

# Sheep, Strongyles and Sequencing: Investigating IVM resistance in UK *T. circumcincta* field populations

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The BUG Consortium  
BUILDING UPON THE GENOME

## AHDB

- Mary Vickers
- Sam Boon
- Emma Steele

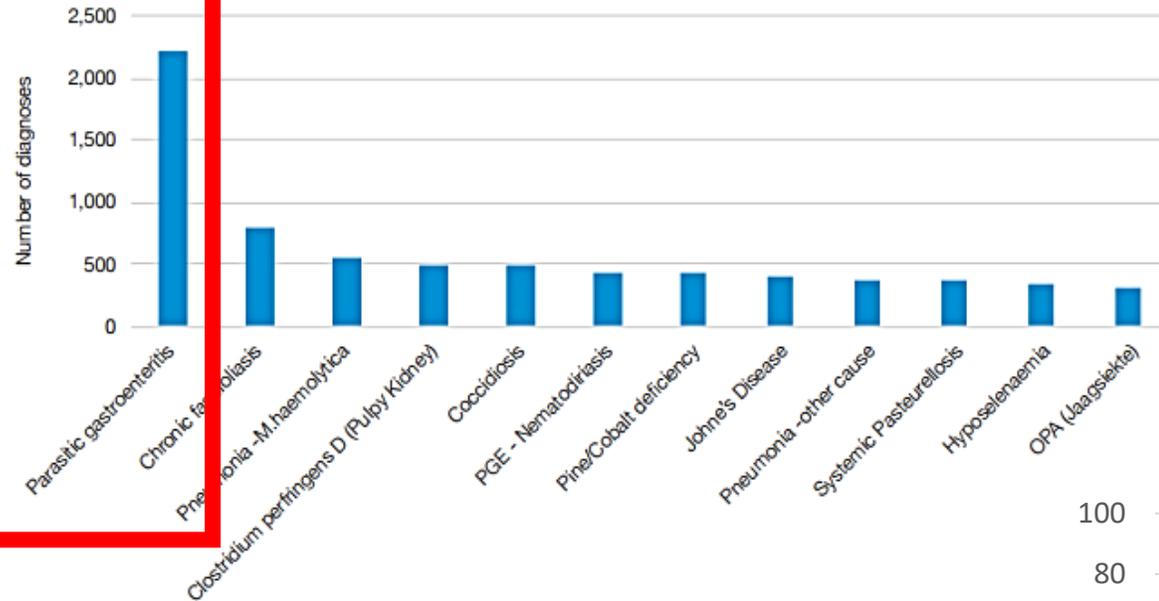
And all the farmers!



# Why *T. circumcincta*? Why ivermectin?



Figure 18. The most common VIDA diagnoses of disease in sheep of all ages (excluding abortion) in Great Britain, 2014–2017



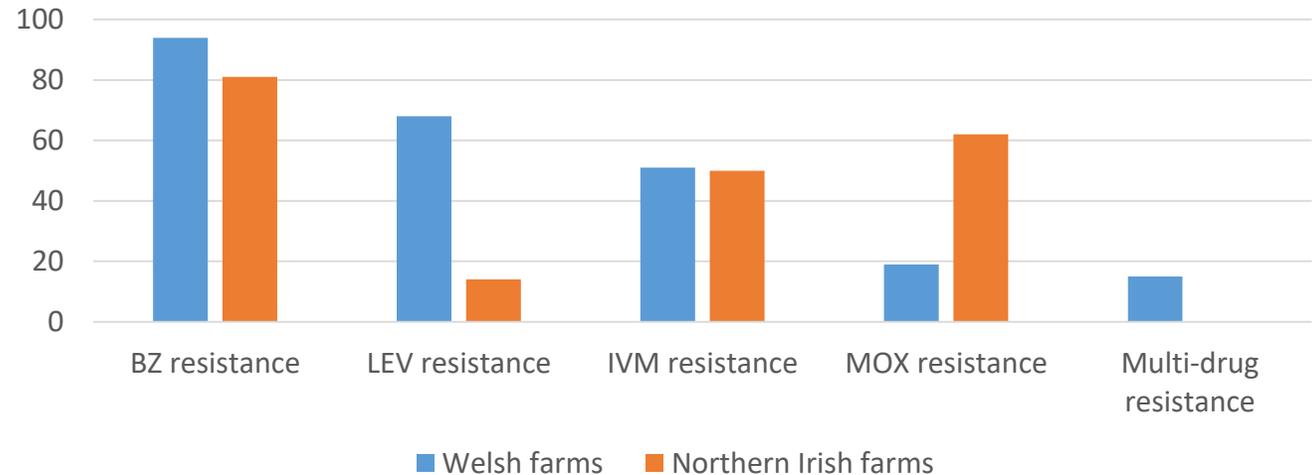
Source: APHA  
Source: SHAWG report 2017/2018 , AHDB Beef and Lamb

## Ivermectin resistance

- Steadily increasing
- Genetic cause unknown

## *Teladorsagia circumcincta*:

- Abomasal nematode
- Primary pathogen in lambs in UK
- Expertly adapted to host and farming year



Source: SHAWG report, AHDB Beef and Lamb: Two studies in Wales (HCC, 2015) and N. Ireland (McMahon et al. 2013)

**Many differences** exist between  
populations or isolates

Which **may not be related to resistance**

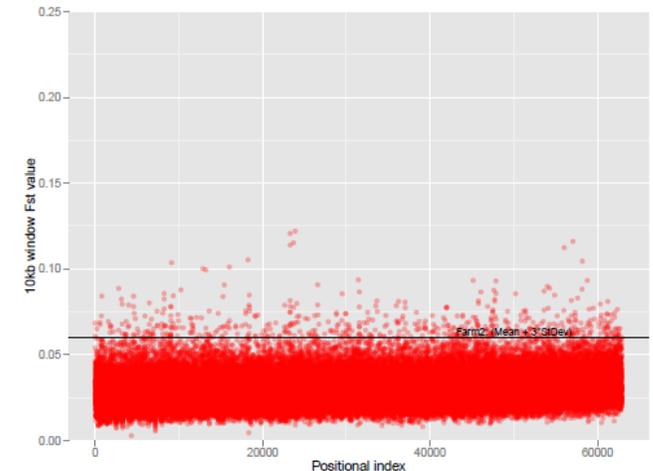
**We used ivermectin treatment to  
select within a population**

# Quick overview

- 2 UK field populations
- Sampled pre- and post-IVM treatment
- 91 *T. circumcincta* larvae (L3) pooled from each sampling time point
- Whole genome re-sequencing as a pool
- $F_{ST}$  analysis comparing pre- and post-IVM samples
- Compared with other studies
- Looked in more detail at certain regions/genes



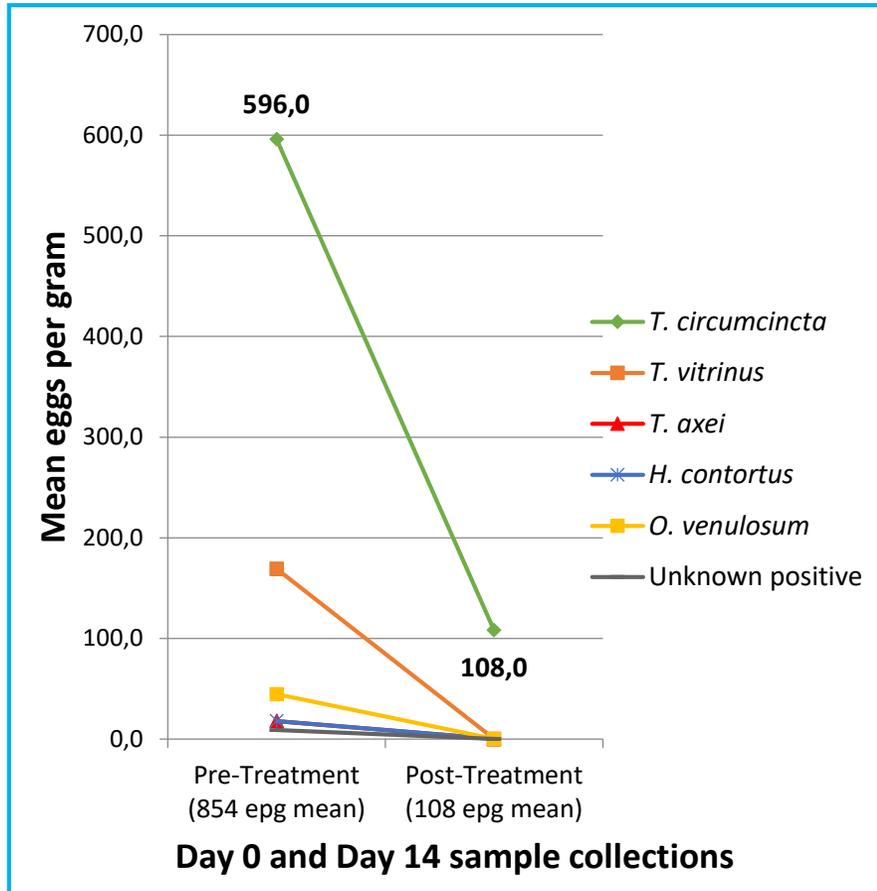
Align to reference genome



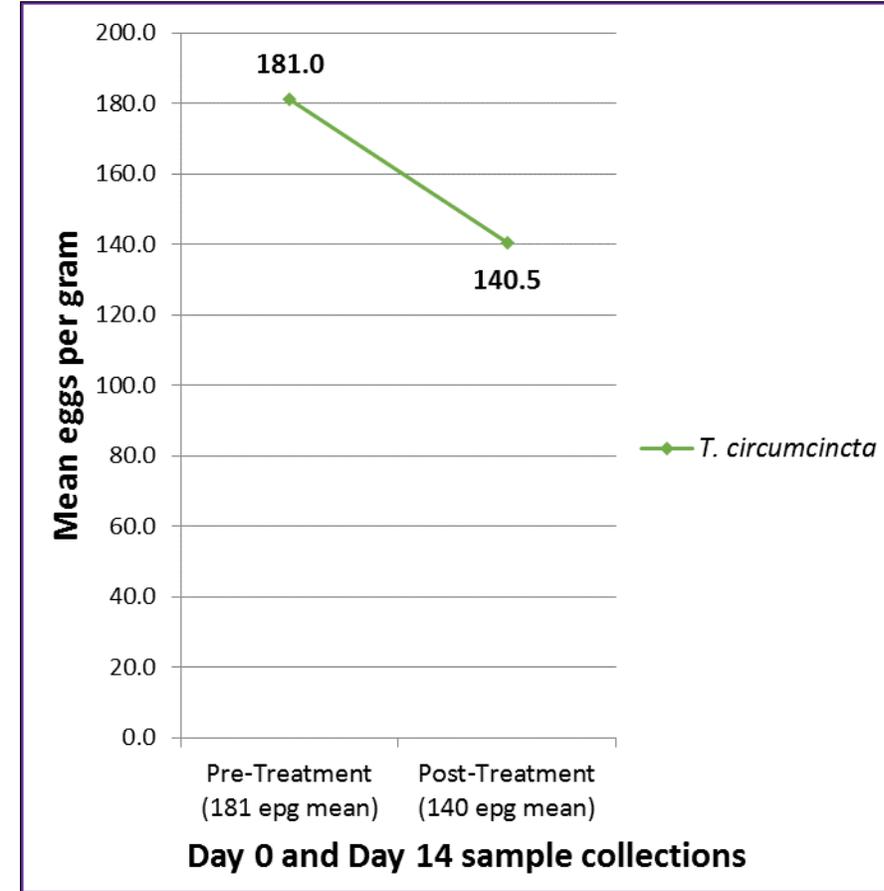
**BZ and IVM resistant +/- LEV resistant**

# Field Populations

Farm 1: 82%



Farm 2: 22%



# Aligning to a reference genome

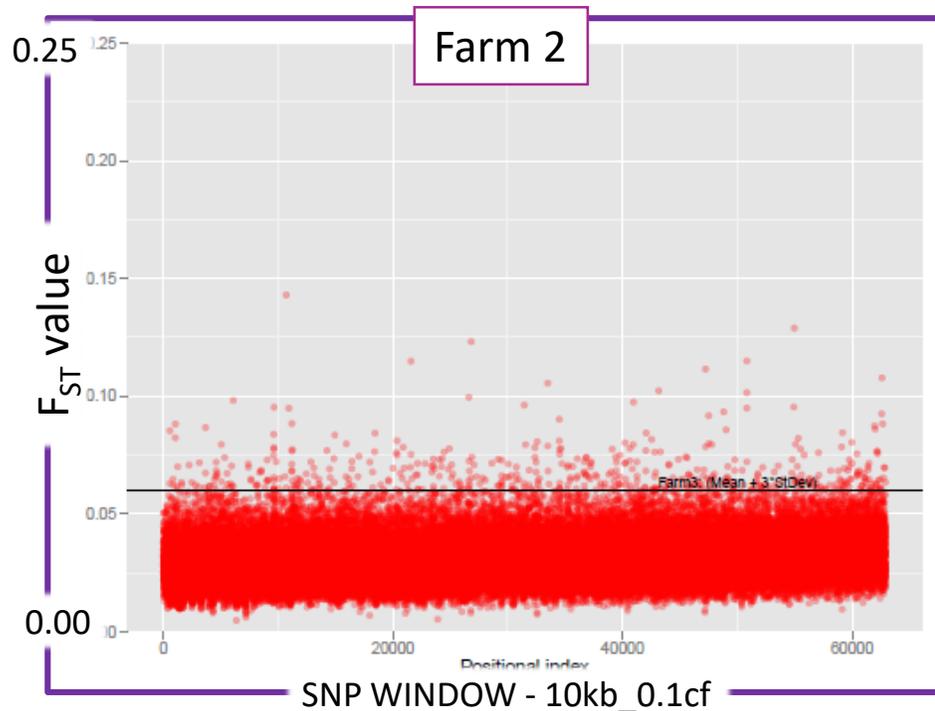
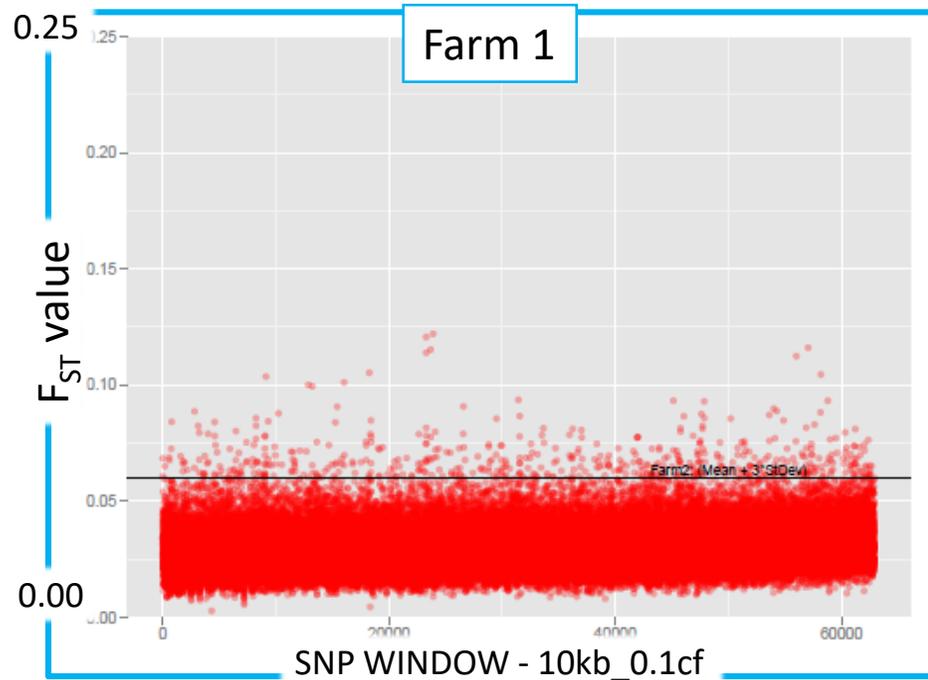
- Two genomes available

Align to reference genome



	Tc_171026	PRJNA72569
Assembled by	WSI	WASHU
Isolate origin	<b>UK (MTci2)</b>	NZ
Genome length (Mb)	685	700
Scaffolds (N)	<b>8000</b>	<b>81,000</b>
N50 (Kb)	200	47
Longest scaffold (Mb)	2	1.5
Annotations	<i>Preliminary</i>	<b>Yes</b>





As the data was quite complex we:

- Filtered the data
- Compared between farms
- Looked at potential SNP impact
- Looked for copy number variation
- Extracted gene ontology terms
- Compared with the literature
- Aligned reads to the Washington University genome

# Key gene groups identified...

- Neuronal genes
  - Glutamate receptor
  - Acetylcholine related genes
  - Sodium:neurotransmitter symporters
  - Other ligand-gated ion channels
  - Neprilysins
- Lipid metabolism genes
- Sex specific genes
- Transcription factors

Locomotion defects

Egg suppression

Pharyngeal paralysis

Inhibited development

Resistance vs Tolerance

# To conclude...

- Offspring of adult survivors
- High diversity
  - Sample size limiting?
  - Difficult to assemble genome – multiple gene copies – real or technical artefacts?
- Fragmented, incomplete genomes
- Field populations – highly outbred = smaller signals of selection
- Interesting genes
- Potential for considerable improvement with improved genome!

# Thanks for listening!



# *T. circumcincta* : Choi et al, 2017

Compared **susceptible** inbred with **triple resistant** introgressed strain.

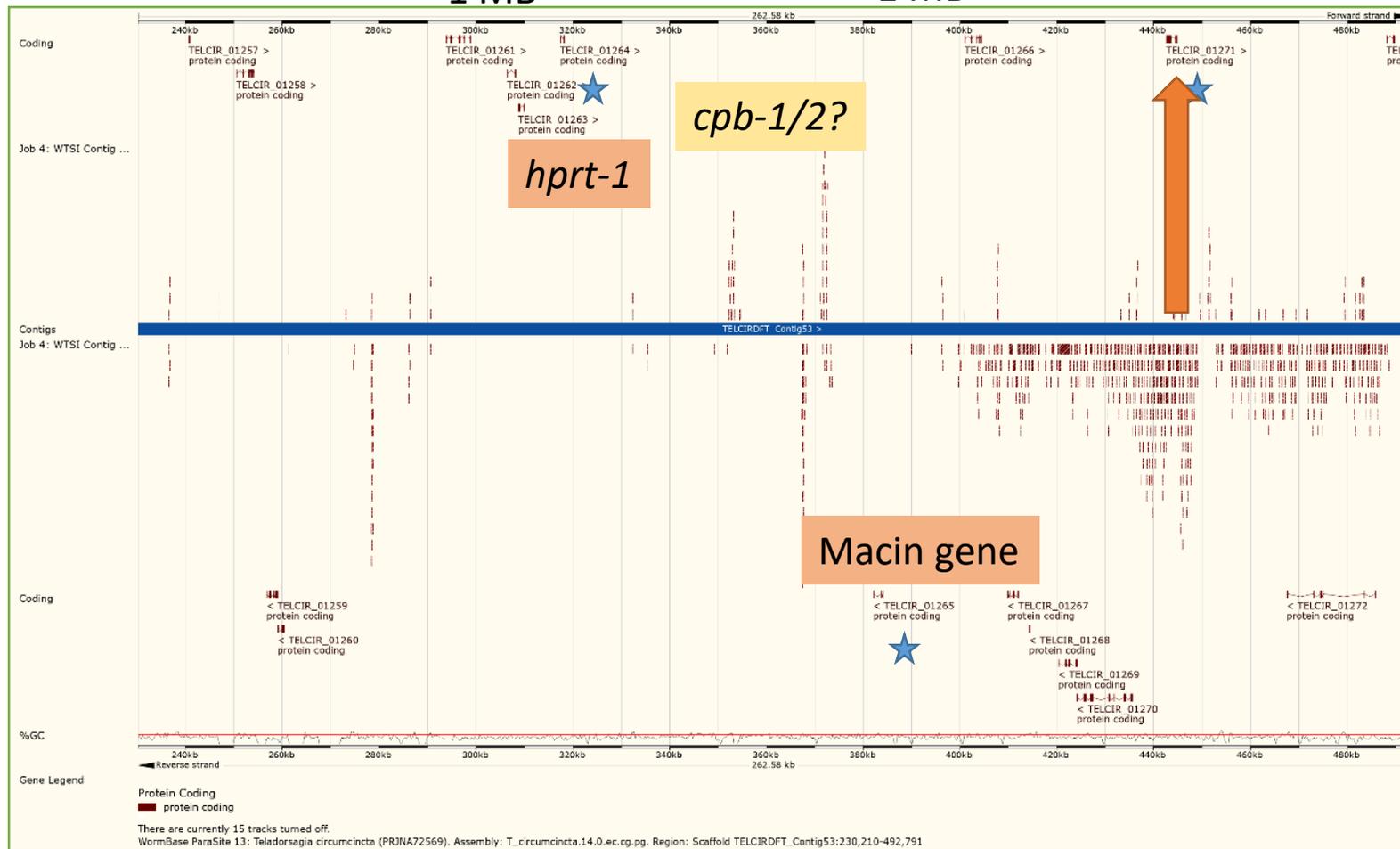
Using the Pool-seq data (on contigs with a ddRAD locus) found 5 genes overlapping.

- Confirmed **single large region of selection** near  *$\beta$ -tubulin isotype-1*
- Choi et al's ddRAD data cannot confirm IVM selection on nearby genes (ddRAD loci absent/<10 individuals).

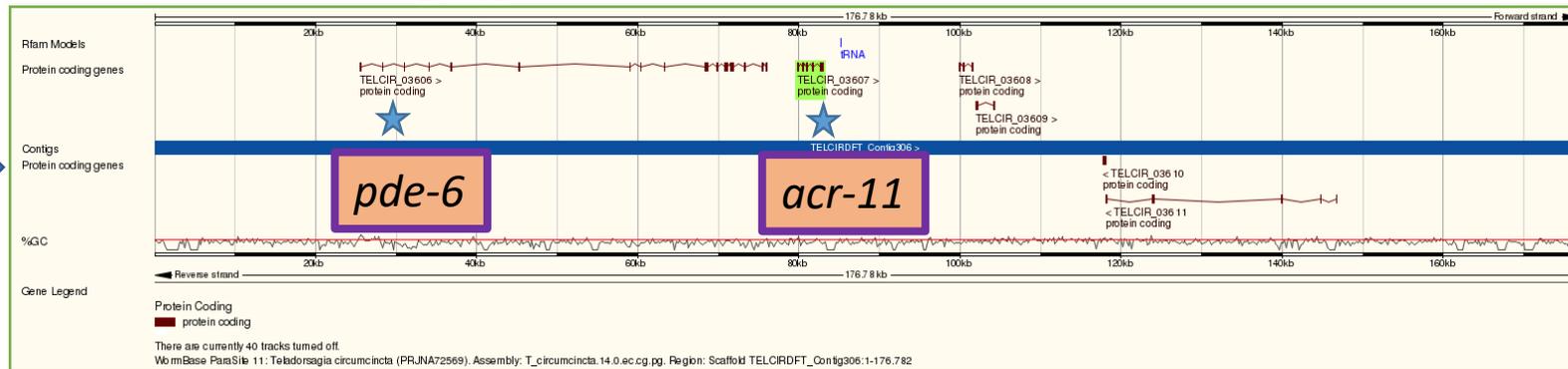
Two genomes are better than one...

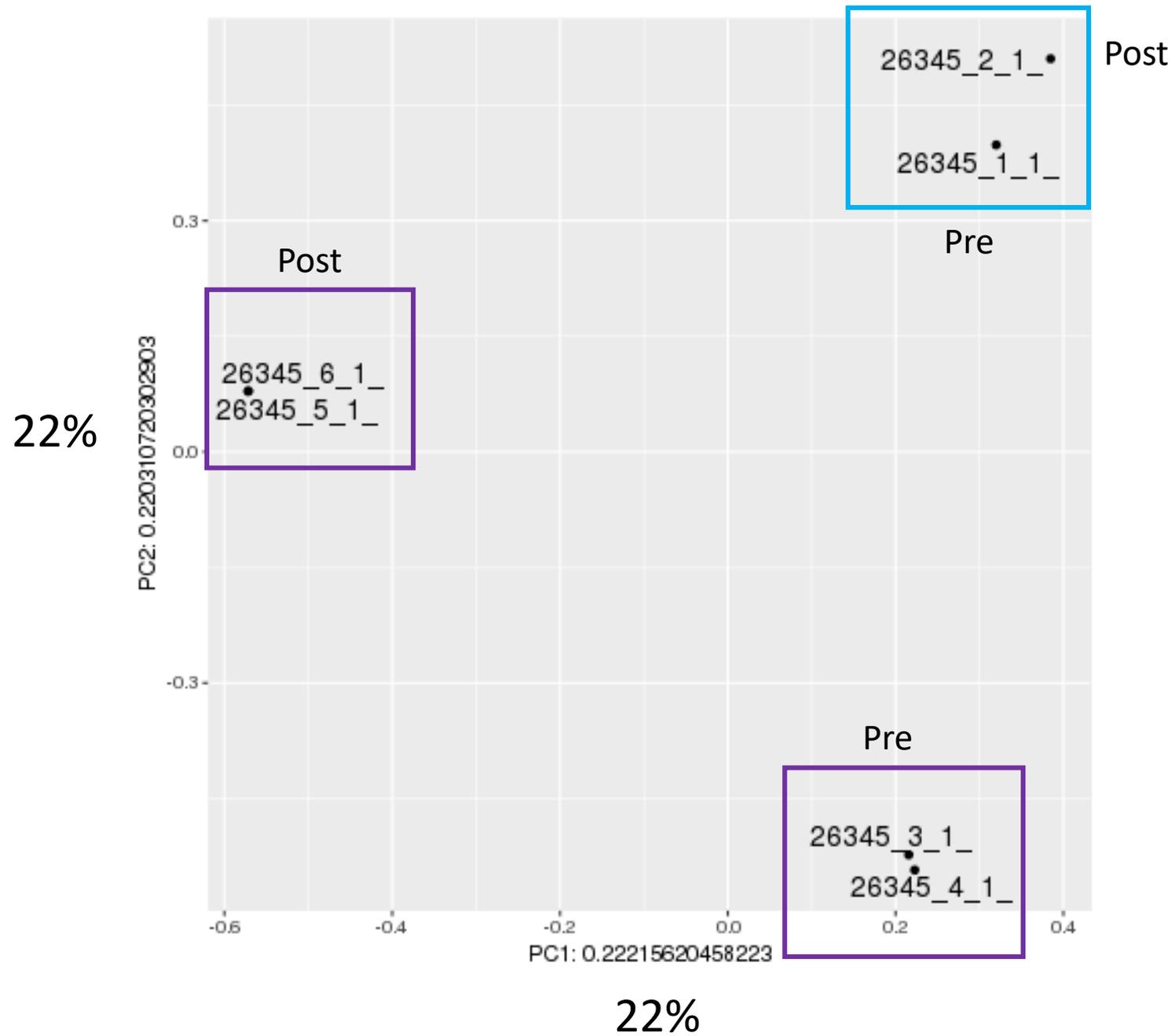
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# Farms used for Pool-seq

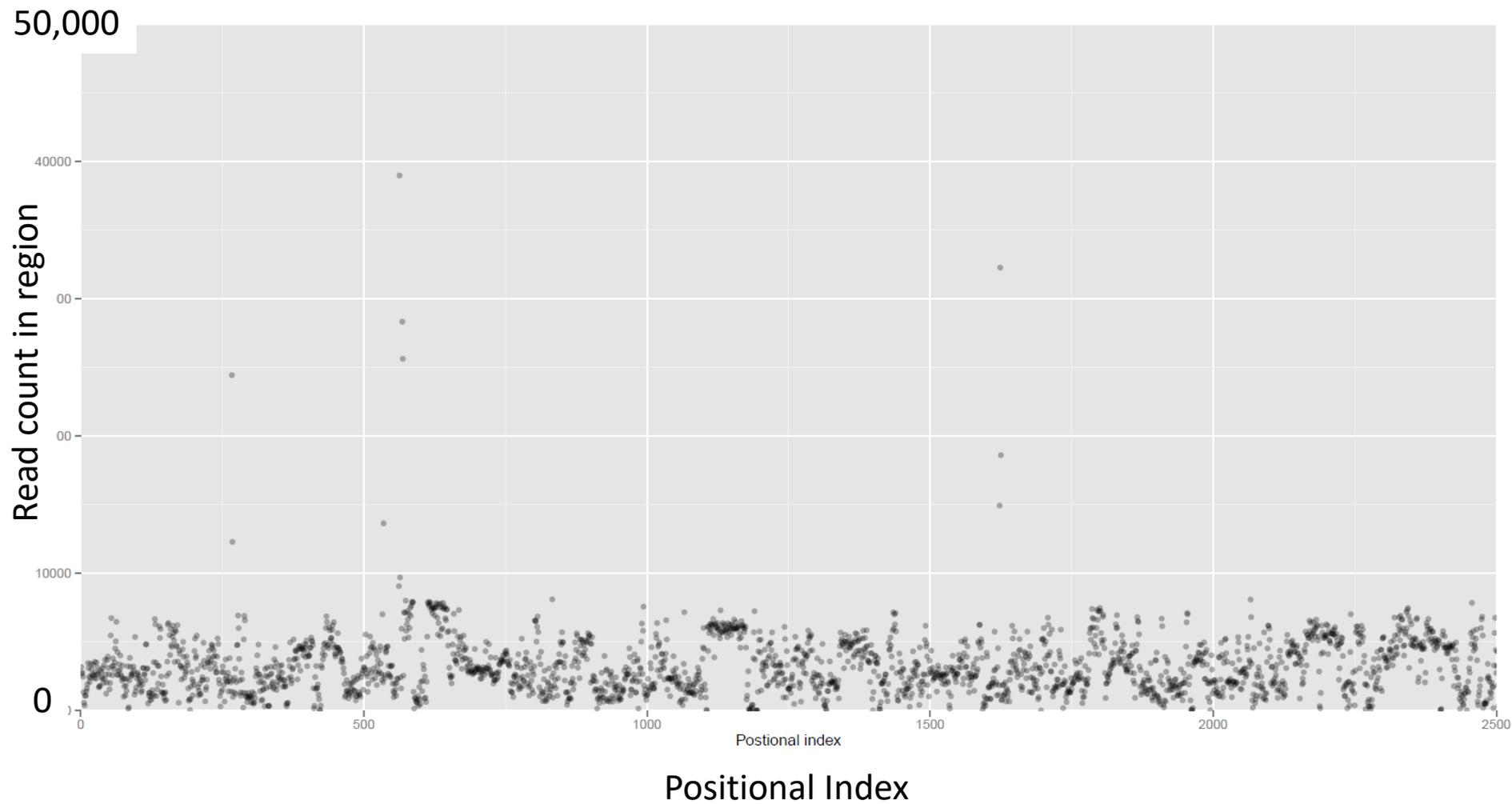
	FECRT 2013 (%)	FECRT 2016 (%)	FECRT 2016 efficacy against <i>T. circumcincta</i> (%)	FECRT 2015 (%)	FECRT 2015 efficacy against <i>T. circumcincta</i> (%)
1-BZ	83.7	87.7	ND	-34.4%	-32.5%
2-LV	92.5	95.4	ND	96.0%	ND
3-IVM	93.0	<b>87.4</b>	<b>81.9</b>	<b>22.4%</b>	<b>22.4%</b>
3-MOX	ND	98.6	ND	ND	ND
BZ+IVM	ND	ND	ND	54.5%	ND
LEV+IVM	ND	ND	ND	89.1%	ND

Farm 1

Farm 2

**BZ and IVM resistant +/- LEV resistant**

# Coverage (6145 bp windows)



# Multiple gene copies – what to do?

- Had considered possibility of removing some gene copies.
- Coverage
- Comparisons of the gDNA....

