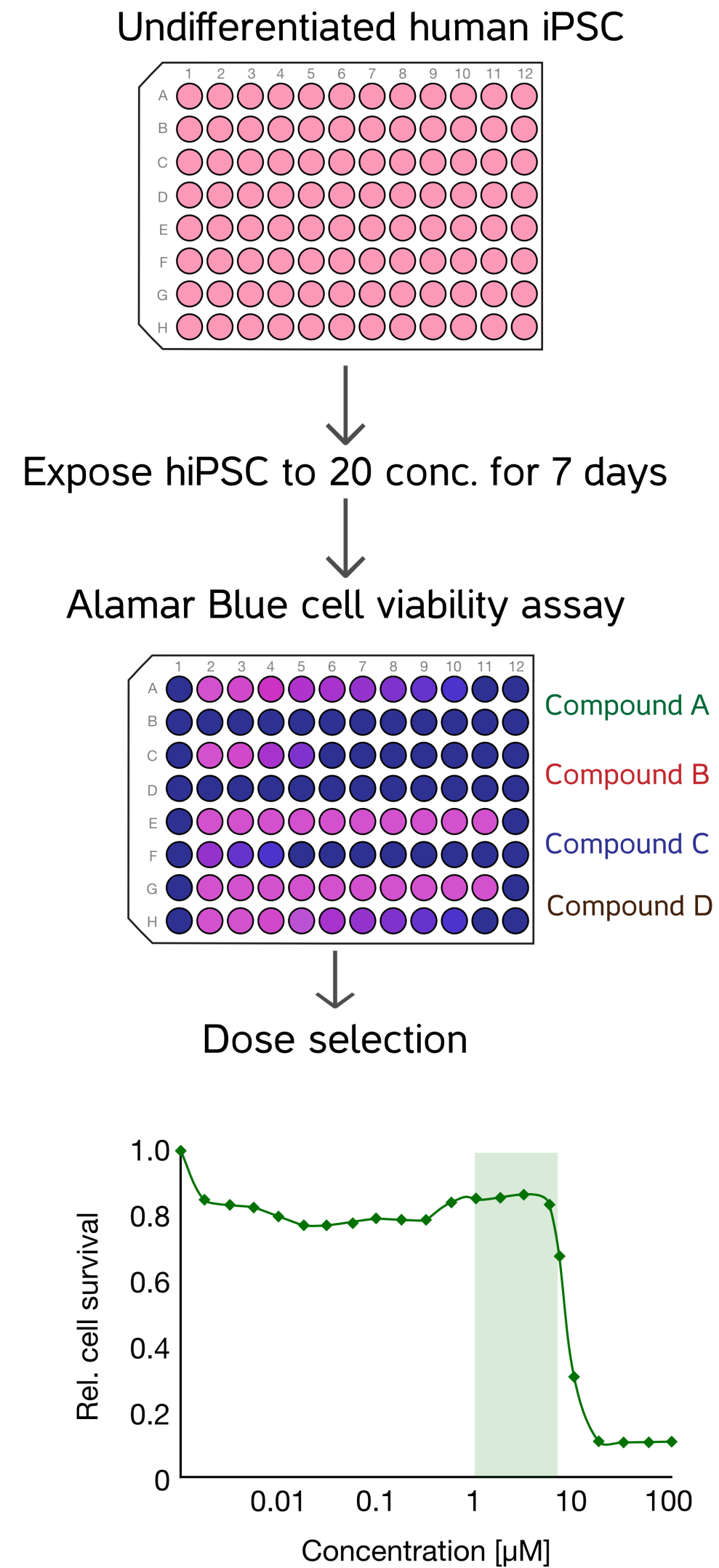
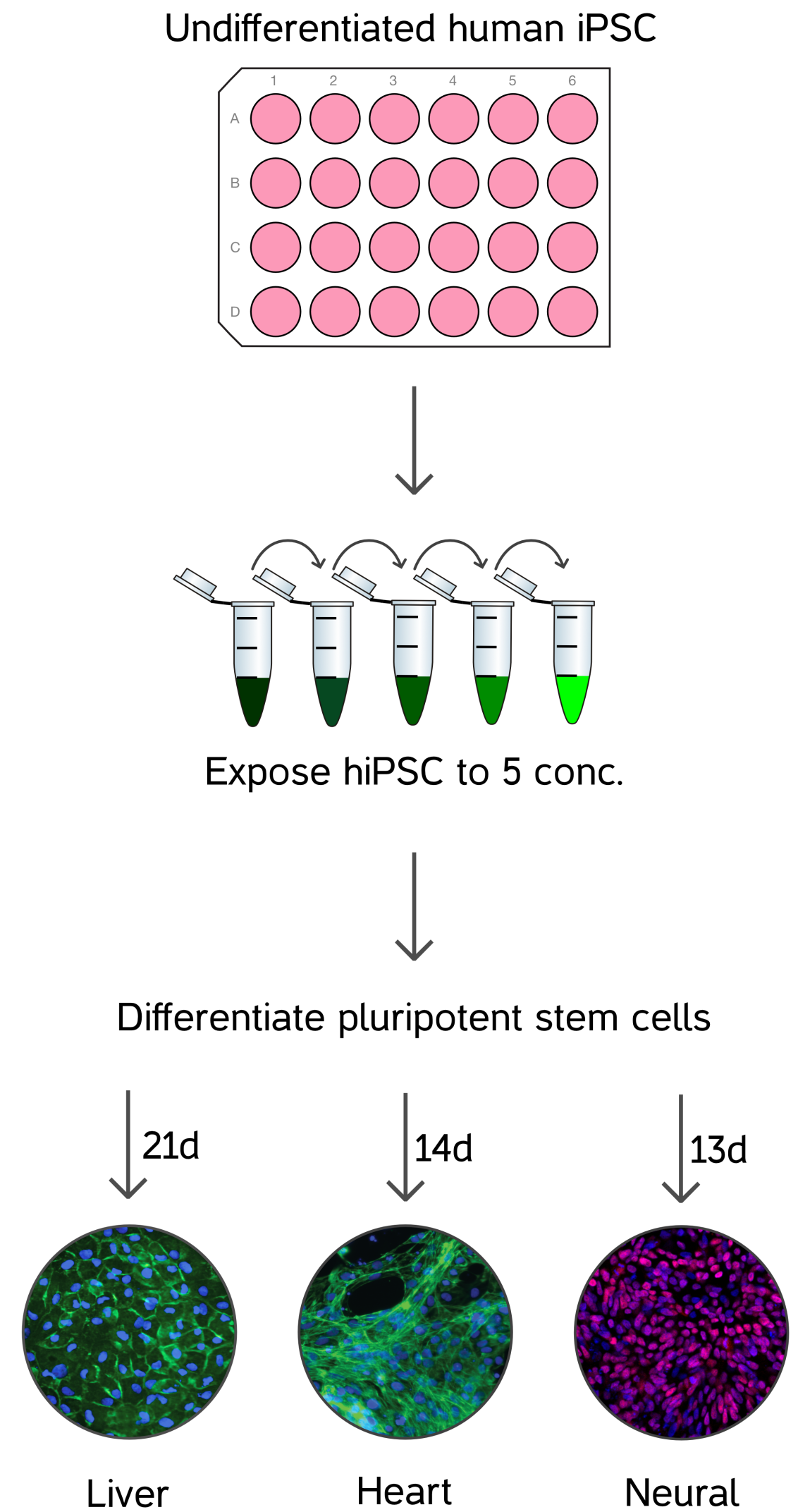


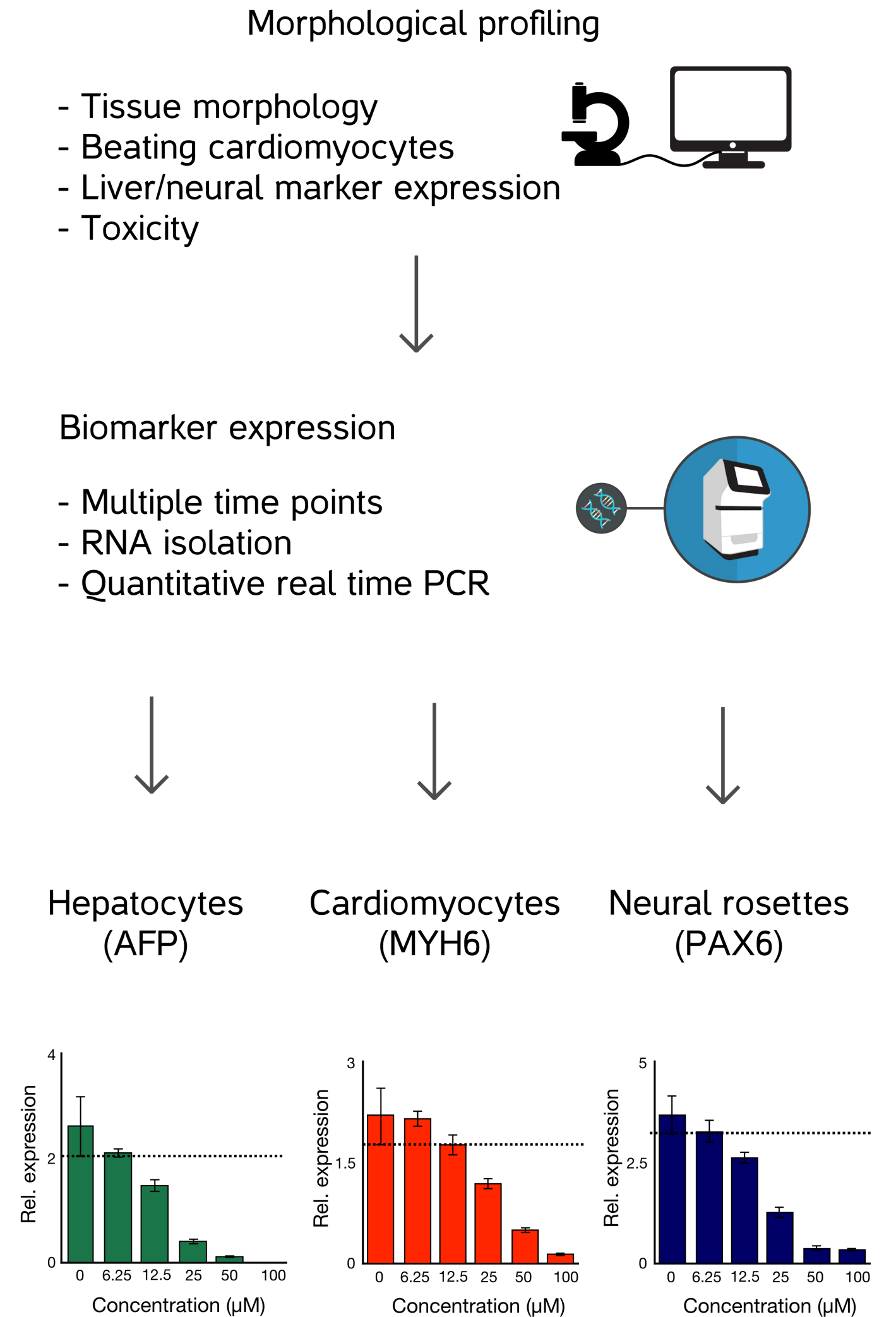
1. Dose range finding



2. Stem cell differentiation

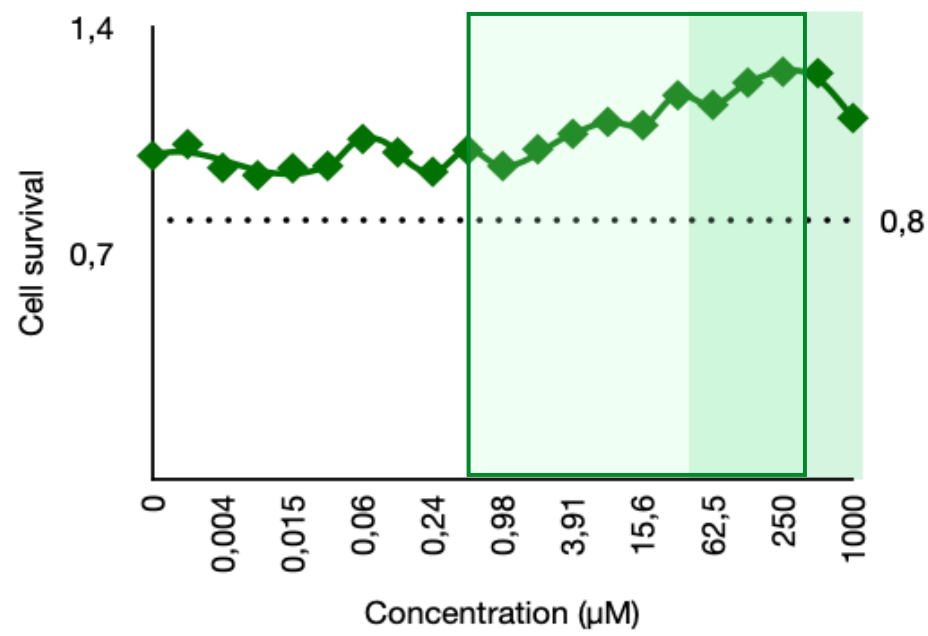


3. Biomarker analysis



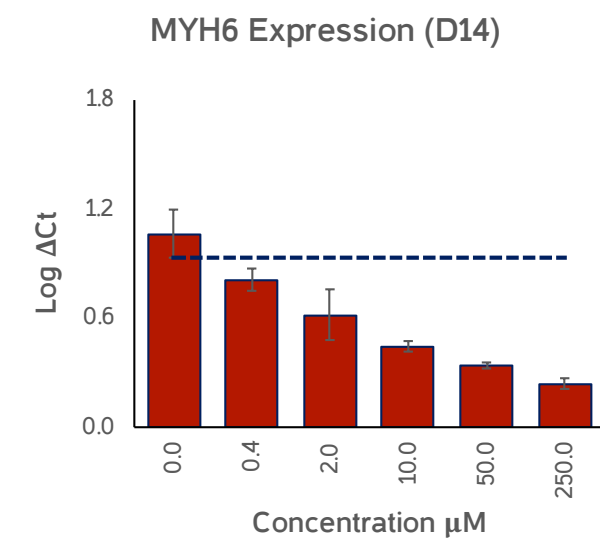
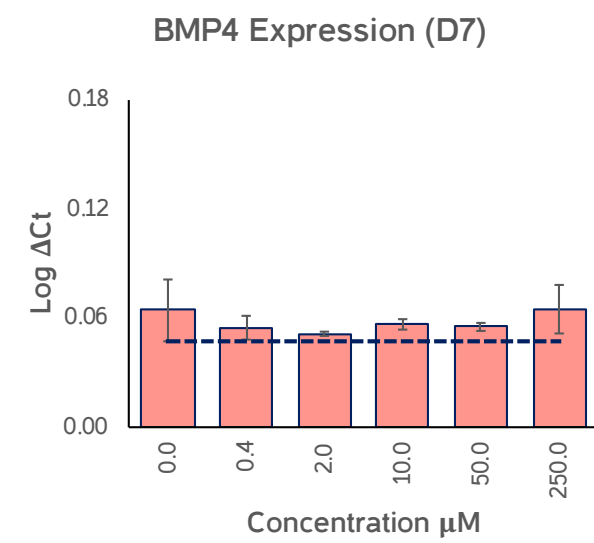
Dose selection

Dose selection: thalidomide

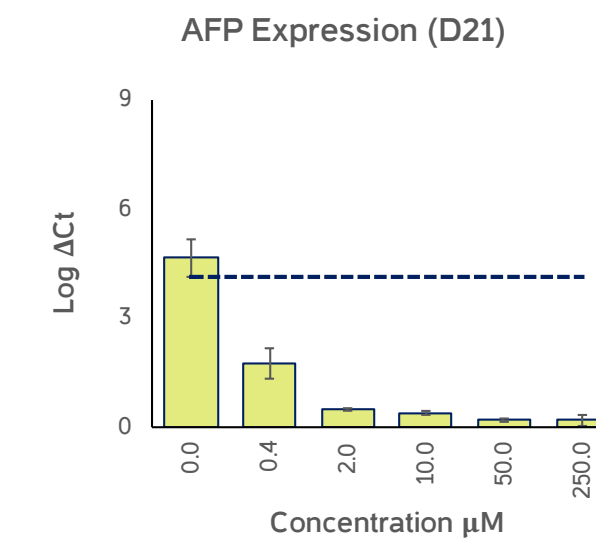
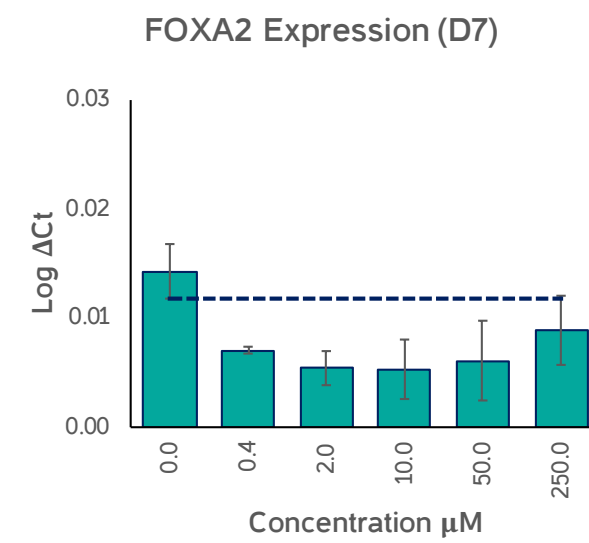


Biomarker analysis

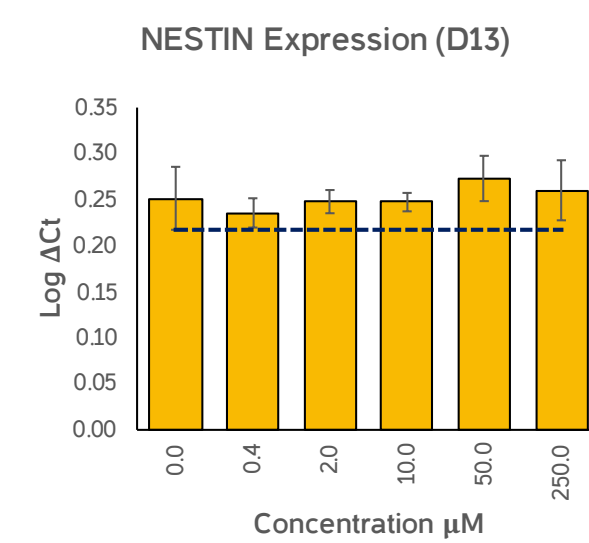
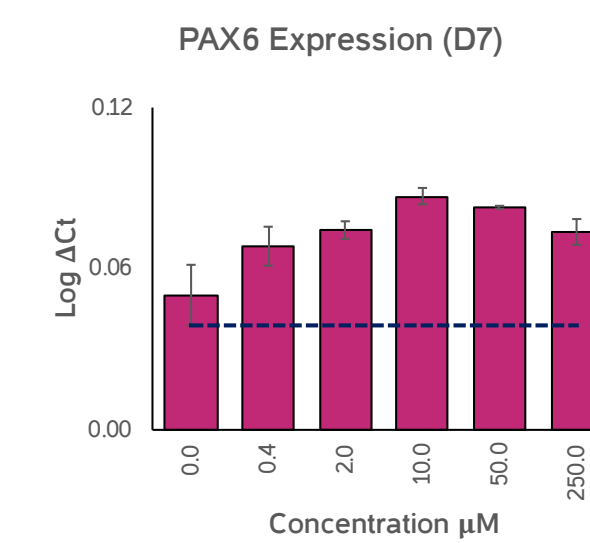
Cardiomyocyte markers



Hepatocyte markers



Neural markers



Clinically relevant concentration is between 1-6 μM

Morphology analysis

Contraction



Increasing concentration

Morphology

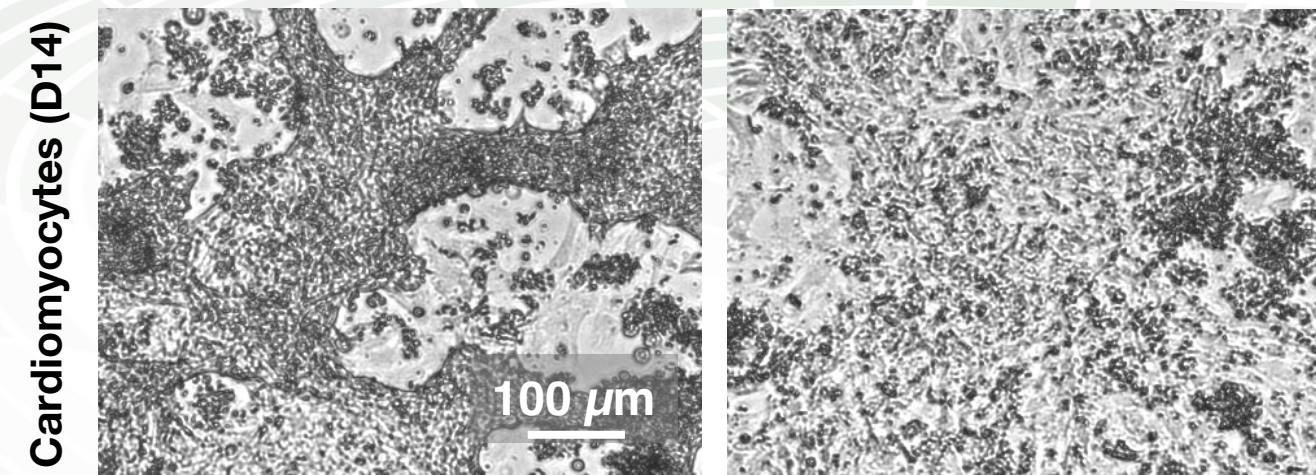


Increasing concentration

Morphology

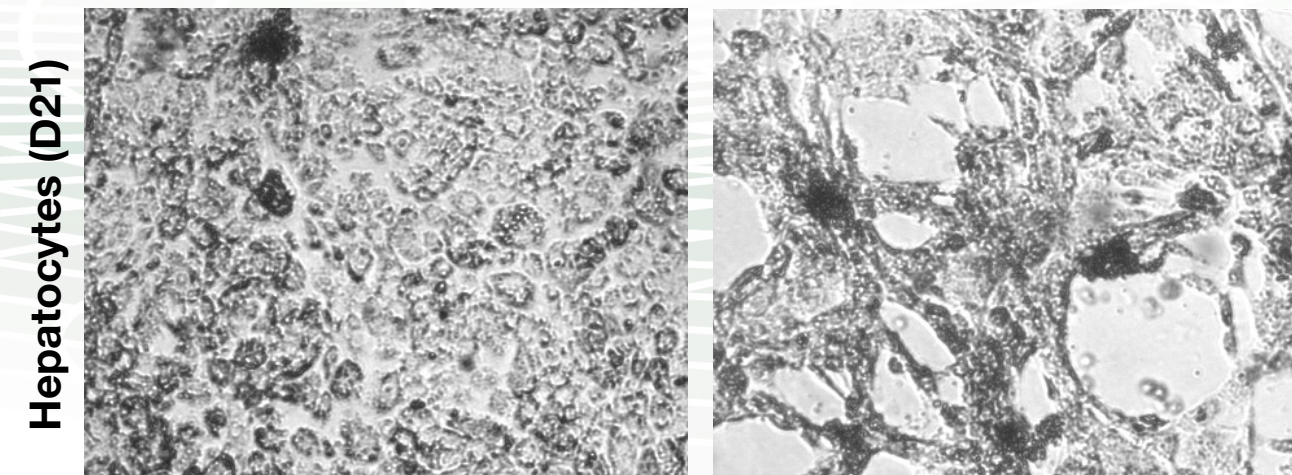


Increasing concentration



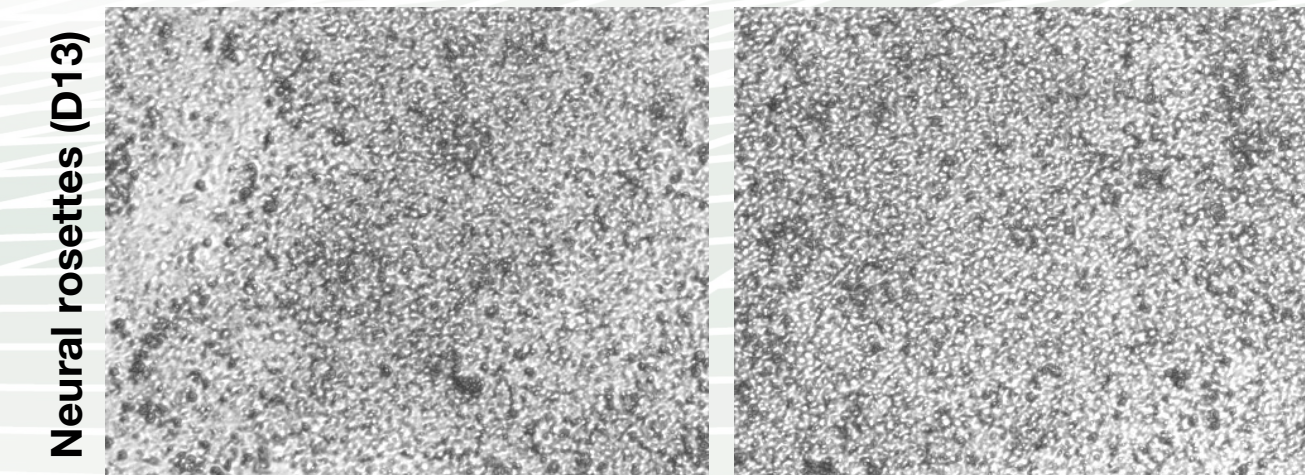
Unexposed

Exposed



Unexposed

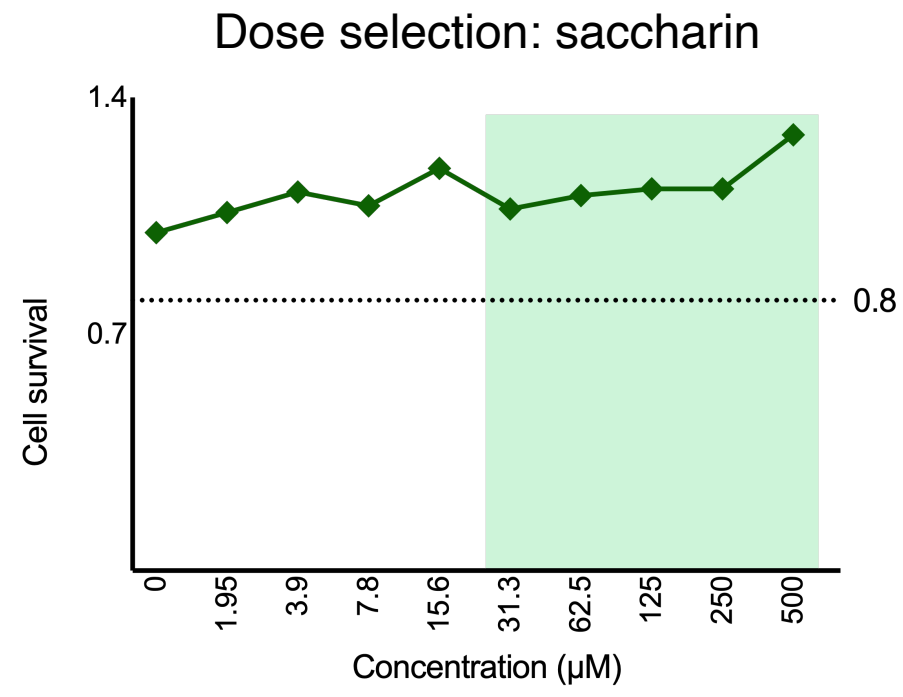
Exposed



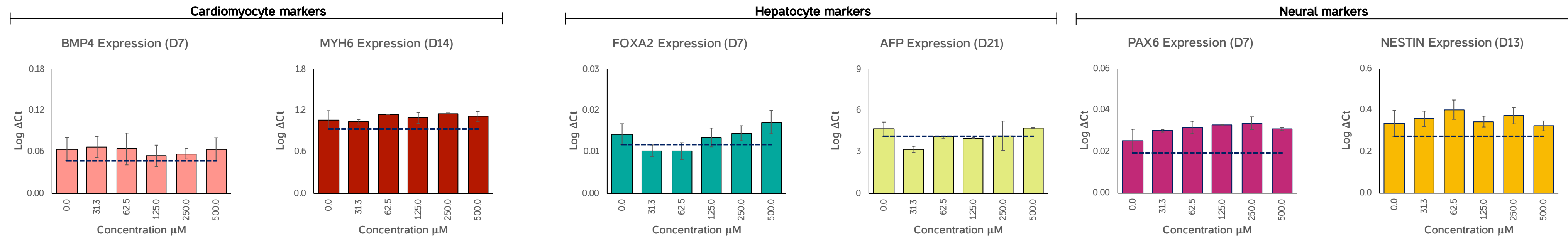
Unexposed

Exposed

Dose selection



Biomarker analysis



Morphology analysis

Clinically relevant concentration is 1.5 µM

Contraction



Increasing concentration

Morphology

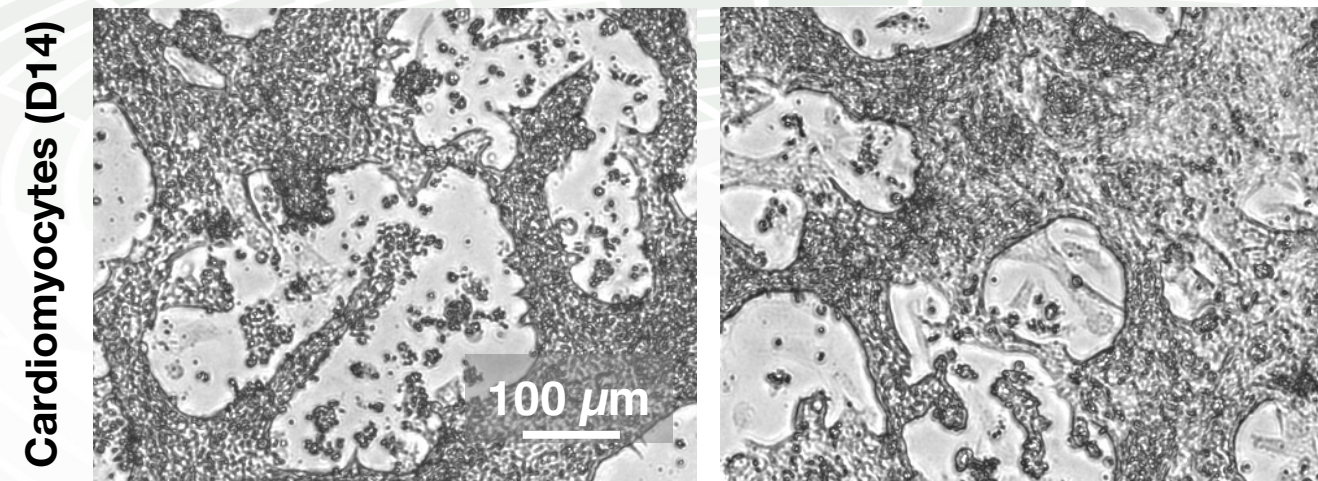


Increasing concentration

Morphology

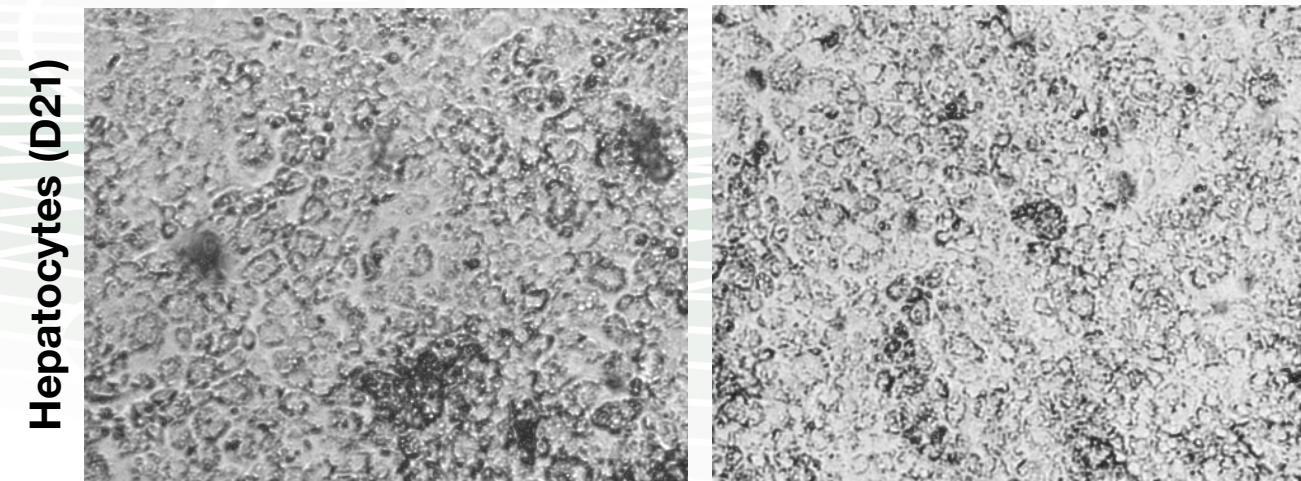


Increasing concentration



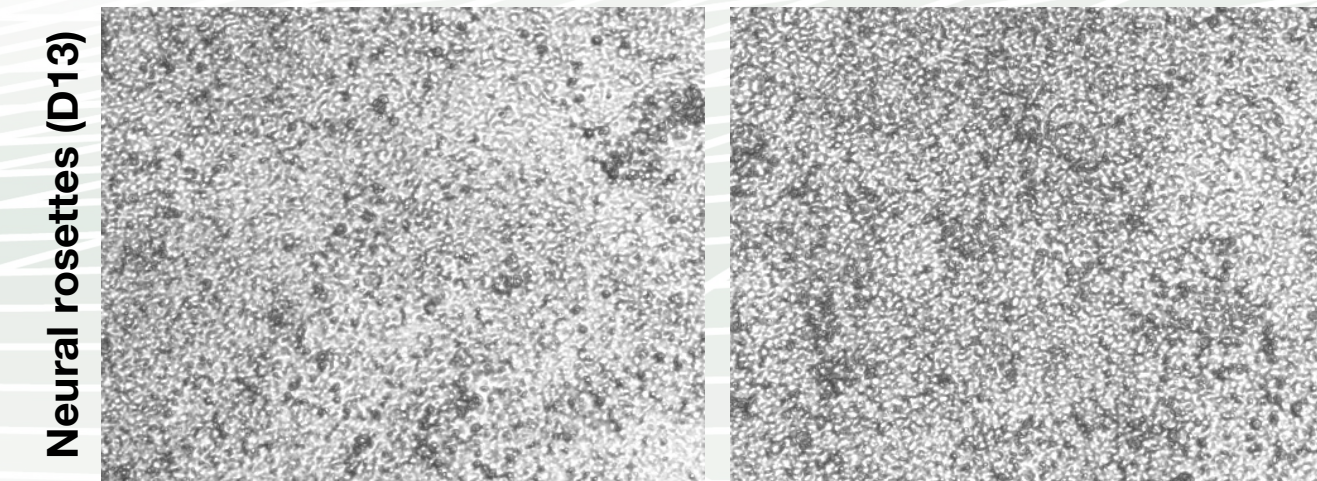
Unexposed

Exposed



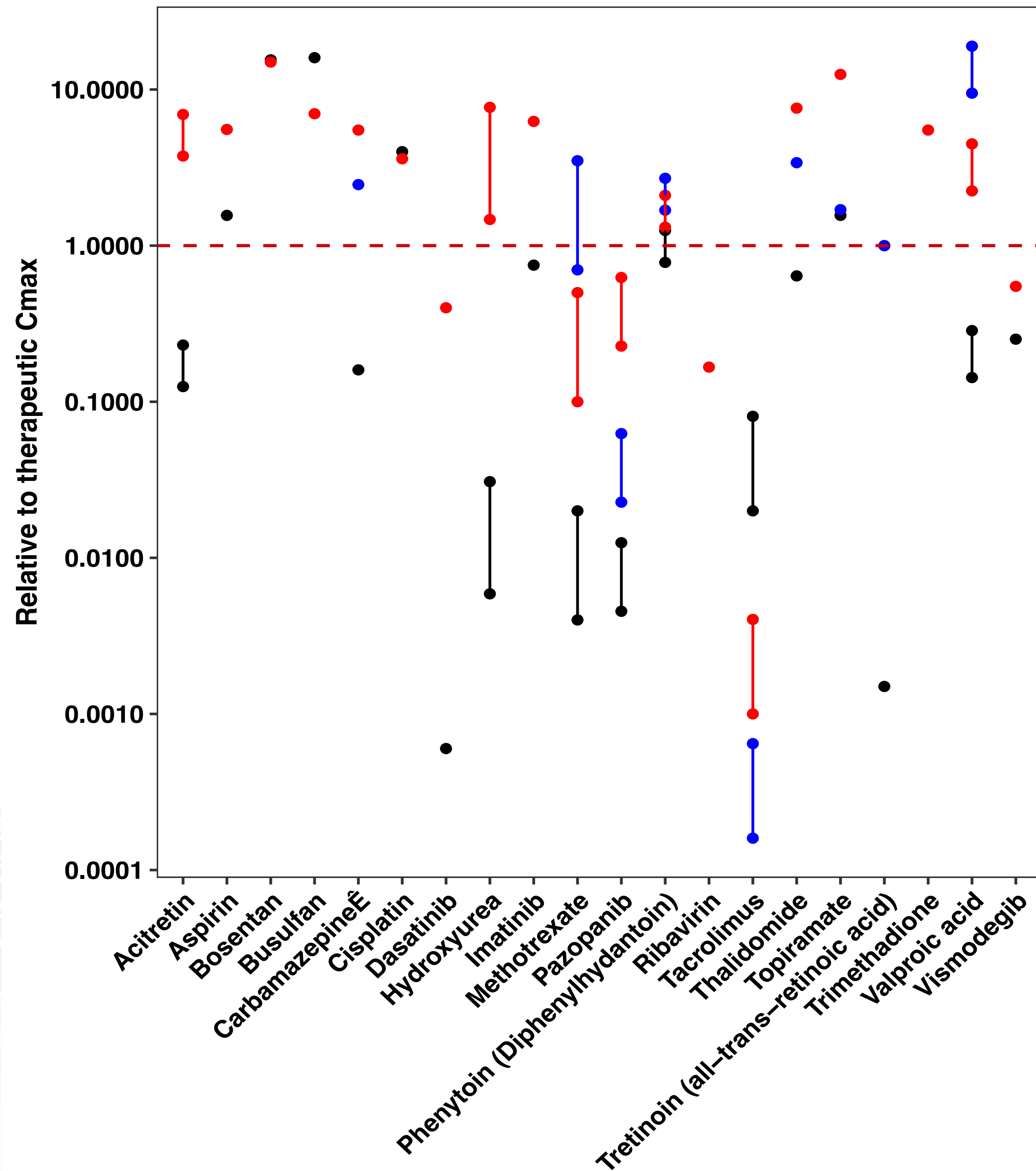
Unexposed

Exposed

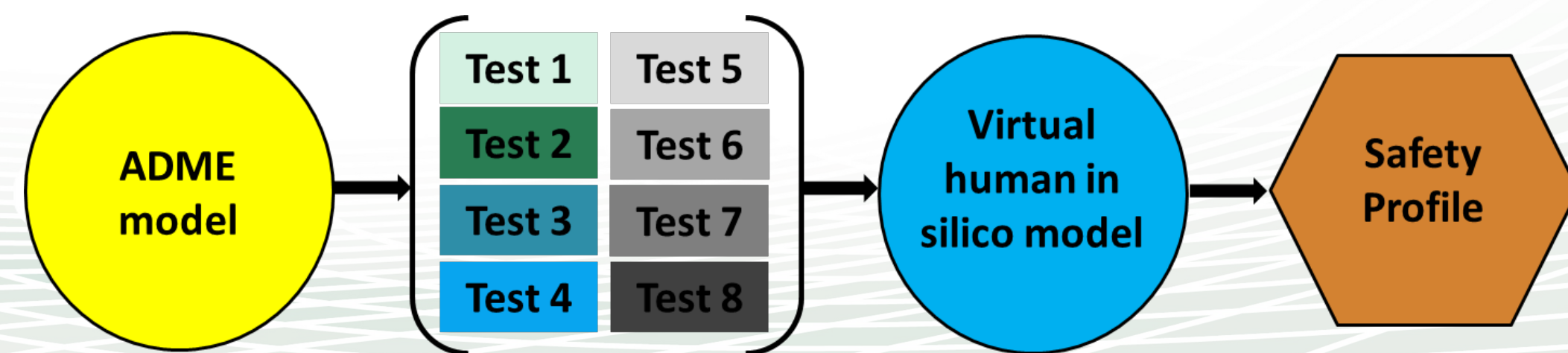


Unexposed

Exposed



- Identification of teratogenic compounds compared to their therapeutic plasma concentrations
- Use in vitro to in vivo extrapolation (IVIVE) → Predict equivalent administration dose



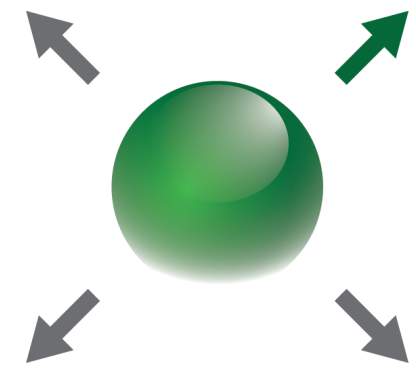
- Human stem cell-based test system
- Combines functional/morphological profiling and expression pattern of selected biomarker genes
- Biomarker based approach – a way to understand biological responses
 - Insight into the molecular mode of action and key events
 - Time-window sensitive gene-biomarkers

Predictability of ReproTracker assay

- Sensitive enough to predict compounds' adverse effects on early embryonic development
- Potency ranking

Applicability

- As part of early drug development phase
- Alternative for animal-free teratogenicity testing of chemicals
- Investigate the mode-of action of teratogenic compounds
- Extrapolate animal-derived results to humans



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The value of understanding

Thank you!



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