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Transposable elements in response to Bisphenol A exposure in zebrafish embryos

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This study delves into potential effects of Bisphenol A (BPA) exposure on zebrafish embryos at environmentally relevant concentrations. BPA is a synthetic compound widely used in various everyday products like plastics and food containers. BPA's estrogenic properties raise environmental concerns as it contaminates water bodies, affecting aquatic organisms and potentially human health.
Zebrafish (*Danio rerio*) is extensively studied across various biological disciplines due to its importance as a model organism. Within the zebrafish genome, Transposable Elements (TEs) makes up over 55%, playing crucial roles in genome evolution and gene regulation. However, little is known about how TE respond to BPA exposure in zebrafish embryos. Therefore, zebrafish might represent a valuable model for studying the role and contribution of TEs to genome adaptation in response to contaminants like BPA. The aim of this study is to investigate the transcriptional activity of TEs and genes involved in TE silencing mechanisms in zebrafish embryos exposed to environmentally relevant concentrations of BPA (0.1, 1, and 4 ppm).

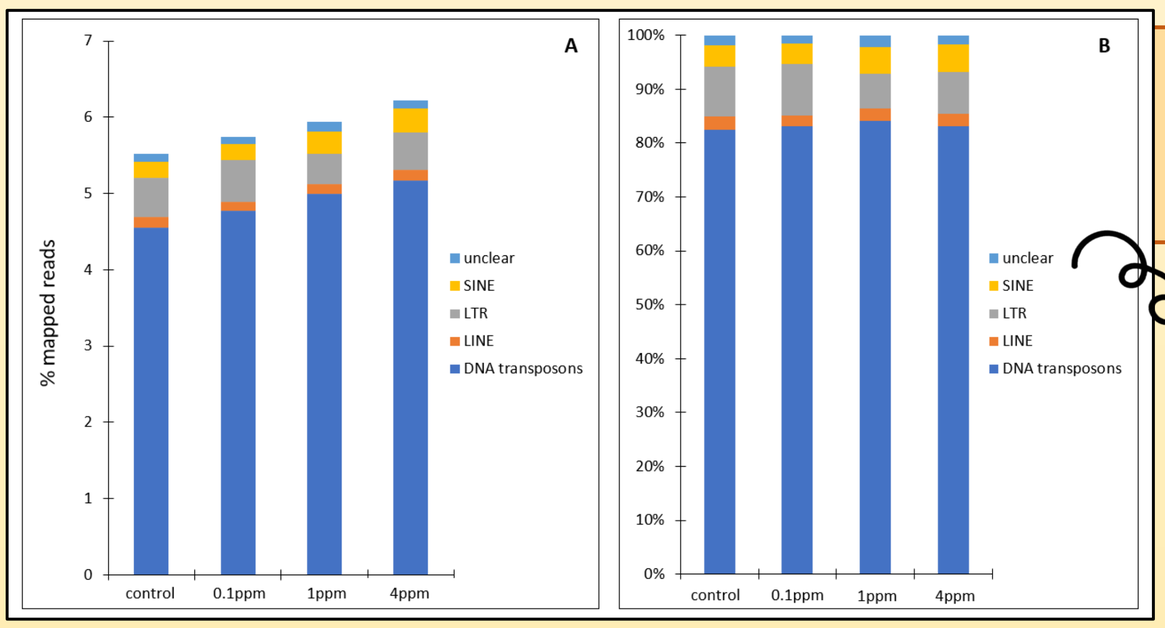


Figure 1. **TE transcriptional contribution on zebrafish embryos treated with BPA. Values are reported for all the tested concentration (control, 0.1 ppm, 1 ppm, and 4 ppm). A**. TE transcriptional activity in zebrafish embryos exposed to different concentration of BPA is reported as percentage of mapped reads. A slight increase in the percentage of mapped reads is observed when comparing the control (5.5%) with 0.1 ppm (5,7%), 1 ppm (5,9%), and 4 ppm (6,21%) concentrations of BPA. Exposure to this compound could have caused a state of stress, leading to increased TEs activity.
B. Relative abundance of TE types to the different BPA concentration observed in zebrafish embryos. At higher BPA concentrations it is notable an increase in the impact of SINE retroelements.

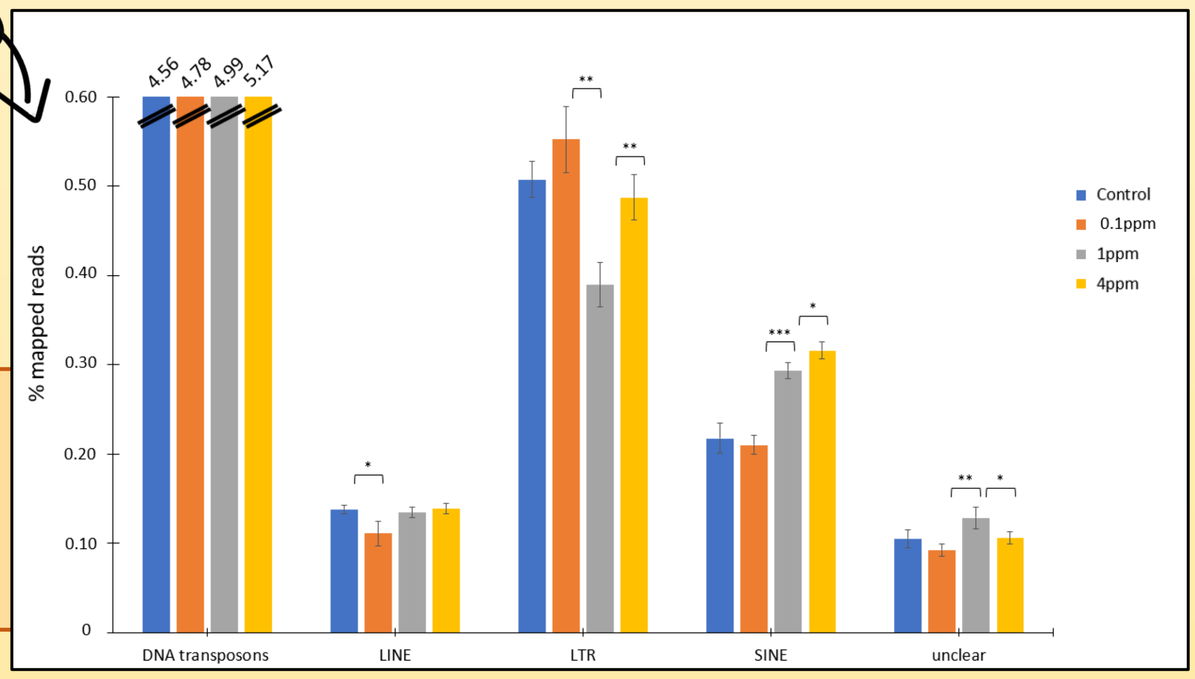


Figure 2. **Transcriptional contribution of each TE type on zebrafish embryos treated with BPA. The percentage of mapped reads for different types of transposable elements (TEs) is reported for all tested concentrations (control, 0.1 ppm, 1 ppm, and 4 ppm).** DNA transposons do not show any significant differences and have the highest percentages in absolute values. The other types of TEs show lower values. Interestingly, LTR retroelements and SINEs show a statistically significant difference when comparing the 0.1 ppm with 1 ppm and 4 ppm conditions. For LTR retroelements, there is a decrease in the percentage of mapped reads from 0.1 ppm to 1 ppm, followed by an increase at 4 ppm. Conversely, for SINE elements, we observe an increase from 0.1 ppm to 1 ppm and a further increase at 4 ppm.
Statistically significant differences are indicated as * for $p < 0.05$, ** for $p < 0.01$, and *** for $p < 0.001$.

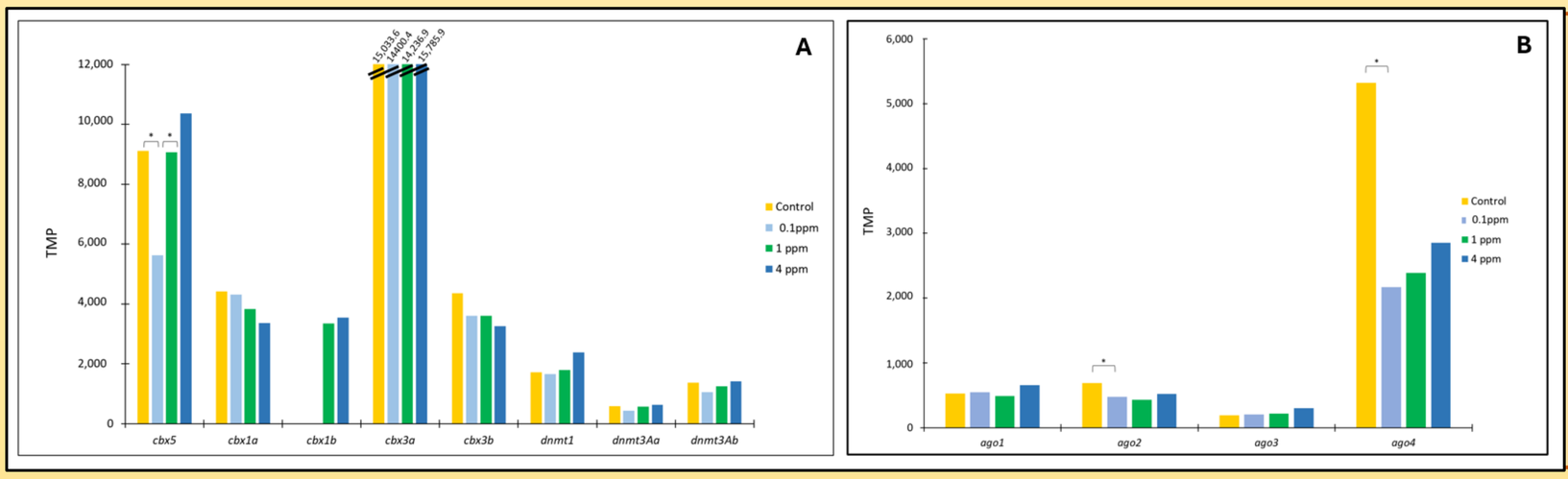


Figure 3. **Transcriptional activity of genes involved in TE silencing mechanisms across all tested conditions (control, 0.1 ppm, 1 ppm, and 4 ppm).**
A. Expression values of genes encoding proteins involved in heterochromatin formation (*cbx5*, *cbx1a*, *cbx1b*, *cbx3a*, *cbx3b*, *dnmt1*, *dnmt3Aa*, and *dnmt3Ab*) are reported. Generally, a reduction in transcriptional activity is observed when comparing the control with embryos exposed to 0.1 ppm. On the other hand, the system appears to increase its activity at higher concentrations as 1 ppm and 4 ppm.
B. Expression values of members of the Argonaute gene subfamily (*ago1*, *ago2*, *ago3*, and *ago4*) are reported. As observed in the graph A in the case of genes involved in heterochromatin formation, there is a decrease moving from the control condition up to 1 ppm of BPA, followed by an increase at 4 ppm.
Statistically significant differences are presented as * for $p < 0.05$, ** for $p < 0.01$, and *** for $p < 0.001$.

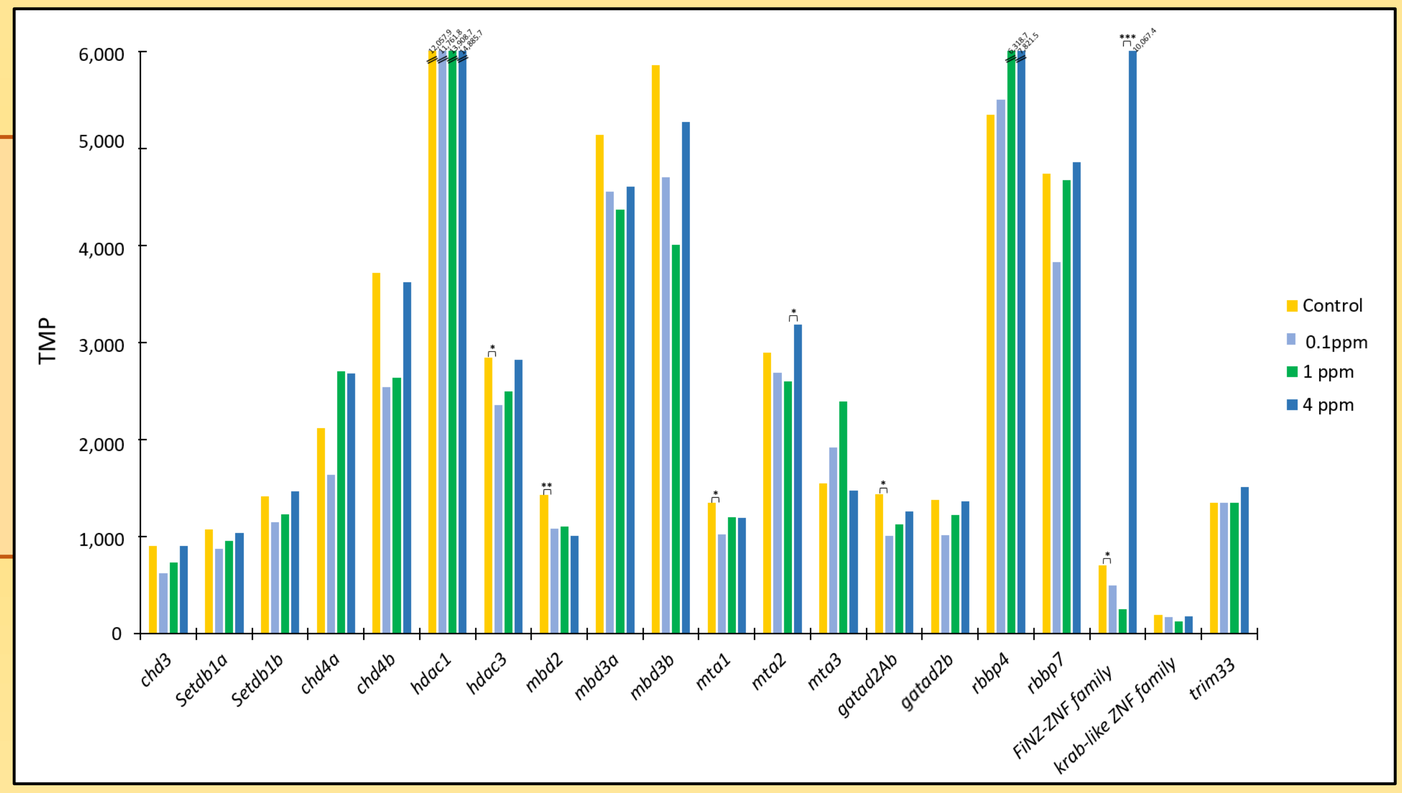
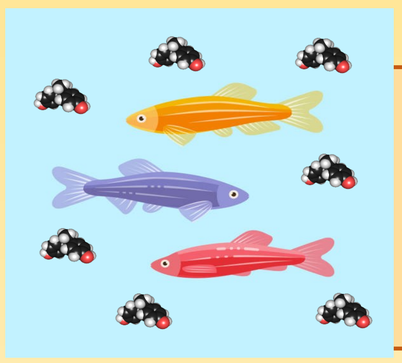


Figure 4. **Expression values of genes encoding proteins constituting the NuRD complex are reported for all the tested conditions (control, 0.1 ppm, 1 ppm, and 4 ppm).**
The transcriptional activity of genes within the NuRD complex (*chd3*, setdb1a, *setdb1b*, *chd4a*, *hdac1*, *hdac3*, *mbd2*, *mbd3a*, *mbd3b*, *mta1*, *mta2*, *mta3*, *gatad2Ab*, *gatad2b*, *rbbp4*, *rbbp7*, *FiNZ-ZNF family*, *krab-like ZNF family*, *trim33*) decreases in zebrafish embryos exposed to 0.01 ppm of BPA compared to the control group. Subsequently, there is an overall increase of transcriptional activity for all genes, returning to baseline levels in samples exposed to 1 ppm and 4 ppm of BPA. The reduced activity of the system could be linked to the slight increase observed in the activity of TEs, suggesting that lower concentrations of BPA may have a greater effect on the entire system. Notably, a statistically significant increase in transcriptional activity was observed specifically for the gene FiNZ-ZNF family in zebrafish embryos exposed to 4 ppm of BPA.

Statistically significant differences are presented as * for $p < 0.05$, ** for $p < 0.01$, and *** for $p < 0.001$.

CONCLUSIONS



BPA is an endocrine disruptor and due to its presence in aquatic environments it is important to understand its effects on aquatic species. In this study, we have highlighted that BPA induces variations, although in a slight manner, in the levels of transcriptional activity of TEs and genes involved in their control. Overall, greater effects are observed at lower tested concentrations of BPA suggesting that this compound behaves following a "non-monotonic dose-response" model, where low doses can provoke a greater effect, differently from higher doses that are less effective. However, it remains crucial to get an holistic view of mechanisms through which BPA influences the activity of TEs.