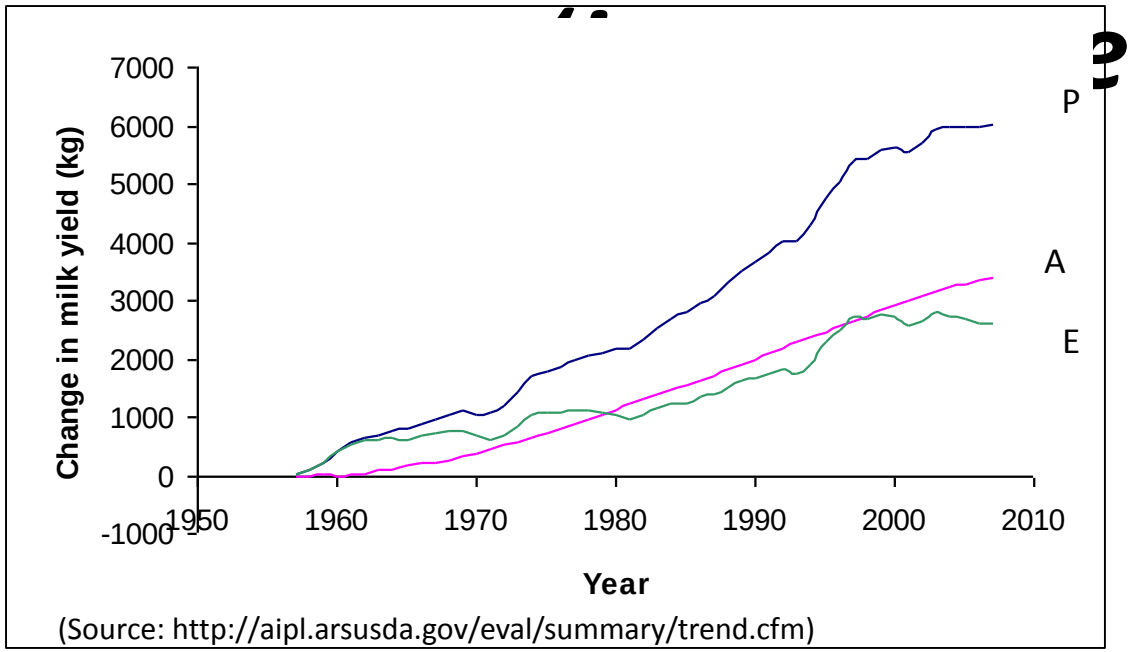
Vision for livestock genetics in Africa

Steve Kemp, ILRI

Animal Genetic Research for Africa (Biosciences for Farming in Africa), Nairobi, 10-11 September 2015

Genetic selection, interacting with environment, drives



(Source: http://aipl.arsusda.gov/eval/summary/trend.cfm)

Changes in milk yields of US Holstein cows

Mean phenotype (P), breeding value (A) and environmental effects (E = A - P). Results relative to 1957 base (mean yield 5859kg).

In the industrial world genetics has driven dramatic improvements in productivity

- Homogeneous environments (systems, markets, health, regulations, policies…….)
- Homogeneous genetics (a handful of well defined breeds)
- Superb data recording driving selection schemes

ILRI CGIAR

Achieving genetic gain in developing countries – the same biological rules but different *environments*

We must take account of the realities of small-scale livestock producers.

Diversity of:

- Environment
- Climate
- Feeds available
- Endemic diseases
- Local market context
- Infrastructure
- Institutions

ILRI CGIAR

Achieving genetic gain in developing countries – the same biological rules but different *environments*

We must take account of the realities of small-scale livestock producers.

Diversity of:

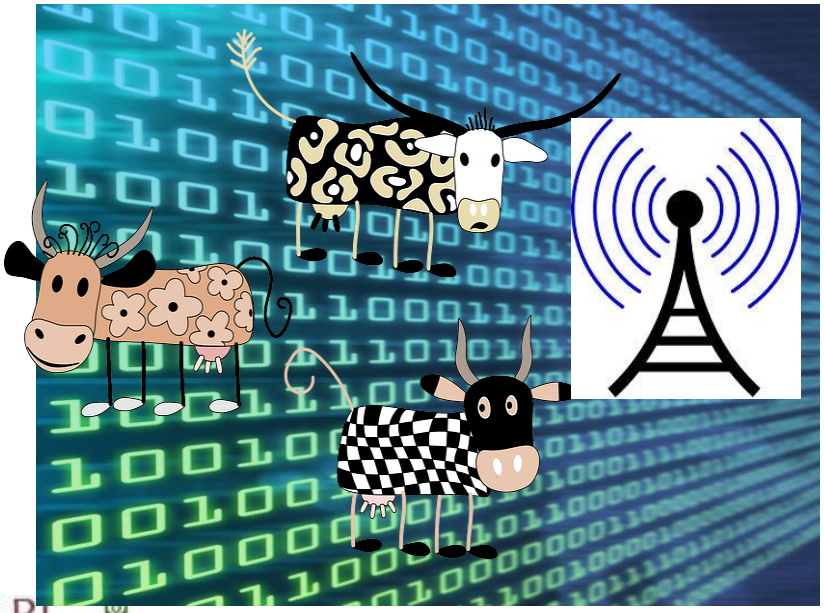
- Environment
- Climate
- Feeds available
- Endemic diseases
- Local market context
- Infrastructure
- Institutions

No data systems to inform selection.

No infrastructure to manage selection.

ILRI CGIAR

Genotype data is cheap and easy to obtain. Phenotype data remains a problem.



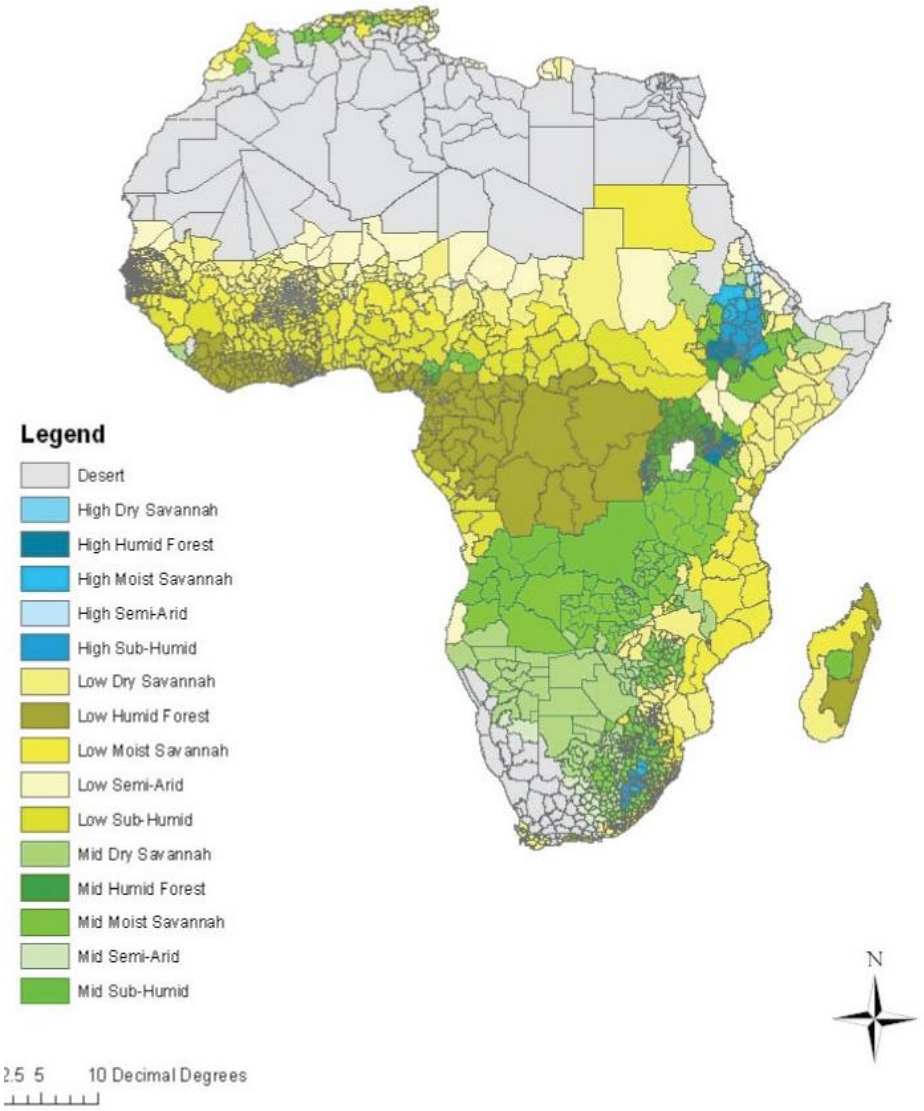
Can we skip a generation of technology?

- Fast, light, cheap performance data harvesting.
  - Cheap sensors, mobile platforms, crowd sensing…..
  - Simultaneously providing management information to the farmer and performance data to the breeder.

ILRI
CGIAR

Diversity of *environments* has created diversity of genetics. Let's not discard it.

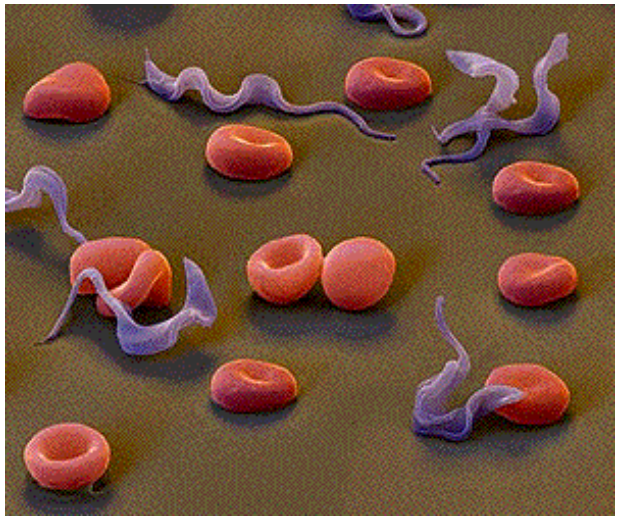
Tailor-made. Acting now to characterize and exploit the unique genomes and adaptations of Africa's livestock, such as the NAMETK cattle (above) could help breed new genotypes tailored to changing local environments.



African Trypanosomiasis

African Trypanosomiasis

- Caused by extracellular protozoan parasites – *Trypanosoma*
- Transmitted between mammals by Tsetse flies (*Glossina* sp.)
- Prevalent in 36 countries of sub-Sahara Africa.



In cattle

- A chronic debilitating and fatal disease.
- A major constraint on livestock and agricultural production in Africa.
- Costs US$ 1 billion annually.

In human (Human Sleeping Sickness)

- Fatal
- 60,000 people die every year
- Both wild and domestic animals are the major reservoir of the parasites for human infection.

ILRI CGIAR

Control and Treatment options for African Trypanosomiasis

Vector Control (Tsetse Fly)

- Using toxic insecticide
- Not sustainable
- Negative impacts on environment

Vaccine

- Tryps periodically change the major surface antigen – variant surface glycoprotein (VSG) and evade the host immune system.
- More than 2 decades, there is no effective vaccine developed.

Drug

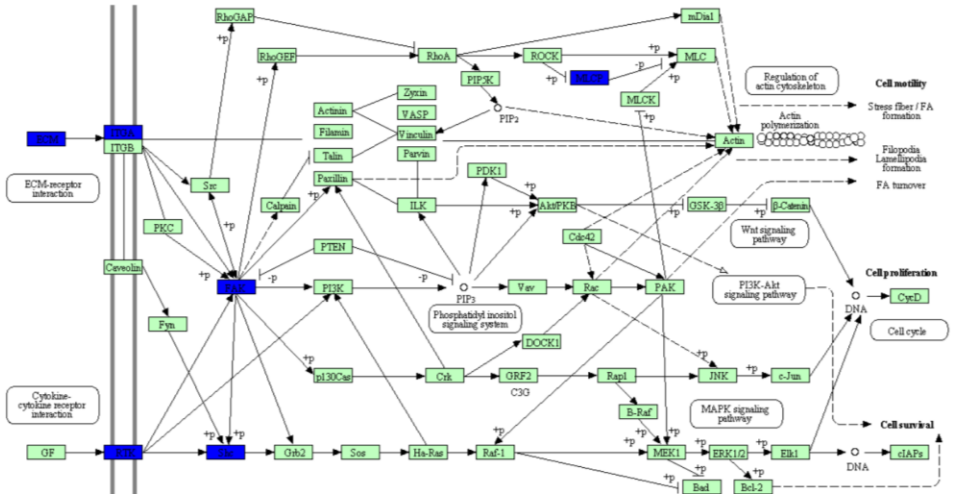
- Drug toxicity and resistance
- Expensive

New tools allow us to look in new places for sources of variation – including wildlife

"traditional" linkage mapping requires crosses – so initial discovery is limited to variants within a species

```
Cow NDama    KFITRRPSLKTLQEKGLIKDQIFGSPLHTLCEREKSTVPRFVKQCIEAVEK
Cow Boran    KFITRRPSLKTLQEKGLIKDQIFGSHLHTLCEREKSTVPRFVKQCIEAVEK
Human        KFISRRPSLKTLQEKGLIKDQIFGSHLHTVCEREHSTVPWFVKQCIEAVEK
Pig          KFITRRPSLKTLQEKGLIKDQIFGSHLHTVCERENSTVPRFVKQCIEAVEK
Chicken      KFISRRPSLKTLQEKGLIKDQIFGSHLHLVCEHENSTVPQFVRQCIKAVER
Salmon       KFISRRPSMKTLQEKGIIKDRVFGCHLLALCEREGTTVPKFVRQCVEAVEK
```

Comparative gene network and sequence analysis allows to ask new kinds of questions about genomes – eg "*what is different about this (group of) species compared to all other mammals*"

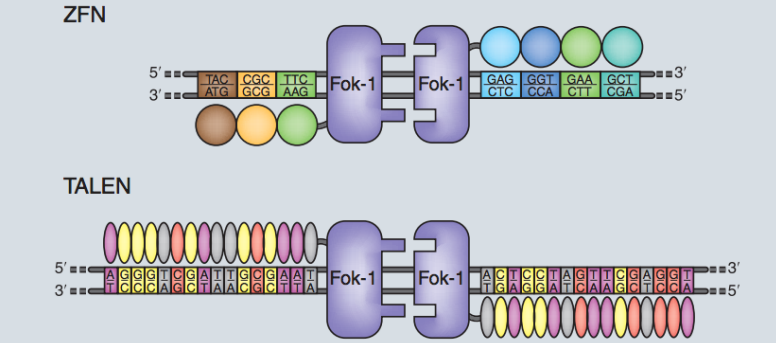


Time for a new search for variation underlying tropical adaptation and productivity

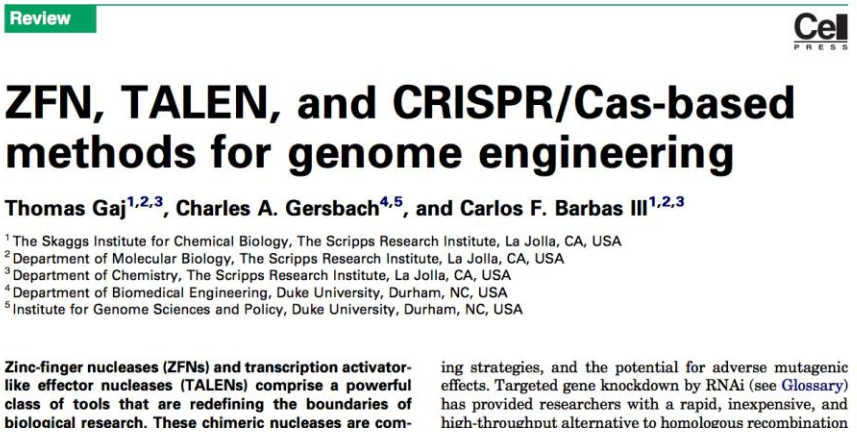
Identify and make use of the genetics underlying natural variation.

There has been no systematic search for the genomic basis of adaptation. Because until now we have had no validation tools and no delivery tools.

New Genome Editing tools change the landscape.



ZFNs and TALENs. Schematic (not to scale) of a ZFN pair (top) and a TALEN pair (bottom) to illustrate the DNA-binding principles of these enzymes. Image modified from *Nat. Methods* **8**, 53–55 (2011).



Review

Cell

ZFN, TALEN, and CRISPR/Cas-based methods for genome engineering

Thomas Gaj[1,2,3], Charles A. Gersbach[4,5], and Carlos F. Barbas III[1,2,3]

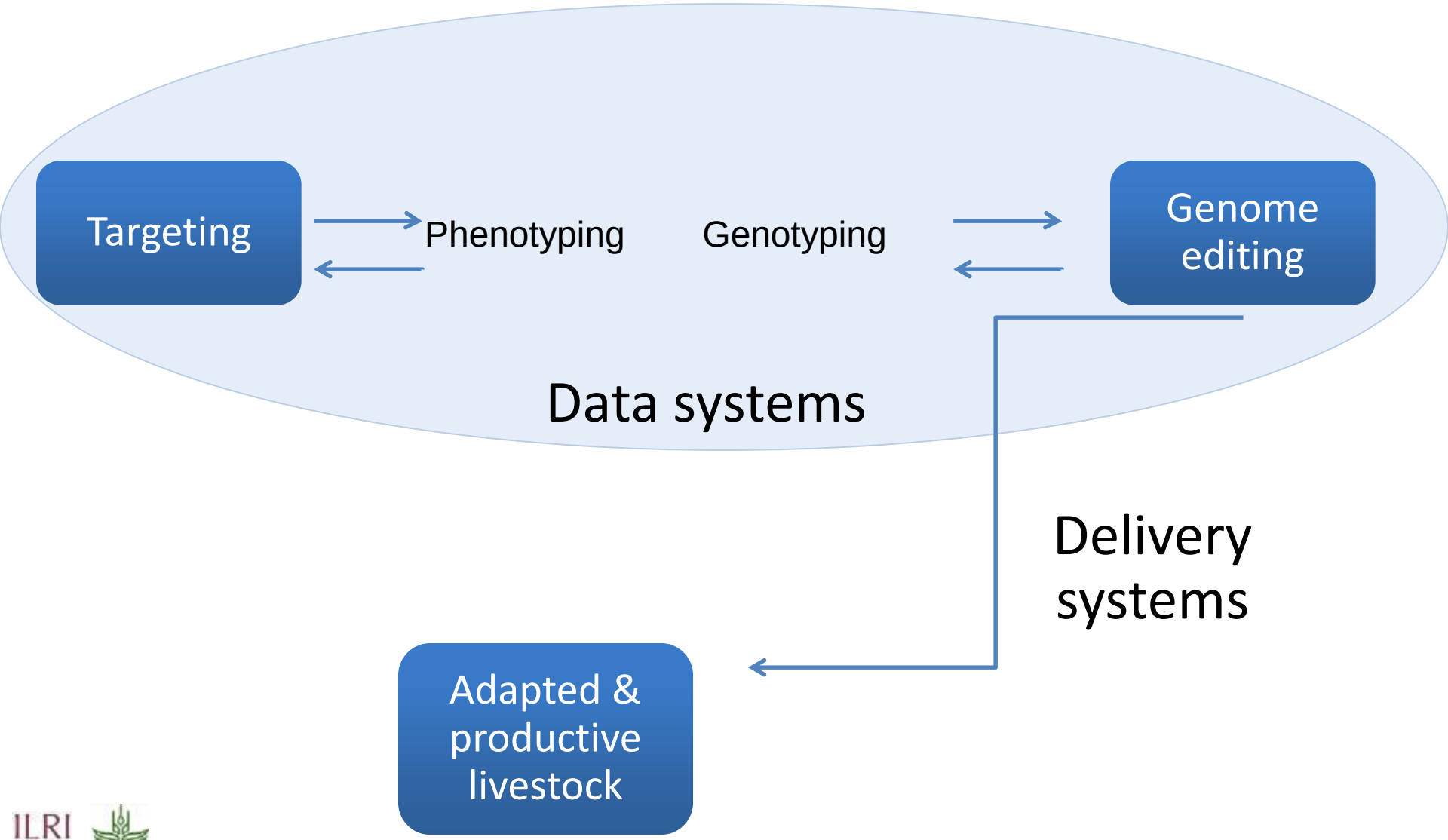
[1] The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, USA
[2] Department of Molecular Biology, The Scripps Research Institute, La Jolla, CA, USA
[3] Department of Chemistry, The Scripps Research Institute, La Jolla, CA, USA
[4] Department of Biomedical Engineering, Duke University, Durham, NC, USA
[5] Institute for Genome Sciences and Policy, Duke University, Durham, NC, USA

Zinc-finger nucleases (ZFNs) and transcription activator-like effector nucleases (TALENs) comprise a powerful class of tools that are redefining the boundaries of biological research. These chimeric nucleases are com-

ing strategies, and the potential for adverse mutagenic effects. Targeted gene knockdown by RNAi (see Glossary) has provided researchers with a rapid, inexpensive, and high-throughput alternative to homologous recombination

ILRI CGIAR

Identify and deliver variants associated with adaptation



ILRI CGIAR

Killing of Tryps by Trypanosome Lytic Factor (TLF)

ApoL-I

TLF

- Apolipoprotein
- **Trypanolytic component**

ApoA-I

- Apolipoprotein
- Found in all HDL subclasses

Hpr

- Haptoglobin-related protein

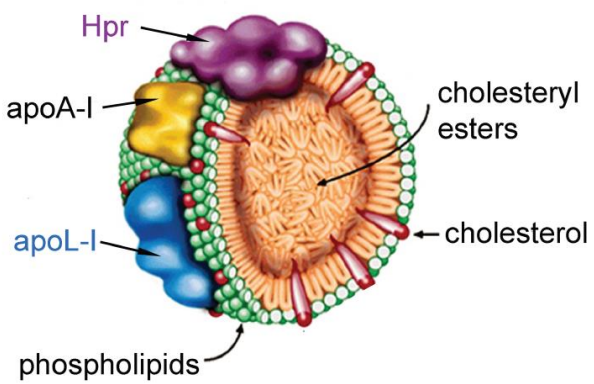
ApoL-I released

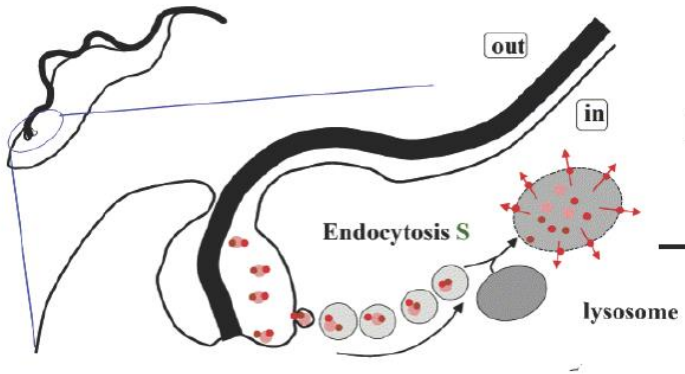
Activated in acidic lysosome

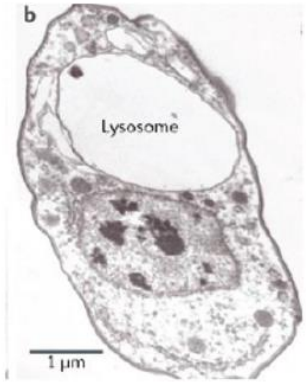
Endocytosed into lysosome by Trypanosomes

Form membrane pores, resulting in ion disregulation and osmotic imbalance

Trypanosomes lysis



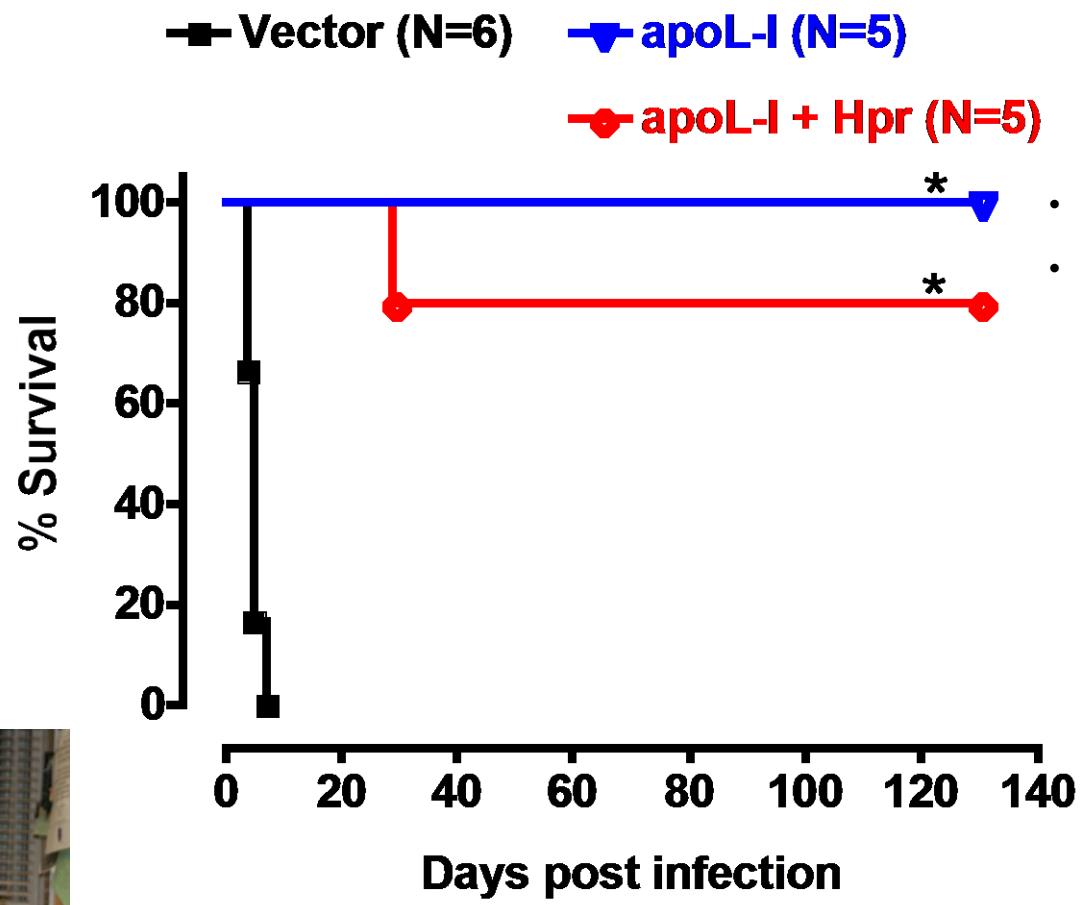




Flagellar pocket of Tryp

ILRI

Complete protection from *Trypanosomes* by baboon ApoL-I in transiently transgenic mice

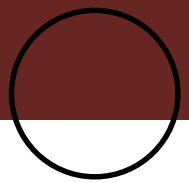


- P = < 0.01
- Vector vs. treatment

Thomson et al PNAS 2009 106:19509-19514

Project Strategy

Kenya Boran



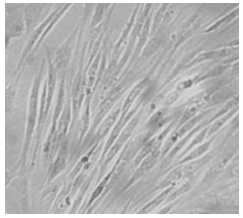
Genomic locus of Baboon apoL-I gene

Vector construction

New York University

Michigan State University

ILRI



Bovine embryonic fibroblasts (BEF) primary culture

Validate the construct in transgenic mouse

Roslin Institute

Transfection & screening

apoL-I Transgenic BEFs

Nuclear Transfer

Transgenic calves

Phenotyping

ILRI

Trypanosome resistant transgenic Boran bull

ILRI CGIAR

Tumaini

A cloned Kenya Boran calf made by SCNT from a Boran embryo fibroblast cell line

better lives through livestock

ilri.org

Video ‘Developing disease-resistant cattle for Africa’

http://vimeo.com/74942619 11 minute version

http://vimeo.com/74940697 3 minute version

ilri.org
better lives through livestock
ILRI is a member of the CGIAR Consortium

Box 30709, Nairobi 00100 Kenya
Phone +254 20 422 3000
Fax +254 20 4223001
Email ilri-kenya@cgiar.org

ILRI has offices in:
Central America • East Africa
• South Asia • Southeast and East Asia
• Southern Africa • West Africa

The presentation has a Creative Commons licence. You are free to re-use or distribute this work, provided credit is given to ILRI.