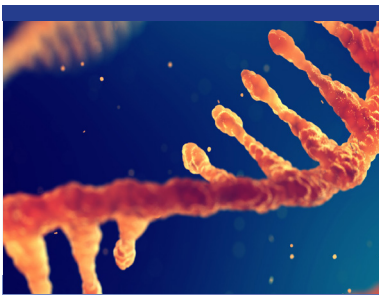


# Safety Prediction and Transcriptomics

## Background Information



'The field of transcriptomics has evolved substantially over the past few decades and made remarkable contributions in biology and toxicology.'

<sup>1</sup>Joseph P. (2017) *Food Chem Toxicol.* **109(Pt 1)**; 650-662

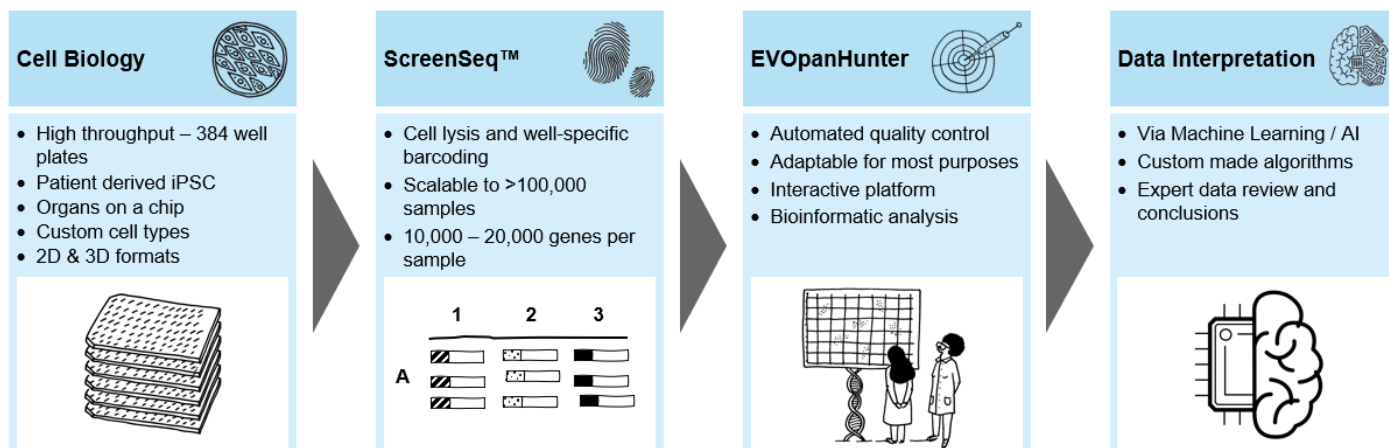
- The lack of translation from animal to human species, coupled with an ethical drive to reduce or ban animal testing has led to a push towards human-relevant cell-based models.
- Mechanisms of toxicity can be complex comprising of a multitude of different and often interlinking pathways resulting in manifestation of a particular toxic outcome.
- Transcriptomic analysis, which identifies transcriptional changes in mRNA and other RNA molecules, is now showing promise in defining these mechanisms and enhancing toxicology prediction.
- Cyprotex, in conjunction with parent company Evotec, has built a complete transcriptomics workflow for whole transcriptome analysis. Using this approach, we are able to evaluate organ-specific models to investigate mechanisms of toxicity and potential safety liabilities.

## Service Benefits

- Advanced cell culture systems for *in vitro* toxicology
- Optimised for cell lines, primary cells, iPSC-derived cells, and complex *ex vivo* tissues
- Sophisticated high throughput 384 well transcriptomics platform using RNA-Seq
- Leading bioinformatics platform for interactive multivariate data analysis
- In depth analysis of complex data using the unique *EVOpAnHunter* software
- Advanced machine learning capabilities
- Large and complex data sets interpreted by expert data scientists
- Toxicity mechanism investigation by expert computational toxicologists
- The largest DILI transcriptomic database in the world

**Figure 1**

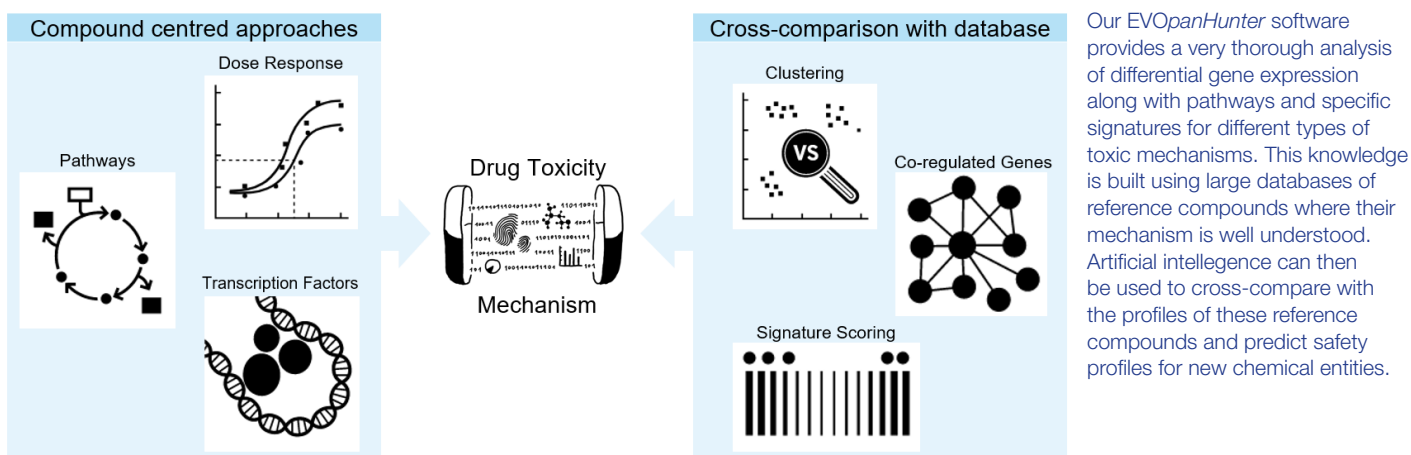
Overview of the high throughput transcriptomics platform



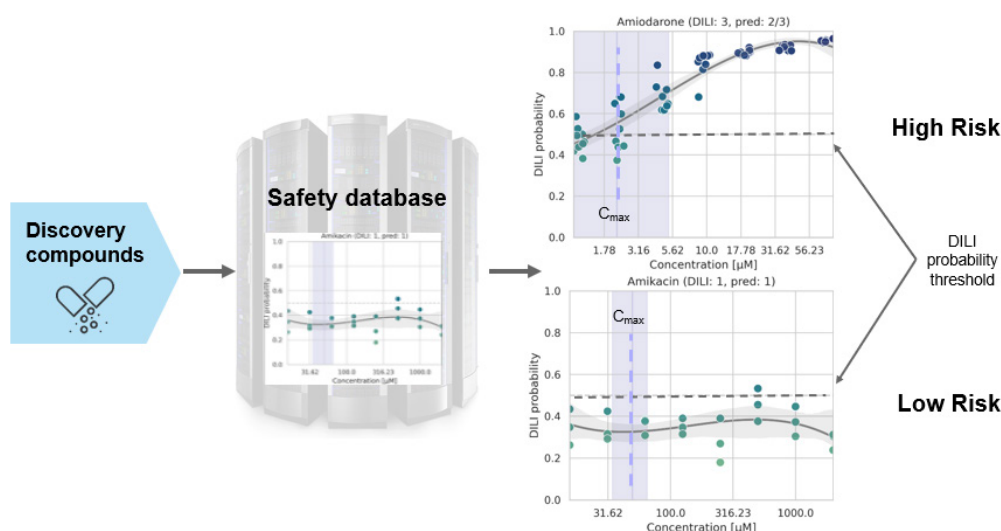
Cyprotex, and parent company Evotec, offer an end-to-end *in vitro* toxicology transcriptomics service that can be customised according to the client's needs. Advanced cell culture systems are combined with the latest NGS sequencing technology (RNA-seq) and a leading bioinformatics platform. Sophisticated machine learning and artificial intelligence are used to interpret the large and complex datasets generated.

**Figure 2**

Transcriptomics data analysis using EVOpanHunter.

**Figure 3**

An example workflow representation of how transcriptomic data and AI are used to predict DILI.



A combination of transcriptomics and AI have been shown to deliver a superior level of DILI prediction. Using the industry current gold standard method; 2D primary human hepatocytes or 3D human liver microtissues with a seven parameter high content imaging read-out, DILI prediction accuracy is reported at 69% and 77% respectively. However, using the new DILI prediction platform, which utilises RNA-seq transcriptomics data generation combined with EVOpanHunter data analysis, accuracies of 80% are achieved using primary human hepatocytes, and 86% using 3D human liver microtissues.

**References**

<sup>1</sup> Joseph P. (2017) Transcriptomics in toxicology. *Food Chem Toxicol* **109**(Pt 1): 650-662

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