓ N-protein
- ✓ Antibody

Therapeutic Application of Aptamer



Vaxine

Advantages over Antibodies

Extremely stable

Small – therefore more potent

Easy to make – large quantities readily available

No risk of ADE – absence of Fc fragment

Simple to modify – can easily address mutation

Vaxine