Feeding Botswana: From Field to Lab to Vaccine

Ferré/Marquet Vaccine Research Center
Keck Graduate Institute and Pitzer College

KGI
KECK GRADUATE INSTITUTE

Pitzer College
A Member of The Claremont Colleges
Chinese Proverb

Give a man a fish and you feed him for a day.

Teach a man to fish and you feed him for a lifetime.
Our Variation

Provide a country with a vaccine and they will need more vaccines forever.

Teach a country to make vaccines and the country will have vaccines forever.
The Mission of the Vaccine Research Center

- Globally, there is a lack of effective and inexpensive vaccines and very few developing countries have the ability to produce vaccines
- At the Vaccine Research Center, we are working with students and faculty from the University of Botswana to teach them how to produce vaccines needed in their country

- Others included in this collaboration
  - Botswana government
  - Botswana Vaccine Institute
  - Botswana National Veterinary Laboratory
  - International Livestock Research Institute (Nairobi, Kenya)
Initial Collaborative Effort: Botswana
Previous Students

Aditi Chandra
Claire Geary
Sally Yang
Perri Hopkins
Jose Cortez
Claire Geary
Somer Drummond
Caitie Tanaka
Claire Willey
Sidra Speaker
Julia Gibas-Jones
Nina Timberlake
Sara Garcia-Dehbozorgi
Aku Ntumy
Sam Jones
Lauren Cole
Lauren Kecskes
Matt Ward
Claire Willey
Stacie Crawford
LeeAnn Allen
Acacia Hori
Dylan Farrell
Amanda Berry
Eva Goa
Michelle Kung

Not pictured:
Rebecca Rubin
Kathleen Coquia
Dennis Duong
Bakang (BK) Baloi
Currently working in the lab
Our Current Targets

• **Rabies (Causative Agent: Rabies virus)**
  This virus is virtually incurable in developing countries and leads to certain death in about 55,000 people / year

• **Anthrax (Causative Agent: *Bacillus anthracis*)**
  This disease is lethal to both humans and animals and there are a number of outbreaks every year in Africa

• **Lumpy Skin Disease (Causative Agent: Capripoxvirus)**
  This virus causes a chronic debility in cattle that leads to serious nutritional and economic losses by decimating cattle in Botswana

• **Rift Valley Fever (Causative Agent: Rift valley fever virus)**
  This virus causes a chronic debility in cattle and other animals

• **East Coast Fever (Causative Agent: Rift valley fever virus)**
  This disease kills about 1.2 million cattle per year in Africa
Traditional vaccine production methods are too slow to respond and too costly

- Many are made by growing viruses in chicken eggs
- Many are produced in cell culture systems
- These methods are labor-intensive, time-consuming, and costly
Newer, western world vaccines are too expensive for the African people (and most of the world)

- Cervarix and Gardasil protect against the Human Papilloma Virus
- Reduce likelihood of cervical cancer
Economic realities for vaccines

• In Africa, vaccines need to be cheap to be effective
  – Herd immunity stops disease spread
• Vaccines for pandemics are needed immediately, and in large supply after an outbreak
• Current technology does not meet these requirements
• Better methods are needed
Current vaccine limitations

- Capital intensive
- Single-product cell production platform
- Requires complex and expensive aseptic culture that usually requires weeks or months for a production run
- Requires highly skilled workforce
- Lengthy product development cycle
Plants can supply vaccines and drugs

- Plants make proteins in the same biochemical way as animal cells with significant economic and commercial advantages
  - Low cost of goods
  - Simplified, low-tech production
  - No animal pathogens
  - Can be scaled easily
HOW?
PLANT VIRUSES: They are awesome! (at least for non-plants – like us)

Plant viruses DO NOT infect or cause disease in humans
But if they got into your body, your white blood cells would mount an immune response (Even though the plant virus cannot cause a disease in humans)
Given these plant virus characteristics, how can we make an effective and low cost vaccine?

✔ We can “decorate” our plant virus (good!) to look it look like a pathogenic human or animal virus (bad) using standard lab techniques.
An illustration of this technique

→ We start with a plant virus (cannot cause disease in humans and other animals)

→ We will have this cowboy with a white hat represent a “good” virus
Whereas, the “villain” disease-causing virus is represented by the cowboy with the black hat.
One major difference: 
*The black hat*
If we change the hat color of the “good” virus, then we can make him “look like” the villain.
What does a good, plant virus look like?
This is the “good”, plant virus

→ It is “good” because it doesn’t cause disease in animals or humans
This is the “bad” virus that is responsible for over 600,000 deaths/year in developing countries.

This is a surface protein, specific to the virus.
We identify surface proteins and clone the genetic sequence for it.
Now we can add the “bad” virus surface protein to the “good” virus using standard lab techniques.

Put the genetic sequence that can make this protein into the “good” virus genetic sequence.
Now “good” virus will **look like** the “bad” virus
How do we produce large volumes of these “decorated” viruses that can be used for vaccines?
Rapid inoculation technique (developed by iBio Therapeutics)
Then grow the plants for 1 week and extract the “vaccine”
Demonstration: Jellyfish gene for fluorescent green protein put into a plant
Extraction and Purification
(to be done in Botswana)
Design for the plant production facility

- Designed to produce 75 million vaccine doses / year in *Nicotiana benthamiana*
- Cost: ~$20 Million
- Greenhouse: 11,335 m$^2$
- Processing: 2,170 m$^2$
- Operations: 52 people
- Estimated cost / dose: 15 ¢
Using plants, therapeutic human antibodies (Zmapp) against the Ebola virus disease have been produced.

- The clinical trial data on ZMapp shows it is 100% effective in monkey studies, even in later stages of the infection.
- In February of this year, Mapp Biopharmaceutical received FDA approval for human clinical trials on patients in Liberia.
Patient- and cancer-specific therapeutic vaccine

Non-Hodgkin’s Lymphoma
General principles

- Introduce cancer-specific cell surface proteins to the patient
- The patient’s immune system is activated against the newly-introduced cancer proteins
- The immunological response cross-reacts with the cancer and the cancer cells are killed by the patient’s own immune system
- Chemo-therapy and radio-therapy could be eliminated
Patient-specific vaccine production

- Biopsy
- Identify cancer-specific Ig proteins
- Obtain and clone cancer-specific DNA sequence
- Make plant viral vectors
- Inoculate plants and produce the cancer-specific proteins (10 days)
- Extract and purify the cancer-specific proteins
- Package and courier vaccine to the clinic
How the patient-specific vaccine works

Inoculate patient once every month for 6 months

The patient builds immunity against the vaccine proteins (humoral and cellular response)

The immune response cross-reacts with the cancer cell-surface proteins (from which the vaccine was made)

The patient’s own immune system kills the cancer cells
Television coverage of clinical trials
Clinical trials at Stanford medical school
One of 16 patients, from whom a biopsy was removed and cancer-specific protein sequenced and cloned (Ms. Ali Gencarelle)
Cancer sequences cloned in plant virus and protein extracted for “vaccine”
Patient inoculated 1x/month for 6 months
Like most of the clinical trial patients, Ali Gencarelle is cancer-free after 10 years.
“Motho le motho kgomo” (one person, one beast)

A symbolic statue on the University of Botswana Campus