Application of Omics for Identification of Mode of Action- Specific Molecular Fingerprints and Protein Biomarkers Induced by the Fungicide Carbendazim in Zebrafish Embryos.

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Abstract

The aim of this work was to predict the early responses induced by carbendazim in zebrafish embryos in terms of transcriptomics supported by proteomic profiling of the same sample. Zebrafish embryos were exposed to sublethal concentrations of carbendazim for 96 hours followed by simultaneous RNA and protein extraction from the respective samples. To further analyse effects induced by carbendazim in transcriptomic and proteomic profiles, RNA-Seq (transcriptome) and mass spectrometry-based proteomics (proteome) analysis were applied. The resulting molecular fingerprints and protein biomarkers will provide the basis for developing a mode of action (MoA)-specific screening approach for active substance precursors under development as well as for monitoring environmental samples in order to detect early responses to environmental contaminants.

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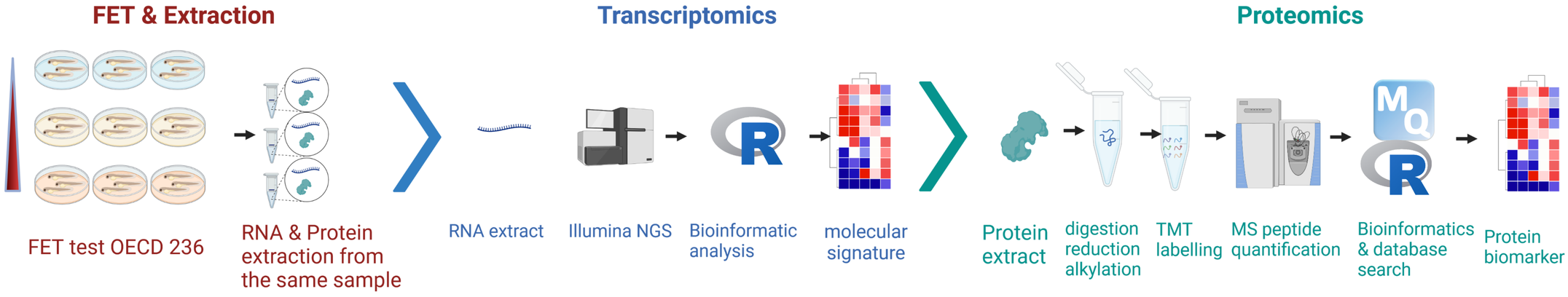
Workflow



findings

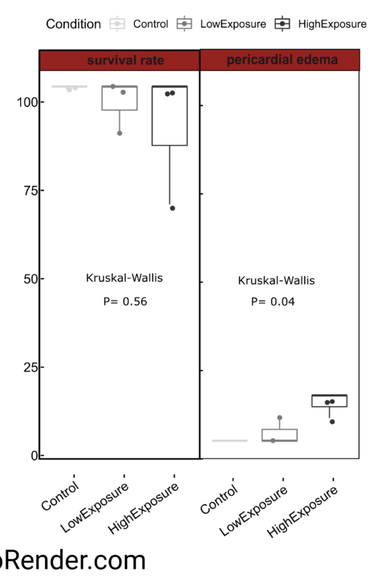


Fig. 1. showing lethality as well as recorded phenotypic effects after 96 hours **FET test** using Carbendazim high exposure (500 µg/l) and low exposure (125 µg/l).

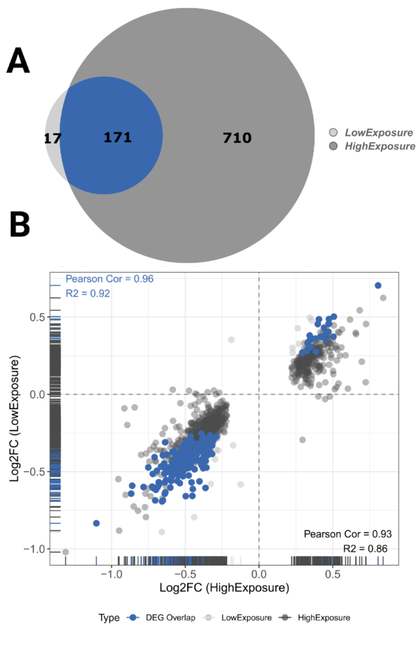


Fig. 2. (A) venn plot displays the differentially expressed genes (DEGs) after **transcriptomics analysis.** for each treatment, a considerable nomber of DEGs was detected in both high and low exposure with 171 DEGs commomn between both treatments. **(B)** a scatter plot indicating the direction of regulation of the detected DEGs. a cnsiderably high correlation was detected especially for the core DEGs (R= 0.96).

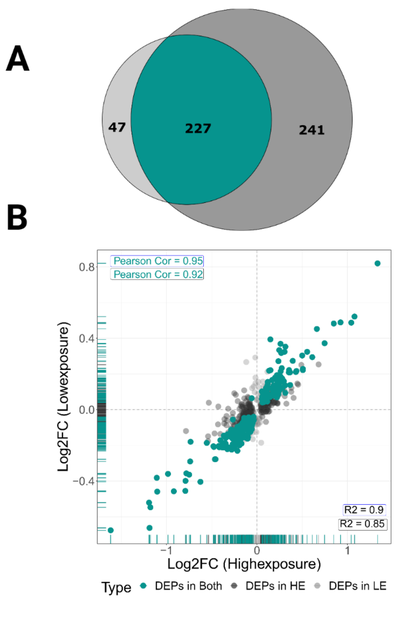


Fig. 3. (A) venn plot displays the differentially expressed proteins (DEPs) for each treatment after **proteomics analysis.** a considerable nomber of DEPs was detected in both high and low exposure with 25 DEPs commomn between both treatments. **(B)** a scatter plot indicating the direction of regulation of the detected DEPs. a cnsiderably high correlation was detected especially for the core DEPs (R= 0.94).

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Conclusion

The reported core differentially expressed genes (DEGs) are especially relevant as potential molecular signatures for the corresponding fungicides in *Danio rerio* due to the strong positive correlation recorded when comparing log2-fold change values of both HE and LE (R= 0.95). As observed in transcriptomics, the DEPs influenced by both low and high exposure conditions (core DEPs) for carbendazim were also significantly dysregulated showing high positive correlation (R= 0.94) when comparing log2-fold change of both exposure conditions. For those reasons, those core DEPs are also particularly interesting as mode of action specific protein biomarkers.

Bibliography:
OECD, 2013. Test Guideline 236: Fish Embryo Acute Toxicity (FET) Test.

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