Objectives

- Review the definition of a vaccine and list its components.
- Discuss the characteristics of an ideal vaccine.
- Explain the workflow within a veterinary vaccine production facility.
- Allow students to discover possible vaccine development targets.
- Show examples of successful vaccine development from Cairo University and from around the world.

Viral vaccines

A biopharmaceutical preparation containing a material originating from a virus (or mimicking a virus structure) that induces an immunological resistance to diseases. The preparations also contain additives and, excipients as well as residual material from the production process.

5/10/2020 Vaccinology-Ausama 3

What is a vaccine?

The viral antigen or mimic is only one of the components

Resistance/protection [A successful immune response must encompass all the following parameters: Time, Type, Level, Location, Feed back mechanism]

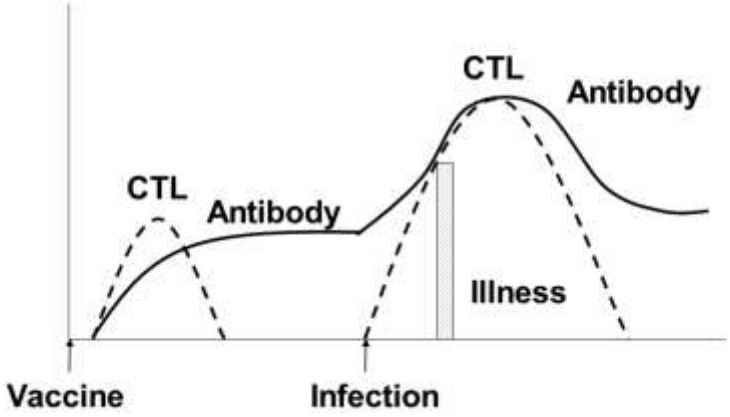
Stabilizer for live virus vaccines or viral antigens and proteins

Substances from the production host.

Residual inactivating agents.

Adjuvants for many inactivated vaccines.

The goal of vaccination
Is it just prevention of disease?



What is protection/immunological resistance?

But may be prevention of disease is not the only thing….. Sometimes it means prevention of replicat

Ideal vaccines

1- Produce effective resistance to infection. (Measures of protection?)

2- Produce long lasting immunity. (At what compartment(s)?)

3- Safe for vaccinated animals (What aspects of safety can you think of?).

4- Free from adventitious agents (no other viruses; how can an adventitious virus enter the formula).

5- Sterile (no microbial contaminants; how do microorganisms gain access).

6- Stable. (Where? For how long?)

7- Affordable. (To whom? Rem: Socioeconomic)

8- Produce early response following vaccination.

Limitations of live virus vaccines (one or more of the following)

1- Mutation and reversion to virulence (Major disadvantage).
2- Shedding of the virus.
3- Instability in tropical conditions.
4- Poor uptake in tropical conditions.
5- May cause abortions in pregnant animals.
6- May be dangerous to immunocompromised individuals.
7- May be subject to interference.

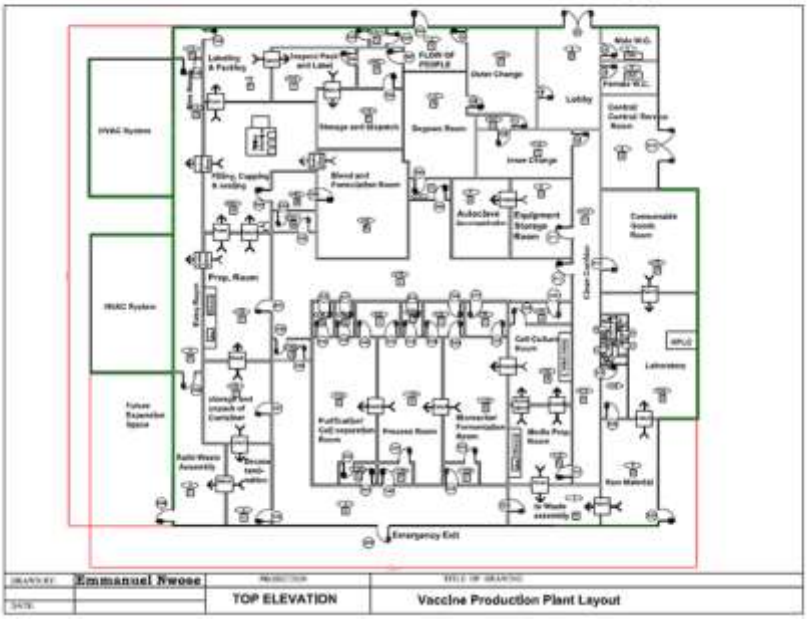
That means that there is reason to attempt development here.

Limitations of inactivated vaccines

1- Booster doses needed?!
2- Short duration of immunity!?
2- No local immunity in the different body compartments!?
3- Administration by injection !?
4- Adjuvants essential to stimulate cell-mediated immunity.
5-Takes a relatively long time for the immune response to develop.

That means that there is reason to attempt development here.

Production Technology



Each aspect of the complex production environment or technology is also target for development.

Production Technology

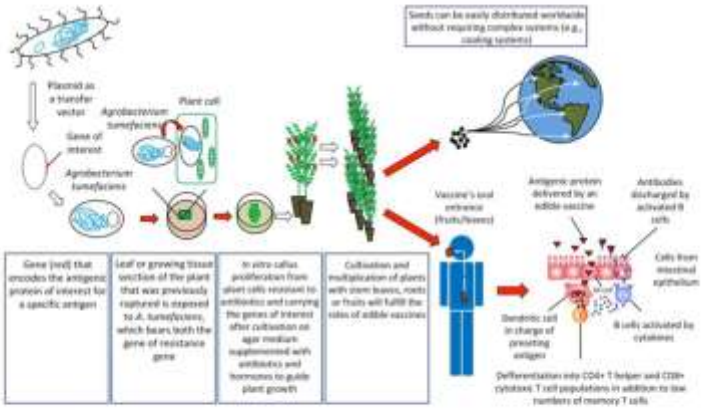
https://www.youtube.com/watch?v=J0SvutsCHrU

Example targets for vaccine development

1. Duration of immunity.
2. Protection from a single immunization.
3. Rapid protection.
4. Can be used in emergency situations.
5. Protection of all compartments of the body/immune system.
6. Can be used in multiple route (non injectable).
7. Stability enhancement.
8. Type of adjuvant.
9. Production economics.
10. Reduction of transient of immune suppression.

Examples of successful vaccine development

Production Platform: Plant-Based



Examples

Ther Adv Vaccines. 2015 Sep; 3(3-4): 139–154.
doi: 10.1177/2051013615613272
PMCID: PMC4667769
PMID: 26668752

Plant-based vaccines for animals and humans: recent advances in technology and clinical trials

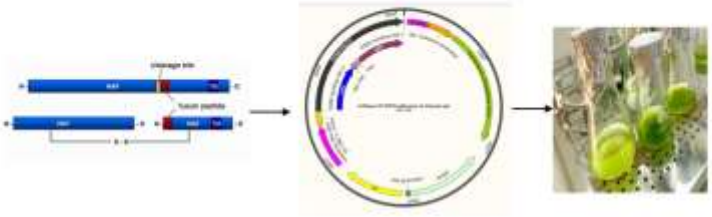
Natsumi Takeyama, Hiroshi Kiyono, and Yoshikazu Yuki

Table 3.

Plant-based vaccines for veterinary use.

Host	Pathogen	Antigen	Plant	Administration route	Treated animal	Reference
Chicken	Newcastle disease	Hemagglutinin-neuraminidase	Tobacco suspension cells	Subcutaneous	Chicken	Yeung et al. [2006] Approved by USDA
Chicken	Newcastle disease	F protein	Maize	Oral	Chicken	Guerrero-Andrade et al. [2006]
Chicken	Newcastle disease	F protein	Rice	Oral	Mice	Yang et al. [2007]
Chicken	IBV	S1 glycoprotein	Potato	Oral	Chicken	Zhou et al. [2004]
Chicken	IBDV	VP2	Rice	Oral	Chicken	Wu et al. [2007]
Pig	ETEC	Fimbriae (F4)	Tobacco (chloroplast)	N/D	Pig (in vitro assay in intestines)	Kolotilin et al. [2012]
Pig	ETEC	Fimbriae (F4)	Alfalfa	Oral	Piglet	Joensuu et al. [2010]
Pig	ETEC	Cholera toxin B subunit	Rice	Oral	Pig	Takeyama et al. [2015]
Pig	ETEC	Fimbriae (F4)	Barley	Subcutaneous	Mice	Joensuu et al. [2010]
Pig	Foot and mouth disease virus	VP1	*Nicotiana benthamiana*	Intramuscular	Pig	Yang et al. [2007]
Pig	TGEV	S protein	Tobacco	Intramuscular	Pig	Tuboly et al. [1800]
Cattle	Bovine Herpesvirus	gD protein	Tobacco	Intramuscular and subcutaneous	Cattle	Perez Filgueira et al. [2003]
Cattle	Bovine Viral Diarrhea Virus	E2 protein	Alfalfa	Intramuscular	Cattle	Perez Aguirreburualde et al. [2013]
Cattle	Rinderpest virus	Hemagglutinin	Peanut	Oral	Cattle	Khandelwal et al. [2003]

Production Platform: Algae-Based



The is another example from the Department of Virology of the Faculty of Veterinary Medicine of Cairo University.

What advantages can you think of when algae are used instead of conventional technology.

Examples

PUBLIC RELEASE: 14-MAY-2007

Students devise oral quick-dissolve strips for rotavirus vaccine

Simple drug-delivery system could cure illness that kills children

JOHNS HOPKINS UNIVERSITY

SHARE PRINT E-MAIL

A thin strip that dissolves in the mouth like a popular breath-freshener could someday provide life-saving rotavirus vaccine to infants in impoverished areas. The innovative drug-delivery system was developed by Johns Hopkins undergraduate biomedical engineering students.

During a two-semester course, the seven-student team fabricated a thin film that should melt quickly in a baby's mouth, prompting the child to swallow the vaccine. The dissolved medication is coated with a material to protect it in the child's stomach. This coating is also designed to release the vaccine in the small intestine, where it should trigger an immune response to prevent a rotavirus infection.

IMAGE: AS ENVISIONED BY THE DESIGN TEAM, A SMALL PIECE OF THIS FILM WOULD STICK TO AND THEN DISSOLVE QUICKLY ON AN INFANT'S TONGUE, CAUSING THE CHILD TO SWALLOW THE ROTAVIRUS... view more >

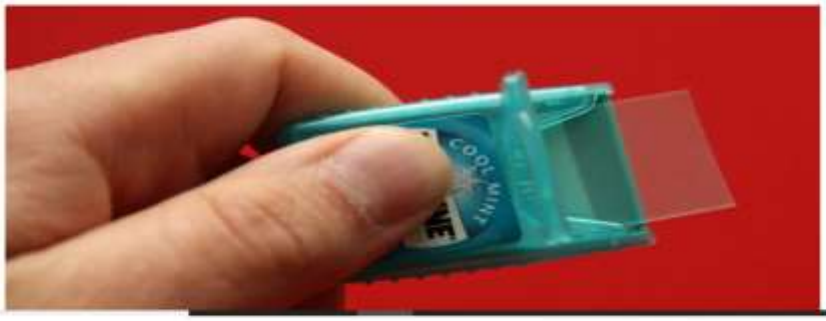
CREDIT: WILL KIRKPATRICK

Examples

McMaster scientists working on new melt in your mouth vaccine

Group receive $100K grant to study how breath strip-like tablets hold up in the heat

CBC News · Posted: Sep 22, 2014 7:25 AM ET | Last Updated: September 24, 2014



Examples

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NEWS | April 29, 2020

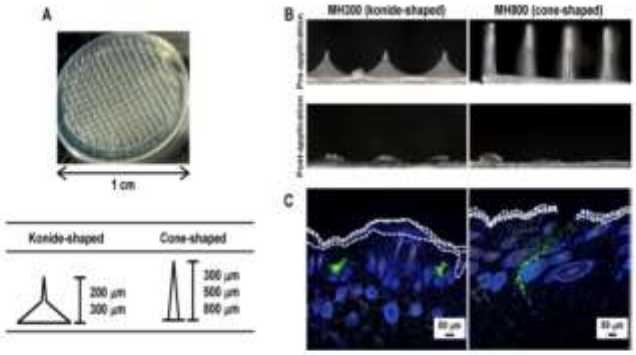
COVID-19 vaccine with patch delivery technology enters preclinical testing at UC Davis

(SACRAMENTO) — Verndari Inc., a biopharmaceutical company, announced today that it will begin preclinical testing this week at **UC Davis' Mouse Biology Program** to evaluate a potential vaccine and delivery system for COVID-19.

Verndari's VaxPatch is a single-dose vaccination kit that uses a dermal patch with a metal microneedle array to deliver vaccines. The company states that the technology eliminates the need for refrigeration, facilitates high-volume, automated manufacturing of vaccines and can potentially be self-administered on the subject's arm.

"Verndari was founded to enable a rapid response to new viral threats as well as to produce more effective vaccinations for existing viruses, such as seasonal flu, while sharply reducing costs and making vaccine administration much simpler," said Verndari's Chief Executive Officer Daniel R. Henderson in a **release**. "Our new approach and previous work enabled us to quickly bring a potential vaccine against COVID-19 to preclinical testing. UC Davis provides a world-class forum for testing, with

Delivery:
Transdermal Patches



NANO-FORMULATED VACCINES TRIGGER AN OPTIMAL IMMUNE RESPONSE

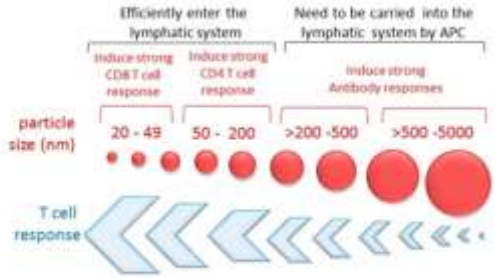
Vaccines 2016, 4(4), 45; doi:10.3390/vaccines4040045

Review

Synthetic Biodegradable Microparticle and Nanoparticle Vaccines against the Respiratory Syncytial Virus

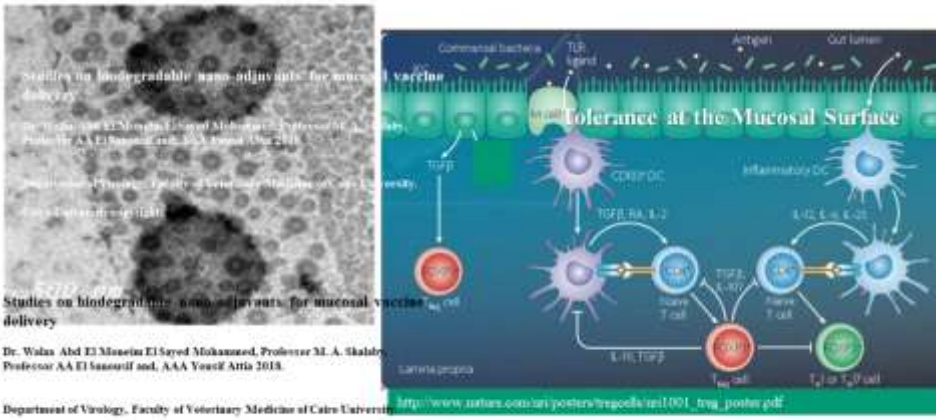
Patricia A. Jorquera and Ralph A. Tripp *

Department of Infectious Disease, College of Veterinary Medicine, 111 Carlton Street, University of Georgia, Athens, GA 30602, USA



Graph from NanoVic

Adjuvant Development: Mucosal Adjuvants



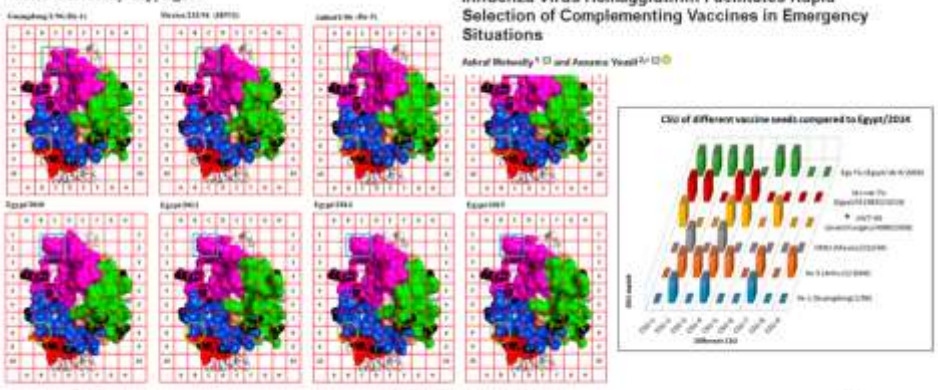
Stimulation of mucosal immunity is a hard challenge because it is designed to function in the presence of food and other harmless substances/antigens.

Antigen Selection: Selection of Complementing Structural Units

Department of Virology, Faculty of Veterinary Medicine of Cairo University.

Cairo University copyright.

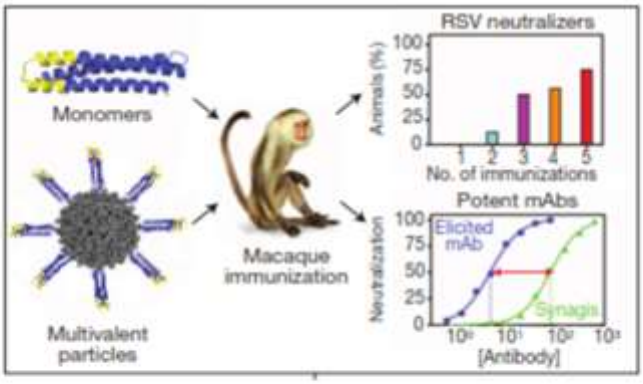
Visualization of Alternative Functional Configurations of Influenza Virus Hemagglutinin Facilitates Rapid Selection of Complementing Vaccines in Emergency Situations



If you know that the new virus looks like, then you can select from available vaccines to make a mixture of vaccines that will provide the required protection against the emerging strain.

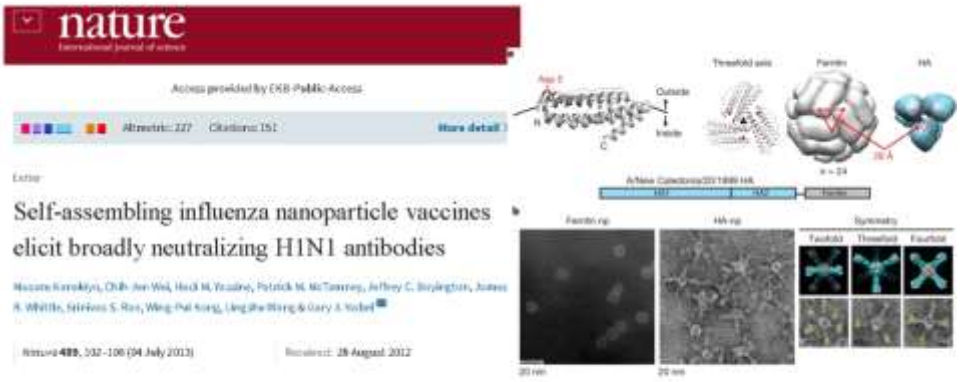
ARTICLE

Proof of principle for epitope–focused vaccine design



How many developments were done here?

Antigen Design:
Enhanced Epitope Presentation



nature

Access provided by CKB-Public Access

Altmetric: 227 Citations: 151 More detail

Letter

Self-assembling influenza nanoparticle vaccines elicit broadly neutralizing H1N1 antibodies

Masaru Kanekiyo, Chih-Jen Wei, Hadi M. Yassine, Patrick M. McTamney, Jeffrey C. Boyington, James R. Whittle, Srinivas S. Rao, Wing-Pui Kong, Lingshu Wang & Gary J. Nabel

Nature 499, 102–106 (04 July 2013)

Received: 28 August 2012