

COMBAR for ECI



Name of ECI (with title): Dr Jennifer McIntyre

Institution: IBAHCM, University of Glasgow

Country: UK

Who I am:

Hi, I'm a researcher interested in finding sustainable futures for agriculture. I trained as a vet and worked in practice for a few years before transitioning to research with a PhD looking into ivermectin resistance in the common sheep parasite, *Teladorsagia circumcincta*. I finished my PhD a few months ago and I'm staying on with the same lab to work on a different sheep worm, *Haemonchus contortus* and both ivermectin and moxidectin resistance.

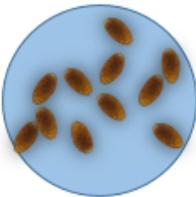
My research project:

We use anthelmintic drugs to combat sheep worms. All ruminants, including all sheep, will have worms, no matter where they are in the world. Farmers need to effectively manage these worms in order to maintain high welfare standards and good growth rates in their sheep. The worms are a massive drain on their enterprise, reducing profit and increasing production costs and time. Most farmers will use anthelmintics to a certain extent to treat sheep. But the worms are rapidly developing resistance to these anthelmintics. One class of anthelmintics – the macrocyclic lactones, which includes the products ivermectin and moxidectin, is widely used. It is highly efficacious and these are broad spectrum drugs, also useful in human parasite infections, cancer and as antivirals. However, resistance in *Haemonchus contortus* (a haematophagus worm of sheep) and *Teladorsagia circumcincta* (a worm which causes severe damage to the sheep's stomach), is already present to both ivermectin and moxidectin, and is fast increasing globally. To test for resistance we currently use an indirect measure – we look to see a reduction in worm eggs in the sheep poo after treatment. But this has multiple limitations. We want a sensitive and specific test which will allow us to detect resistance without treatment, and can be used to determine how different management practices affect (and perhaps slow) the development of resistance. Our research project looks to identify mutations within the DNA of the worms which survive treatment compared with those that are sensitive to ivermectin or moxidectin. We want to find a mutation which can be used as a 'genetic marker' – a diagnostic test for the presence or absence of resistance. I have been sequencing the entire genome of worms collected before and after treatment in field populations of UK worms to identify genetic markers of ivermectin resistance in *T. circumcincta*. This proved rather difficult for various reasons – the reference genome (the 'blueprint' of the worm genome for this species) was incomplete and greatly hampered interpretation of the data. So that has been put to one side while we wait on the reference genome improving. Instead, I am currently testing genes which might be involved in ivermectin resistance in *H. contortus* in the lab. This is based on work by the BUG consortium, which identified a large region on a chromosome of the *H. contortus* reference genome (a beautiful 'blueprint'), which we are confident holds one or more mutations related to ivermectin resistance. The genes I have been testing in the lab lie within this region. We had hundreds of genes in the region initially but are narrowing it down to a

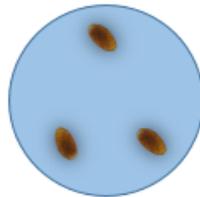
much shorter list. I am testing some of the most promising genes using resistant and susceptible strains of *H. contortus*. This worm has some lifecycle stages which live outside the host in faeces and on grass, so I am using those stages to test our ideas. It involves lots of trial and error – we want them to grow well, but not too fast, so that we can test our ideas. If we can find a test for ivermectin resistance, and in the future, moxidectin resistance, it will be a big help to farmers across the world, and may also help in managing human diseases.

On the hunt for a sensitive and specific genetic test of ivermectin resistance:

Sheep worms are a problem worldwide. Treatment includes drugs like ivermectin. Resistance is increasing to these drugs.



Day 0
Treat sheep
with ivermectin



Day 14
after
ivermectin

**Resistance present if
 < 95% reduction in faecal
 egg count**

What if we could detect resistance quickly, and without using the drug itself?



We sequenced the DNA of lots of worms, collected before and after treatment

We identified mutations which might be associated with ivermectin resistance

We are now investigating these further using other sequencing techniques and testing individual genes in the lab

My plans or ambitions for after my project/COMBAR:

I would love to continue working in research which would be of benefit to farmers in the UK and elsewhere – finding solutions to improve sustainable farming for the future. An alternative would be to work with human parasites – to improve the livelihoods of people across the world, but especially in the poorest places.