Vision for livestock genetics in Africa

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Genetic selection, interacting with environment, drives improvement.

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

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).

(Source: http://aipl.arsusda.gov/eval/summary/trend.cfm)
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
Achieving genetic gain in developing countries – the same biological rules but different environments

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Diversity of:

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No data systems to inform selection.

No infrastructure to manage selection.
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.
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 NAMEK cattle (above) could help breed new genotypes tailored to changing local environments.
African Trypanosomiasis

- Caused by extracellular protozoan parasites – *Trypanosoma*
- Transmitted between mammals by Tsetse flies (*Glossina* sp.)
- Prevalent in 36 countries of sub-Saharan 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.
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: KFITRRPSLKTQEKLGDQIFGSPLHTLCERKSTVPRFKQCEAVEK
Cow Boran: KFITRRPSLKTQEKLGDQIFGSPLHTLCERKSTVPRFKQCEAVEK
Human: KFISRRPSLKTLQEKGLKDQIFGSPLHTVCEREHSTVPFWVKQCEAVEK
Pig: KFITRRPSLKTQEKLGDQIFGSPLHTVCERENSTVPRFKQCEAVEK
Chicken: KFISRRPSLKTLQEKGLKDQIFGSPLHLVCEHENSTVPQFRQCIKAVEK
Salmon: KFISRRPSTMKTQEKGIKDRVFCPLLLAECREGTTVPKFRQCVEAVEK

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.

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

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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 complementing strategies, and the potential for adverse mutagenic effects. Targeted gene knockdown by RNAi (see Glossary) has provided researchers with a rapid, inexpensive, and high-throughout alternative to homologous recombination.
Identify and deliver variants associated with adaptation

Data systems

Delivery systems

Targeting

Phenotyping

Genotyping

Genome editing

Adapted & productive livestock
Killing of Tryps by Trypanosome Lytic Factor (TLF)

**ApoL-I**
- Apolipoprotein
- Trypanolytic component

**ApoA-I**
- Apolipoprotein
- Found in all HDL subclasses

**Hpr**
- Haptoglobin-related protein

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

![Graph showing survival rates](image)

- Vector (N=6)
- ApoL-I (N=5)
- ApoL-I + Hpr (N=5)

- P = < 0.01
- Vector vs. treatment

Thomson et al PNAS 2009 106:19509-19514
Project Strategy

Kenya
Boran

ILRI

Genomic locus of Baboon apoL-I gene

Vector construction

Validate the construct in transgenic mouse

New York University
Michigan State University

Bovine embryonic fibroblasts (BEF) primary culture

Roslin Institute

Transfection & screening

apoL-I Transgenic BEFs

Nuclear Transfer

Transgenic calves

Phenotyping

Trypanosome resistant transgenic Boran bull

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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