REDUCED TRANSCRIPTOMIC APPROACH IN CHEMICAL TOXICOLOGY

Full dose range testing of hundreds of chemicals or mixtures can be performed with human cells or zebrafish embryos by a reduced transcriptomic approach. Points of departure of genes and pathways are used for potency ranking and to classify chemicals by disrupted biological pathways.

**STEP 1**
**INPUT: DOSE-RESPONSE MODELING OF GENES**

- **U-shaped**
  - POD \( \text{gene-1} \)
  - Fold change
  - Concentration

- **Sigmoid**
  - POD \( \text{gene-2} \)
  - Fold change
  - Concentration

- **Linear**
  - POD \( \text{gene-3} \)
  - Fold change
  - Concentration

**STEP 2**
**PATHWAY MAPPING**

- **PATHWAY-1**
  - POD \( \text{path-1} \)
  - Gene-1
  - Gene-2

- **PATHWAY-2**
  - POD \( \text{path-2} \)
  - Gene-1
  - Gene-2

- **PATHWAY-x**
  - POD \( \text{path-x} \)

**STEP 3**
**DOSE-DEPENDENCE OF PATHWAY PERTURBATIONS**

- **Rank**
- **Path-x**
- **Path-2**
- **Path-1**

**STEP 4**
**CLASSIFICATION**

- **CHEMICAL A**
- **CHEMICAL B**
- **CHEMICAL C**
- **CHEMICAL D**
- **CHEMICAL E**
- **CHEMICAL I**
- **CHEMICAL H**
- **CHEMICAL K**

Proportional ranks of POD

**STEP 5**
**RANKING BY POTENCY**

Proportional ranks of POD vs. concentrations