# Understanding the Molecular Mechanisms of Contaminant Exposures in Fish and Their Interaction with Nutrients

**OVERVIEW**

Dr Rasinger and Dr Lie work on multi-level omic (molecular) analyses that combine gene expression profiles (transcriptomes), protein profiles (proteomes), and small molecule metabolite profiles (metabolomes).

*“Typically, we are looking at thousands of changing features and it’s great to have those summarised in a PCA plot or heat map”*

Fish in our diet provides us with key nutrients such as marine omega-3 and -6 fatty acids, vitamins A and E, iodine and selenium. But eating fish may also expose us to harmful substances in the environment such as persistent organic pollutants (POPs), pesticides, and heavy metals that fish ingest.

POPs detected in fish include legacy chemicals such as dioxins and polychlorinated biphenyls as well as more recent pollutants like brominated flame-retardants (BFRs) - substances that accumulate in fatty tissues potentially causing chronic exposure.

The study of environmental contaminants and nutrients is at the heart of the work carried out by Norway’s National Institute of Nutrition and Seafood Research (NIFES) - a leading centre of research into fish nutrition and the effects of fish and seafood consumption on human health.

**TECHNICAL SITUATION**

Dr Josef Rasinger, a nutritional toxicologist coordinating food and feed safety testing, and Dr Kai Kristoffer Lie, an ecotoxicologist, are using Qlucore’s Omics Explorer to study the molecular mechanisms of exposure to environmental contaminants on fish and humans, including how the contaminants may interact with the nutrients in fish. “Compared to conventional measurements like organ-weights, clinical chemistry and microscopic histopathology, molecular marker studies enable us to explore mechanisms of toxicity at much lower doses. This allows us to discover earlier if an environmental contaminant is more or less of a problem than we thought. By seeing these trends, it means we can react faster and design focused toxicology experiments around the most problematic substances out there,” says Dr Rasinger. Based at Norway’s National Institute of Nutrition and Seafood Research (NIFES), both scientists have a strong background in data analytics and a keen interest in the development of molecular, bio-statistical and bio-informatics tools. However, the sheer volume and complexity of data generated at NIFES remains a challenge.

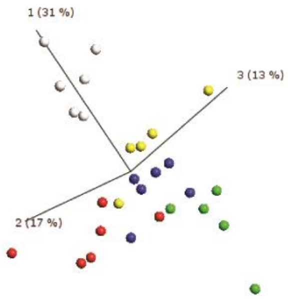
**SOLUTION**

“Omics Explorer has become our ‘go-to’ tool for getting a first glance of any multivariant data problem,“ explains Dr Rasinger. “It provides us with simple and fast visualisation of data, irrespective of the data source.“ He adds: “Typically we are looking at thousands of changing features and it’s great to have those summarised in a PCA [principal component analysis] plot or heat map. It means we can very quickly see if there is something interesting going on and if so whether we should dig deeper." By using these techniques, they are learning about the mechanisms of nutrient and contaminant exposures and discovering novel biomarkers for health and disease. One early project that showed the capabilities of the tool looked at the effect of a fish diet spiked with persistent organic pollutants (POPs) on gene and protein expression in the brains of young mice. "We had a huge amount of data: around 20k to 30k gene transcripts and around 2000 proteins and there were a lot features changing. We wanted to relate these changes to the exposure conditions, to find sets of proteins and genes that were changing at the same time, and to find out which changes are important," he adds.

**BENEFITS**

"With Omics Explorer, we could work together with the proteomics and transcriptomics data on the same platform so there was no need translate the outputs from one tool to another. It made it very easy to compare data, to communicate amongst the researchers, and to discuss the next steps," comments Dr Rasinger. Exporting data, he says, for downstream analysis was also straightforward.

The study concluded that all four POPs (non-dioxin-like BFR chemicals CB-153, BDE-47, HBCD and the dioxin TCDD) accumulated in the mouse brains. Based on the analysis of the omics data, the NIFES team hypothesised that this accumulation caused damage by dysregulation of the otherwise tightly controlled homeostasis of calcium and zinc. Interestingly, subsequent studies by Dr Rasinger and Dr Lie have shown that nutrients such as selenium, vitamin E and vitamin A in fish may counteract some of the adverse effects of environmental pollutants.




PCA plot of significant responses detected after dietary exposure to BDE-47 (blue), CB-15(yellow), HBCD (green) and TCDD (red), respectively. Control group - white. Rasinger, J. D., T. S. Carroll, A. K. Lundebye, and C. Hogstrand. 2014. "Cross-Omics Gene and Protein Expression Profiling in Juvenile Female Mice Highlights Disruption of Calcium and Zinc Signalling in the Brain Following Dietary Exposure to CB-153, BDE-47, HBCD or TCDD." Toxicology, 321, 1–12.







QLUCORE SWEDEN IDEON SCIENCE PARK, SCHEELEVÄGEN 17, 223 70 LUND.
QLUCORE USA 900 THIRD AVENUE, 29TH FLOOR, NEW YORK, NY 10022.