Developing non-antibiotic options to manage Mycoplasma bovis

Project Code: ANH.01.19

Completed: *In Progress. Results expected in September 2023.*

Project Title:

A screen for drugs that reveal Mycoplasma bovis to the bovine immune system

Researchers:

Antonio Ruzzini and Murray Jelinski (Western College of Veterinary Medicine)

Background:

Mycoplasma bovis is involved in bovine respiratory disease, and mycoplasma treatments are estimated to cost the beef industry $30 to $50 per head. *M. bovis* also causes significant welfare (lameness) problems. There is no vaccine for *M. bovis*. One challenge for vaccine development is that *Mycoplasma* can alternate which antigens proteins it expresses on the cell membrane surface. This means that *M. bovis* antigens might stimulate an immune response, but the bacteria may be expressing different surface antigens by the time the animal's antibodies are circulating. As a result, the immune response is always playing catch-up and doesn't effectively combat *M. bovis* infections.

These researchers want to explore molecules that may be able to interfere with the *M. bovis* cell membrane, so that it releases more of its cell membrane proteins. This would allow the animal's immune system to recognize more of the *M. bovis surface* antigens and help it to mount a more effective immune response.

These researchers are targeting an *M. bovis* enzyme that is involved in cell membrane growth. They will use results recently obtained from other bacteria that also add lipids (fats) to proteins to anchor them within the cell membrane (these are called lipoproteins).

Objectives:

- Develop an assay to screen for compounds that elicit the release of lipoproteins from *M. bovis* cells
- Screen and validate safe, commercially available compounds for their ability to induce the release of *M. bovis* lipoproteins

What they will do:

They will develop and validate an assay to screen for drugs that can disrupt the *M. bovis* enzymes involved in cell membrane maturation. This will be done by replacing an *E. coli* gene with the *M. bovis* enzyme gene, along with a second gene to reports when the first gene is functioning. The reporter gene will indicate the status of lipoproteins in the cell membrane. The researchers are using this approach because *M. bovis* is a very difficult organism to grow and work with, while *E. coli* is well understood, easy to grow, and easy to work with.

The second step is to screen 2,368 FDA-approved and commercially available compounds and validate whether they can disrupt the *M. bovis* cell membrane. They will be tested at three different concentrations in bovine nasal and kidney tissue culture for a preliminary evaluation of animal safety. If necessary, 200 other natural extracts derived from livestock microbiomes are available for screening and testing. Compounds that work will be tested in *M. bovis* under different environmental conditions, using well-characterized *M. bovis* isolates isolated from the lung and joint of feedlot cattle.

Implications:

M. bovis has been a big problem for a long time, and we still don't have effective solutions. This project is very early stage drug discovery research. It will not solve the mycoplasma problem, but it will explore a potential new approach that may lead to an effective solution in the future.

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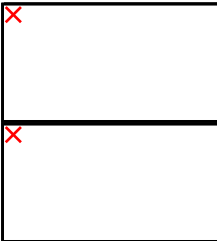
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