Effects of early life stage exposure to thyroid-altering chemicals on the developing immune system of a small fish model

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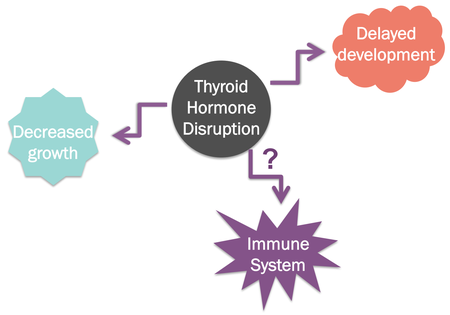
Introduction

- Thyroid disrupting compounds are prevalent in the aquatic environment and have been shown to elicit a wide range of negative physiological effects.[1]
- The thyroid system is responsible for regulating a variety of processes, especially during early life stages. Though thyroid hormones are most well-known for their ability to regulate growth and development, there is evidence to suggest that thyroid hormones also play a role in proper immune system development and function.[1,2]
- Prior studies from our lab have revealed that early life stage exposures to polybrominated diphenyl ethers (an environmentally-relevant thyroid disruptor) cause alterations in the immune development of fathead minnow (*Pimephales promelas*) and impair their ability to survive pathogen exposures later in life.[3]
- However, little research has been done to determine how early life stage exposure to thyroid disrupting compounds affects the developing immune system.



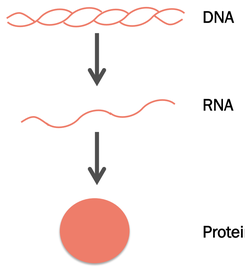


Figure 1. General schematic of gene expression.

Study Goal & Objective

GOAL: To determine the effects of early life stage exposures to thyroid altering compounds on the development of the immune system using the fathead minnow as a model.

OBJECTIVE: To identify differences in immune-related gene expression in developing fathead minnows following exposures to thyroid-altering chemicals.

Methods

- Newly hatched fathead minnow larvae (<24 hours post hatch) were exposed to various doses of propylthiouracil (PTU, a thyroid inhibitor) or thyroxine (T4, a thyroid stimulator) as shown in Figure 3.
- Three replicates of the experiment were performed, with exposures lasting 35 days.
- Larvae were sampled from each exposure group at 7 and 35 days post hatch for immune-related gene expression analysis by qPCR.
- Target genes: *Ikaros, recombination activating gene 1 & 2 (rag1,2), human T-cell receptor Cα (tcrac4), immunoglobulin lambda constant 1,2, &3 (iglC1,2,3)* See Figure 2 for functions of target genes.

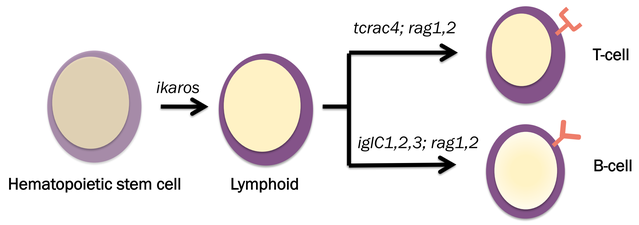


Figure 2. Target genes analyzed in the present study and their function.

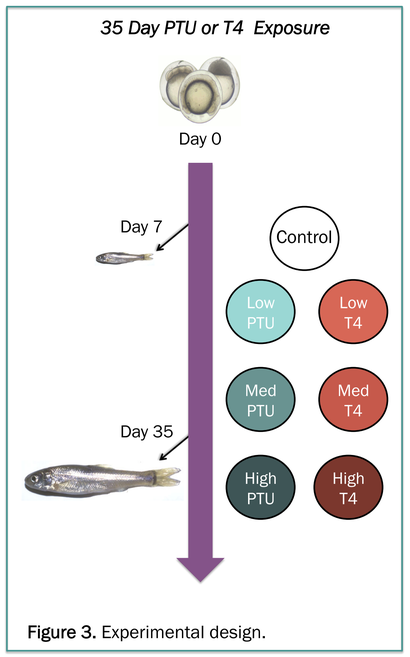


Figure 3. Experimental design.

Results

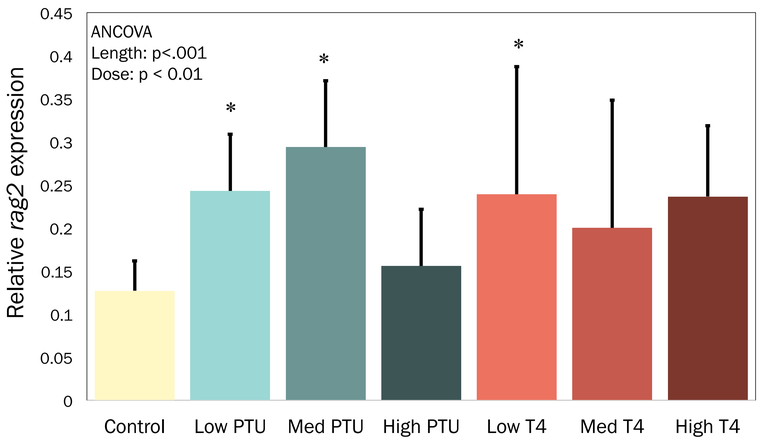


Figure 4. Mean relative recombination activating gene 2 (*rag2*) expression in 7 day old fatheaed minnow larvae following exposures to proplythiouracil (PTU) and thyroxine (T4). Error bars represent standard error and * denote a significant differences from controls.

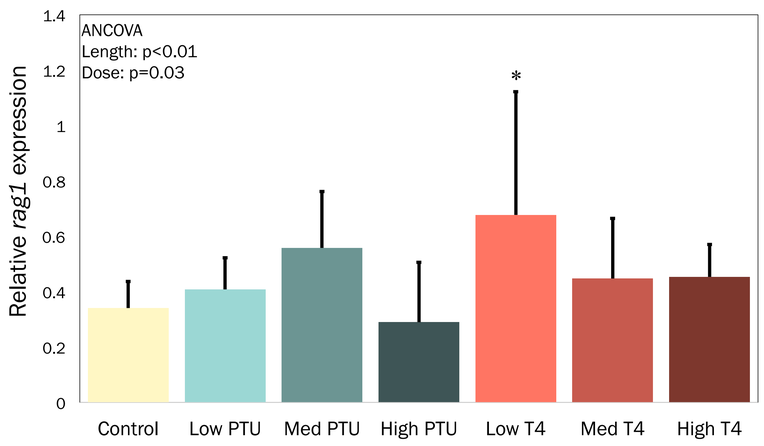


Figure 5. Mean relative recombination activating gene 1 (*rag1*) expression in 7 day old fatheaed minnow larvae following exposures to proplythiouracil (PTU) and thyroxine (T4). Error bars represent standard error and * denote a significant differences from controls.

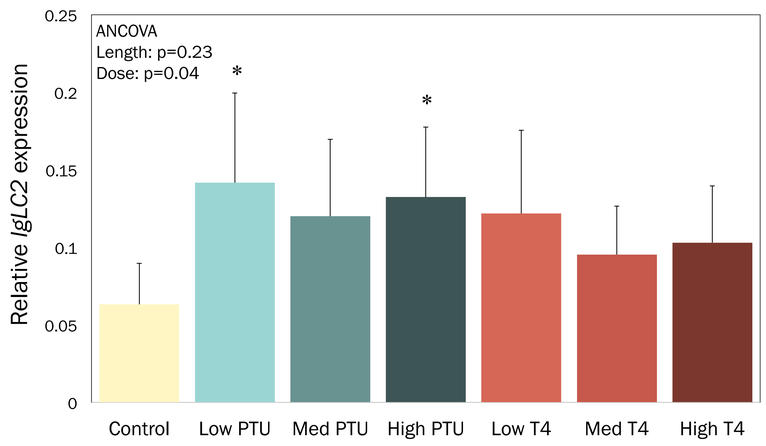


Figure 6. Mean relative immunoglobin lambda constant 2 (IglC2) expression in 7 day old fatheaed minnow larvae following exposures to proplythiouracil (PTU) and thyroxine (T4). Error bars represent standard error and * denote a significant differences from controls.

Conclusions & Future Directions

- The observation of changes in gene expression of *rag1, rag2,* and *igLc2* suggest that immune system development has been altered in response to PTU and T4.
- The results of this study suggest alterations in immune development in response to thyroid disruption at the level of gene expression. However, future studies should elucidate what effects alterations in expression cause, at both the cellular level (i.e. alterations in immune cell populations) and the whole animal level (i.e. ability to resist disease).
- The results of this study provide evidence that exposures to thyroid-disrupting compounds during early development lead to alterations in immune system development. Whether these immune system changes have long-term consequences remains unknown. Therefore, future studies should evaluate the effects of early life stage exposures on adult immune responses and disease resistance.

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References. **(1)** Boas et al. (2006). Eur. J. Endocrinol. *154*, 599-611. **(2)** Power et al. (2001). Comp. Biochem. Phys. C. *130*, 447-459. **(3)** Thornton et al. *In Review*. Environmental Science & Technology Letters.