Investigating the evolution, zoonotic transmission and population structure of the intestinal worm *Ascaris* using genomics approaches

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BACKGROUND

Ascaris is a large soil-transmitted helminth that infects both humans (***A. lumbricoides***) and pigs (***A. suum***). Approximately 700 million are infected worldwide, with higher prevalence in Asia and South America [1]. Infections result in significant morbidity, particularly in children, and economic losses in pigs [2]. *Ascaris* infection has been linked to developmental delays, increased allergies and reduced vaccine responses, posing a major threat to public health [3-5].

The World Health Organization aims to eliminate helminth infection morbidity by 2030, but treatment resistance is a growing concern [6]. Understanding the evolutionary history and transmission dynamics of *Ascaris* will be crucial to achieving this goal.

ASCARIS LIFECYCLE

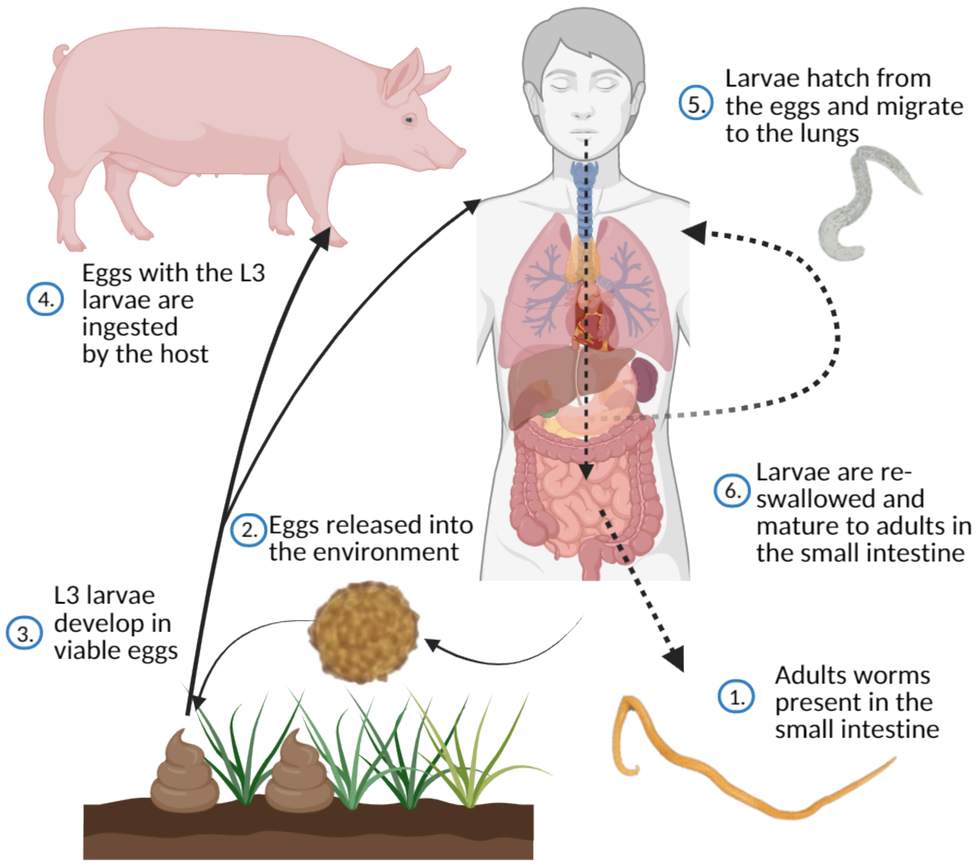

Figure 1: *Ascaris* lifecycle [7]

- Eggs are highly resilient and can survive in the environment for several years [2].
- Open defecation and using faeces for fertilizer in personal and agricultural purposes is common.
- Eggs can contaminate vegetables and be transported to areas with lower prevalence.
- Agricultural runoff can also contaminate water sources, making control measures difficult [8-9].
- Working closely with pigs increases risk of infection
- Cross-transmission and interbreeding between *Ascaris* species can occur [8].

ASCARIS GENOMICS

Ascaris's genome is approximately 300Mb, with 24 germline chromosomes. Programmed DNA elimination results in ~20% of germline DNA being lost in somatic cells during normal development [10].

Ascaris Evolution

- A large proportion of the *A.suum*, and *A.lumbricoide*s genome is shared, resulting in debate as to whether they are two distinct species [10].
- The origin of ascarids remains unclear.
- Identification of clades and distinct haplotypes in both nuclear and mitochondrial DNA may indicate a historical speciation event.
- Domestication of pigs and subsequent cross-over and hybridisation events may have led to contamination of the true evolutionary pattern [10].

Population Genomics

- Geographic reproductive isolation has resulted in a large proportion of the differences identified between *Ascaris* populations [10].
- Mitochondrial marker COX-1 has highlighted three clades (A-C) [11-12].
- Combining nuclear and mitochondrial markers has indicated multiple cross-over and hybridisation events.
- Zoonotic transmission is the leading source of infection in developed countries [13].
- Nuclear and mitochondrial markers alone may not be able to determine the difference between prior introgression, incomplete lineage sorting or recent hybridisation [14].
- Further exploration is required to understand what epidemiological factors may be contributing to infections.

OBJECTIVES

- Generate new whole-genome data for *Ascaris* samples from different hosts.
- Identify evolutionary relationships and population structure
- Explore transmission dynamics between humans and swine.
- Create models to see how genomic regions respond under different selection pressures.
- Identify markers to investigate *Ascaris* genetic variation.
- Optimise these markers using environmental samples in the UK to create a multi-locus typing scheme, which can then be used in a pilot field survey in the Philippines.
- Understand how the environment plays a role in *Ascaris* transmission in different geographical regions.

METHODS

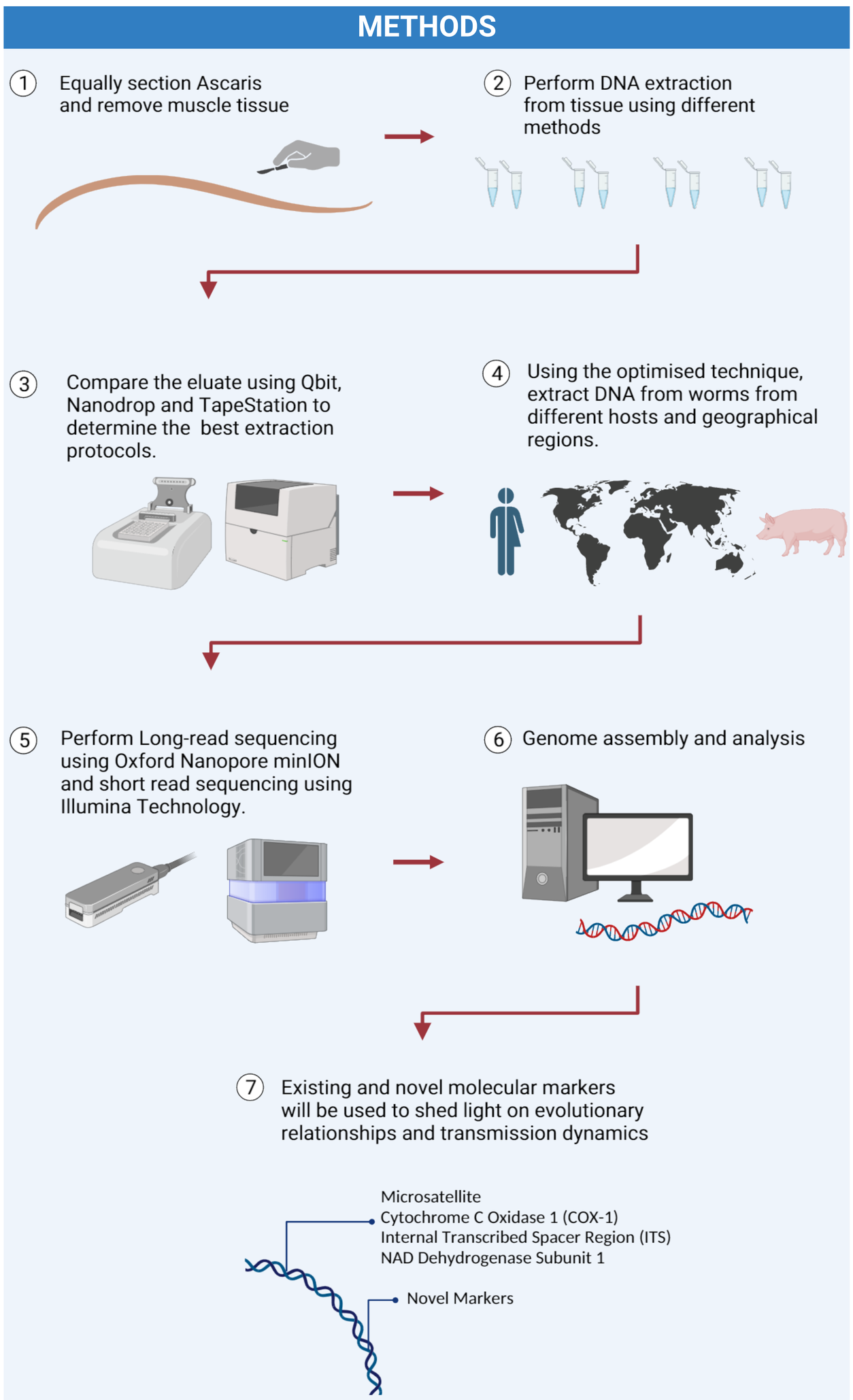

Figure 2: Methodology pipeline

OUTCOMES

- Add to the existing pool of *Ascaris* genomic data to help create an open access comprehensive genome library.
- Shed light on the evolutionary origin of *Ascaris*, providing further information to the debate if *A. suum* and A. *lumbricoides* are a single species, or not.
- Provide new insight into the relationship between *A. suum* and A. *lumbricoides*, focusing on the likelihood of zoonotic transmission, the potential for transfer of genes (particularly those involved in anthelmintic resistance) between parasite populations in different hosts, and the effects of different selection pressure on the *Ascaris* genome.
- Generate a multi-locus typing scheme, and other tools for monitoring zoonotic transmission and effects of anthelmintic drugs on *Ascaris* populations in faecal and environmental samples.

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References: [1] Holland, C. et al. (2022) doi.org/10.1186/s40249-022-01038-z. [2] Dold, C. and Holland, C.V. (2011) doi.org/10.1016/j.micinf.2010.09.012. [3] EZEAMAMA, A.M.A.R.A.E. et al. (2005) doi.org/10.4269/ajtmh.2005.72.540. [4] Caraballo, L., Acevedo, N. and Buendía, E. (2015) doi.org/10.1007/s40475-015-0058-7. [5] Cadmus, S.I. et al. (2020) doi.org/10.1371/journal.pntd.0008069. [6] World Health Organization. https://www.who.int/publications/i/item/9789240010352. [7] Evangelista, F (unpublished). [8] Tran-Thi, N. et al. (2017). doi.org/10.1371/journal.pntd.0006088. [9] Bowman, D.D. (2021). doi.org/10.1016/j.rvsc.2020.12.017. [10] Wang, J. (2021). doi.org/10.3390/genes12040493. [11] Betson, M. et al. (2014). doi.org/10.1093/infdis/jiu193. [12] Peng, W. and Criscione, C.D. (2012). doi.org/10.1016/j.meegid.2012.01.012. [13] Nejsum, P. et al. (2012) doi.org/10.1017/s0022149x12000193. [14] Loreille, O. and Bouchet, F. (2003) doi.org/10.1590/s0074-02762003000900008.