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| Supplementary Table 1. The top portion of the table presents the mapping statistics for individual each *Parascaris* spp. sample to the *Parascaris univalens* reference genome (Wang et al., 2017) generated in Part 2 of this study.  |
| Mapping statistics |
| Sample | Uniquely Mapped Reads (%) |
| *In vivo* control, Female | 72.73 |
| *In vivo* control, Male | 76.65 |
| Ivermectin (1 µg/mL), Female | 76.06 |
| Ivermectin (1 µg/mL), Male | 68.03 |
| Ivermectin control, Female | 71.94 |
| Ivermectin control, Male | 62.65 |
| Oxibendazole (10 µg/mL), Female | 77.67 |
| Oxibendazole (10 µg/mL), Male | 73.94 |
| Oxibendazole control, Female | 43.02 |
| Oxibendazole control, Male | 71.80 |

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| Supplementary Table 2. Concentrations and RIN scores for samples used in RNA-seq analysis analyzed by the Agilent Bioanalyzer (Agilent, Santa Clara, CA, USA) at the University of Kentucky Genomics Core Lab.  |
| Sample ID | Concentration Average (ng/μl) | Average RIN |
| *In vivo* Male | 432 | 9.75 |
| *In vivo* Female | 1105 | 9.75 |
| OBZ (10) Female | 459 | 9.8 |
| OBZ Control Female | 583 | 9.75 |
| IVM (1) Female | 440.5 | 9.8 |
| IVM Control Female | 531.5 | 10 |
| OBZ (10) Male | 328.5 | 9.5 |
| OBZ Control Male | 366 | 9.35 |
| IVM (1) Male | 487 | 9.35 |
| IVM Control Male | 574.5 | 9.45 |
| *Abbreviations: IVM, ivermectin; OBZ, oxibendazole; RIN, RNA integrity number* |

**Materials and Methods Supplementary Information**

*2.2.1 Collection of Parascaris spp.*

 Collection of live worm specimens at necropsy occurred as previously described (Scare et al., 2018). Briefly, all worms were milked out of the small intestine onto a mesh sieve, rinsed with room temperature (RT) tap water, and placed in a container of RT RPMI-1640. The container was placed in a water bath maintained at 37˚C for transport to the laboratory. Worms were classified as adult or L4, and adult worms were further characterized by sex as described by Scare et al. (2018).

*2.6.2 RNA-seq analysis*

Adaptor trimming and quality control were performed using TrimGalore Version 0.4.4 (Babraham Bioinformatics) and reads were subsequently aligned to the *Parascaris* *univalens* reference genome (Wang et al., 2017) using STAR Version 2.5b (Dobin et al., 2013). Reads were annotated to the *Parascaris* reference transcriptome (Wang et al., 2017) using Cufflinks (Release 2.2.1) (Trapnell et al., 2012). The parasite sources used to develop the genome and transcriptome by Wang et al. (2017) were obtained from the same drug naïve *Parascaris* spp. population used in the current study (section 2.2). Read counts were normalized as fragments per kilobase of exon per million mapped reads (FPKM) and differential gene expression analysis was performed on normalized read counts.

*2.8 Statistical analyses*

*2.8.1 Part 1: Initial assessment of parasite responses to* in vitro *drug exposure*

Two mixed model analyses with repeated measures over time were performed where ‘percent viability’ was the response variable. The first analysis examined the differences between worm stage (adult or immature) and between adult males and females. The covariates examined were ‘time’, ‘stage/sex’, and the interaction term of ‘time’\*‘stage/sex’. The variable ‘drug’ was kept as a random effect. The second analysis examined the effects of drugs (IVM or OBZ) at each concentration (0.1, 1, or 10 μg/mL), and RPMI-1640 and DMSO (10%) controls for all worms over time. The covariates examined were ‘time’, ‘drug/concentration’, and the interaction term of ‘time’\*‘drug/concentration’. The variable ‘stage/sex’ was kept as a random effect.