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Title: Developing an enhanced experimental work-flow for maximising the use of 'omics data within
the Adverse Outcome Pathway framework
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Abstract: Developments in ‘omics technologies have opened new possibilities for assessing the molecular and
biochemical responses of organisms to chemicals. Feature selection tools are increasingly being used to discover
responses within the ‘omics datasets that may be predictive of adverse outcomes. These molecular responses
can help to define the “key events” (KEs) underpinning the toxicity pathway within an Adverse Outcome Pathway
(AOP) framework. KEs are deviations from a healthy state, through a stress response, that may predict an
adverse outcome and therefore indicative of a chemical’s potential health hazards. Here we investigate the
potential of multi-omics technologies to discover KEs of specific acting chemicals and baseline narcotics. The
first phase of this work has been the development of a proposed work-flow of how to utilise the non-targeted,
information rich, data attainable from omics investigations; incorporating this into an enhanced AOP driven risk
assessment approach. The second phase has been to start to develop comparative multi-omics approaches as
part of an integrated (weight of evidence) approach in combination with available in silico or in vitro data to
support the categorisation of chemicals by their KEs based upon their molecular and biochemical responses in
Daphnia and algae. We aim to achieve this by elucidating the relevant KEs of specifically acting chemicals and
baseline narcotics and measuring the strength of the association with the subsequent adverse outcome. The use
of organisms that span two trophic levels could enable qualitative assessment of the predictive capability of the
KE(s) both within and across species, improving toxicity predictions for untested species and in setting exposure
thresholds in environmental risk assessment. To identify target homology and further enhance cross species
applicability, molecular target sequence analysis tools; such as the US-EPA developed SeqAPASS (Sequence
Alignment to Predict Across-Species Susceptibility), will be utilised. Sampling at high temporal resolution
(spanning the acute and chronic experimental stages) for the ‘omics assays will provide reproducible
toxicological effects measurable by gene expression and metabolite profiling. By detecting the point of
departure from a healthy state, we aim to use acute exposure scenarios to predict chronic outcomes, ultimately
streamlining the experimental design to capture just the KEs making the work flow rapid and cost effective.