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Editorial

Spotlight on environmental omics and toxicology: a long way in a short time☆

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ABSTRACT

The applications for high throughput omics technologies in environmental science have increased dramatically in recent years. Transcriptomics, proteomics, and metabolomics have been used to study how chemicals in our environment affect both aquatic and terrestrial organisms, and the characterization of molecular initiating events is a significant goal in toxicology to better predict adverse responses to toxicants. This special journal edition demonstrates the scope of the science that leverages omics-based methods in both laboratory and wild populations within the context of environmental toxicology, ranging from fish to mammals. It is important to recognize that the environment comprises one axis of the One Health concept - the idea that human health is unequivocally intertwined to our environment and to the organisms that inhabit that environment. We have much to learn from a comparative approach, and studies that integrate the transcriptome, proteome, and the metabolome are expected to offer the most detailed mechanism-based adverse outcome pathways that are applicable for use in both environmental monitoring and risk assessment.

1. Introduction

As the acting editors for this special edition, we welcome you to read the articles here within Comparative Biochemistry and Physiology-Part D: Genomics and Proteomics. This edition shines a spotlight on the diverse applications of omics-technologies in environmental toxicology. Together, "Omics" and "ecotoxicology" are only ~15 years young, and exciting discoveries are on the horizon. The amount of both nucleotide and protein information continues to increase at an exponential rate, as does the number of model and non-model species included in databases such as the National Center for Biotechnology Information (NCBI) (Fig. 1). As per its mission, CBP-Part D: Genomics and Proteomics aims to publish hypothesis-driven research in the broad fields of genomics, transcriptomics, proteomics, metabolomics, and bioinformatics; ecotoxicology has embraced these approaches to (1) answer questions related to the modes of action of environmental toxicants; (2) identify molecular initiating events in order to construct adverse outcome pathways, a conceptual framework that has gained popularity in both human and environmental toxicology; (3) achieve an integrated understanding of how chemicals are associated to higher level responses in individuals and populations; and (4) monitor adverse effects in organisms inhabiting polluted ecosystems. The purpose of this special paper symposium is to demonstrate the scope of the science that leverages omics-based methods in both laboratory experiments and wild populations. It is important to recognize that the environment comprises one axis of the One Health concept - the idea that human health is unequivocally intertwined to our environment and to the organisms that inhabit that environment. Interdisciplinary science is therefore essential for integrating medical, animal, and environmental studies to improve global health. It is our opinion that omics-technologies can contribute significantly to this global effort. Below we introduce the technologies, briefly outline the state of the science, and provide examples for how these methods are used to assess chemical effects in a wide array of organisms, truly a comparative approach from invertebrates to vertebrates. We hope you enjoy reading the articles here within CBP-Part D: Genomics and Proteomics, as the research pushes the boundary of knowledge using high-throughput omics-technologies to understand how environmental pollution impacts health.

2. An array of applications, from genes to metabolites

2.1. Transcriptomics: microarray and RNA-seq

Gene expression analysis using both microarrays and RNA-seq has been a significant advance for ecotoxicogenomics. One of the first appearances for the terms "toxicology and microarrays" in the literature (Pub Med, NCBI), (US National Library of Medicine National Institutes of Health) occurred in 1999 (Nuwaysir et al., 1999). A survey

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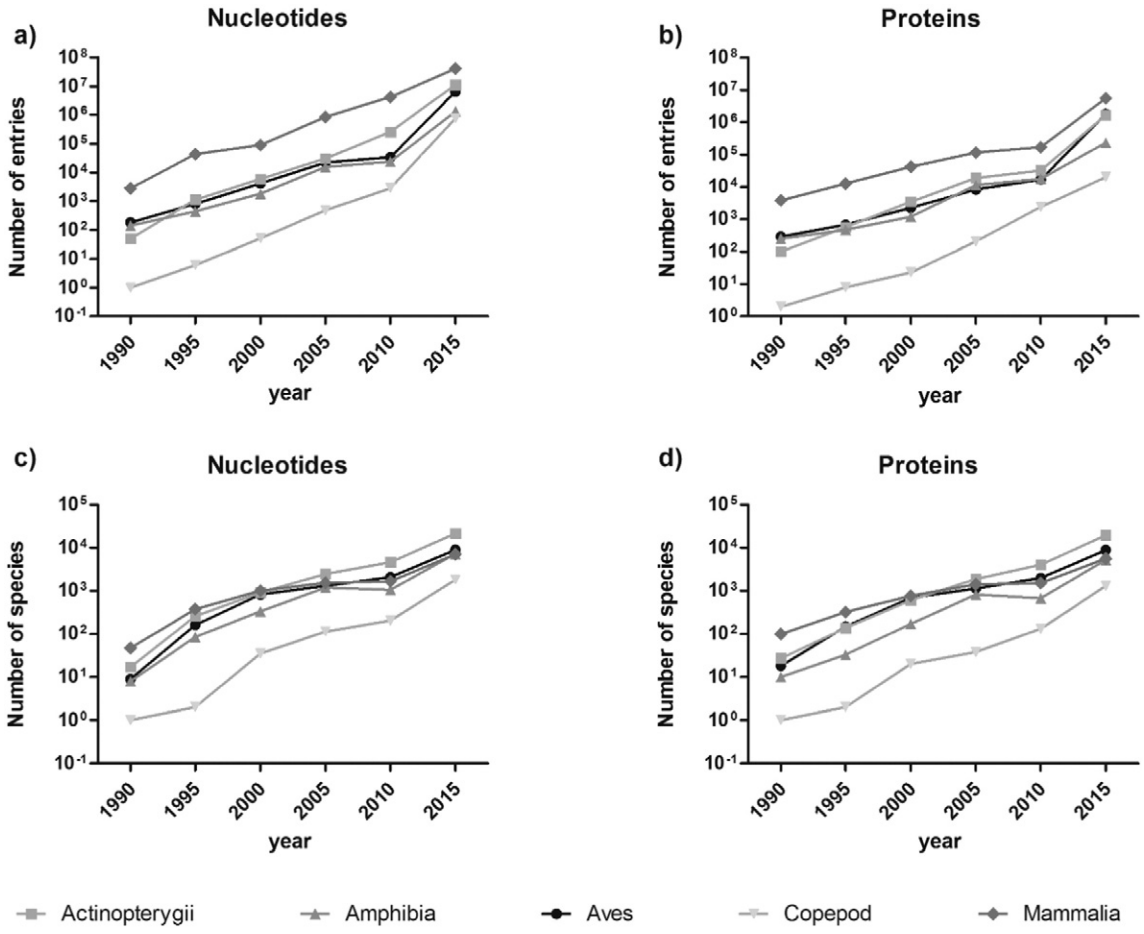

Fig. 1. Number of NCBI database entries for nucleotides (a) and proteins (b) and number of species represented in the NCBInr nucleotide database (c) and NCBInr protein database (d) for five different eukaryotic classes; Aves (black circle), Actinopterygii (medium grey square), Amphibia (grey triangle), Copepoda (light grey inverted triangle), and Mammalia (dark grey diamond).

(December 2015) in NCBI *"Microarray + toxicology"* yielded > 1100 publications and *"RNA-seq + toxicology"* yielded > 50 publications, and it is expected that the use of RNA-seq will dramatically increase over the next several years as the technology becomes more widely available to researchers. Microarrays consist of synthesized oligonucleotide targets on a solid platform that act to hybridize with complimentary probes generated with fluorescent tags (e.g., cyanine 3) from a biological sample. Different technologies exist for microarray analysis, and the strength of these fixed platforms is that many of the targets (and thus the represented genes) are known "a priori". However, for non-model species, uncharacterized targets have been a challenge for many and annotation of microarrays is continuously improving. Prior to synthesized oligonucleotides (ssDNA), microarrays were cDNA-based (dsDNA from PCR amplification of cDNA library inserts). Early efforts in non-mammalian

Genomics Research on All Salmonids Project with a high level of annotation (Rise et al., 2004). cDNA platforms have been used to study an array of chemicals over the past decade (Larkin et al., 2003; Poynton et al., 2007; Liu et al., 2013) and have contributed significantly to toxicogenomics over the past several years. Newer technology, such as RNA-seq, entails massive parallel sequencing of transcripts using methods developed by Illumina (NextSeq, TruSeq), Thermo Fisher Scientific (Ion Torrent), and Pacific Biosystems, to name but a few. Longer reads are now possible, and in 6–7 years, the technology has advanced from <100 base pair reads to >1 Kb reads (PacBio), facilitating whole genome and targeted sequencing, RNA sequencing, and epigenetics.

Gene expression profiling has been used in ecotoxicology to study the effects of pesticides, industrial by- products, pharmaceuticals, and nanoparticles. Moreover, expression technologies have applications both inside and outside the laboratory and include a wide range of aquatic species (Bahamonde et al., 2016). For example, the manuscript in this special issue by Sanchez and colleagues uses transcriptomics (i.e. microarray analysis) in male zebrafish to learn more about the mode of action of a widely used fungicide in Mexico called chlorothalonil (Sanchez Garayzar et al., 2016). Male zebrafish were exposed to 0.007 mg/L and 0.035 mg/L chlorothalonil in a 96-h toxicological assay. Based on the transcriptomics analysis, it was proposed that chlorothalonil may act as a compound that disrupts metabolic capacity in the liver, and based on transcript induction of the egg yolk precursor protein vitellogenin and zona pellucida may also act as an estrogen or anti-androgen in fish. Gene expression analysis revealed that males exposed to chlorothalonil showed changes in transcriptional subnetworks related to cell division, reproduction, immunity, DNA damage, and xenobiotic clearance. This study improves knowledge regarding whole animal exposures to chlorothalonil and identifies molecular signaling cascades that are sensitive to this fungicide in the fish liver, a strong example of how this omics approach can be used to identify new modes of action of emerging contaminants.

The aforementioned study suggests that chlorothalonil may have an estrogenic or anti-androgenic mode of action. The timing of a transcriptome response is very important for biomarker characterization and this must be considered carefully, as pointed out by Osachoff et al. in their study investigating the hepatic response of rainbow trout to estrone (E1), a lesser studied estrogen that is detectable in municipal wastewater effluent (Osachoff et al., 2016). A time course analysis revealed that estrogen receptors were more sensitive to E1 compared to other biomarkers of estrogen exposure, such as vitellogenin. The study