

Cow vaccines go vroom

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In much of Africa, a herd of cattle is more than just cows. It's a savings account, protein store, dowry, funeral fund, symbol of wealth, and hedge against drought. For many smallholder farmers, the loss of even a single cow to disease can spell ruin.

Yet a grievous number of cattle in sub-Saharan Africa get sick: one estimate puts annual losses from disease at \$40 billion, some twenty-five percent of the total value of livestock production in the region.

John Barlow, professor of animal sciences at the University of Vermont, thinks the cows in the university's research herd may be able to help.

"Many cattle diseases in sub-Saharan Africa might be prevented if we had better vaccines," he says, "but the way we have traditionally created vaccines is expensive and takes a lot of time."

That's why he's leading an international project that aims to better understand the molecular workings of cow immune systems -- and accelerate the development of vaccines for two critical cattle diseases: East Coast fever and foot-and-mouth disease.

Barlow and his colleagues in Kenya, Denmark and at the U.S. Department of Agriculture are supported by a new three-year grant from the National Science Foundation.

"In the first year, we will be studying the cattle in the University of Vermont herd to understand the diversity of their [immune function](#)

genes," Barlow says.

Then, applying this knowledge, the team will use a new technology that has been accelerating human vaccine development, but, until now, hasn't been applied to cows: so-called MHC tetramers. These synthetic molecules allow researchers to quickly get a view of what proteins in the invading virus or parasite are likely to spark a strong immune response in the host animal.

"These proteins are the key vaccine candidates," says Barlow -- and can be tested in lab cell lines.

The MHC -- or "major histocompatibility complex" -- is a large family of genes found in most vertebrate animals, including cows. It plays a key role in regulating T-cells, that, in turn, help the organism recognize and attack a wide range of foreigners -- like the foot-and-mouth virus or the parasite the carries East Coast fever. To accomplish this complex task, the MHC itself is a complex set of protein molecules that vary dramatically between individuals -- which is part of the reason some individuals catch a disease while others don't.

"We want to understand the diversity of those molecules within cattle populations," says Barlow. The tetramer technology provides synthetic MHC proteins that act much like the real ones. This allows researchers to largely sidestep the traditional method of infecting an animal with the disease, waiting for the infection, and then extracting tissue.

"Tetramer technology allows us to efficiently and cheaply evaluate the T-cell response, to either natural infections or vaccines," using core research facilities at the University of Vermont medical school, says Barlow. This technology will be combined with several others, including advanced bioinformatics techniques to sort through the soup of genetic data. All of which promises to provide basic science insights needed for

faster and more accurate development of vaccines in developing countries.

Barlow is quick to point out that none of the cows in the UVM herd will be exposed to any diseases -- they're just providing the resource that a highly inbred research herd allows when trying to look at the range of genetic responses. "Then, in later years in the project, we'll start to test vaccines in herds in Africa," he says.

"We can get the data we need without having to expose many animals to the actual diseases," says Barlow's colleague Bill Golde at the USDA's Plum Island Animal Disease Center. The sequestered animals at this center will be the only ones tested with the actual diseases once promising vaccine candidates have been identified.

Foot-and-mouth disease is a highly contagious virus passed from animal to animal. It hasn't been seen in the United States since 1929. The U.S.D.A. and U.S. cattle interests have every intention of keeping it that way, but it is common in parts of Africa and Asia.

"We're studying foot-and-mouth because it's a very small virus that is relatively easy to investigate and there is a strong motivation from the perspective of U.S. global disease control," says Barlow. "And for Sub-Saharan Africa it would be good if they could control it since it will improve their ability to export meat once it's controlled there."

In contrast, East Coast fever is caused by a large parasite with a large genome and complex lifecycle. "It is hugely important to the smaller shareholder farms in Africa as it kills many cattle," says Barlow. "Farmers there are very interested in eradicating and controlling both these diseases."

This goal may be easier to reach because only a few popular breeds

dominate herds around the globe resulting in limited genetic diversity in cows. This means that the tetramer technology is likely to be even more illuminating and powerful in cattle than in human immunology.

"We're doing basic science on the molecular level," says Barlow, "to give the developing world better vaccines."

Provided by University of Vermont

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