Methylation inheritance in three-spined sticklebacks (*Gasterosteus aculeatus*) in response to parasite infection

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Background

Parasite pressure influences the evolution of resistance and tolerance mechanisms in their hosts. In a two-generation infection experiment of three-spined stickleback (*Gasterosteus aculeatus*) by the nematode *Camallanus lacustris*, paternal infection, despite imposing a **cost** on the next generation, also presented **benefits for offspring's tolerance**[1]. The methylation pattern was shown to differ between infected and control parents[2].

Aim: Understanding the role and mechanisms of phenotypic plasticity within and across generations, focusing on DNA methylation. Which of the DNA methylations linked to parasite infection can be transmitted to the next generation?

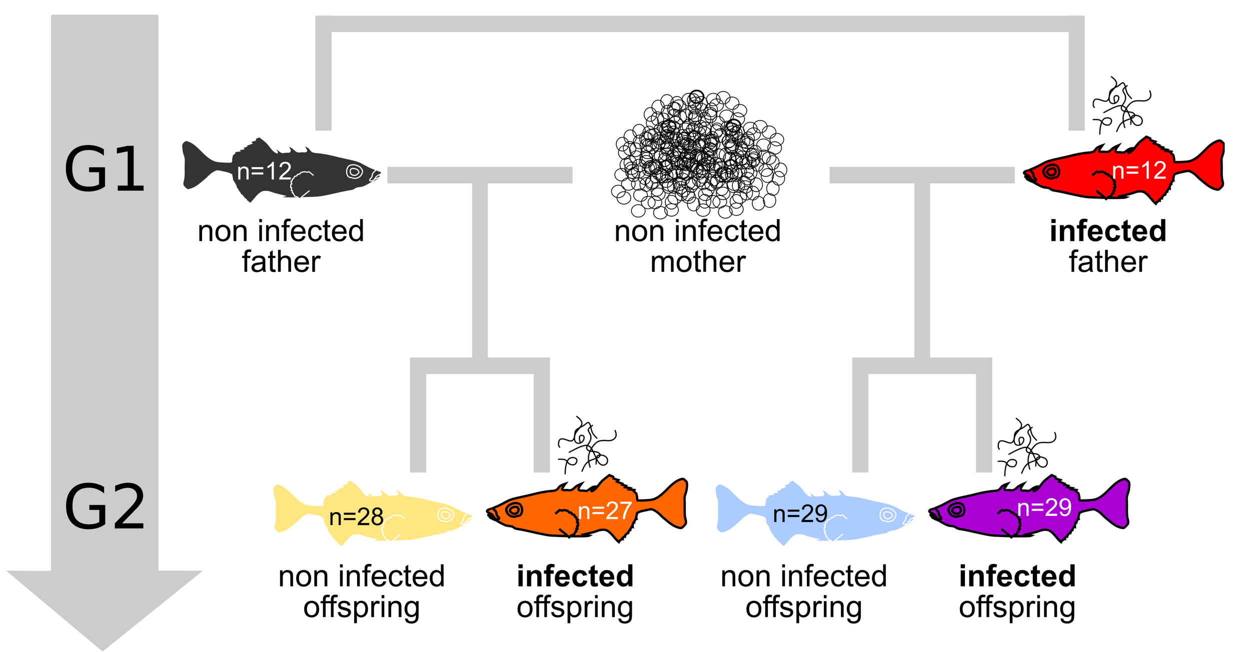

Fig. 1: Experimental design

Material & methods

1. **Experimental design: G0 generation** from natural lake population -> **G1 generation** of full-sib fish families. In vitro mating of G1 males and G1 gravid female from another family serving as egg donor, repeated in brother pairs within each male family (1 from G1 "treatment" group and 1 from G1 "control" group) -> **G2**. Infection of G1 & G2 with *C. lacustris* larvae through copepod ingestion (Fig.1)
2. **Data processing:** Methylome sequencing: Reduced Representation Bisulfite Sequencing (RRBS) single-end reads of 100bp long, Illumina HiSeq 2500. Alignment on a European gynogen genome[3] and methylation call by BSBolt. Downstream analyses by Methylkit.

Preliminary results

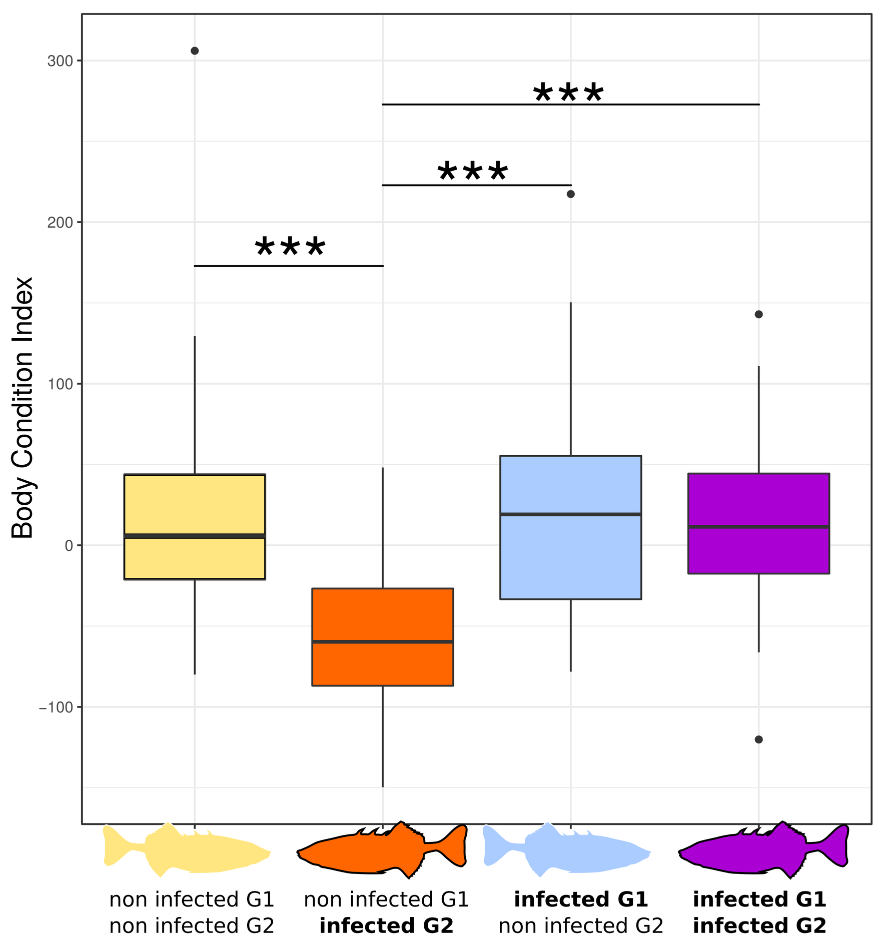

Fig. 2: Paternal treatment effect on offspring body condition

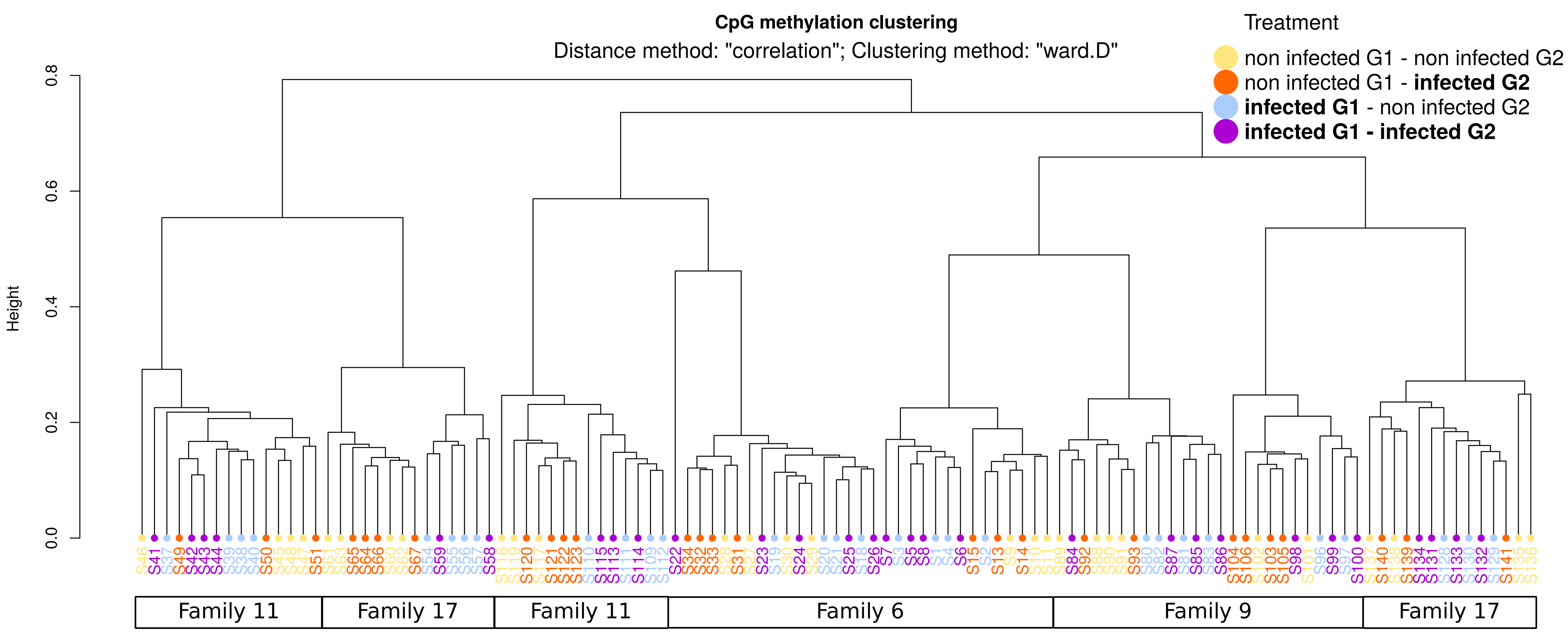

Fig. 3: Hierarchical clustering of individual fish CpG methylation

Paternal treatment affects body condition (BC): infected offspring from non infected father show a decrease in BC after infection; this drop is absent in infected fish from infected father (Fig.2). This confirms on our data subset the results of Kaufmann et al.[1]

Offspring methylomes cluster by family and paternal treatment: within family subgroups, the paternal treatments seems to play a stronger role in clustering than the treatment of offspring itself (Fig.3).

Perspective

1. Compare Differentially Methylated Sites (DMS), hypo and hypermethylation, between offspring groups:
   (a) **Tests of parental effect:**
   comparison of (G1 non infected-G2 non infected vs G1 infected-G2 non infected), and (G1 non infected-G2 infected vs G1 infected-G2 infected)
   (b) **Tests of offspring exposure:**
   comparison of (G1 non infected-G2 non infected vs G1 non infected-G2 infected) and (G1 infected-G2 non infected vs G1 infected-G2 infected)
2. Identification of genes and genes networks (method: WGCNA) involved

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References

[1]Kaufmann, J., Lenz, T. L., Milinski, M., & Eizaguirre, C. (2014). Experimental parasite infection reveals costs and benefits of paternal effects. Ecology Letters; [2]Sagonas, K., Meyer, B. S., Kaufmann, J., Lenz, T. L., Häsler, R., & Eizaguirre, C. (2020). Experimental parasite infection causes genome-wide changes in DNA methylation. Molecular Biology and Evolution; [3]Thornburn et al., in prep.

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