

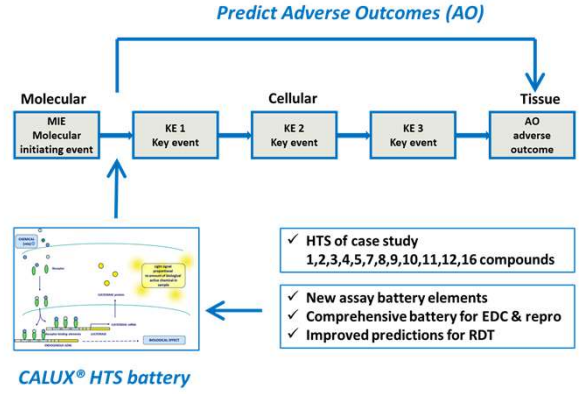
Reporter systems for MIE and KE hazard characterization (WP6)

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Introduction

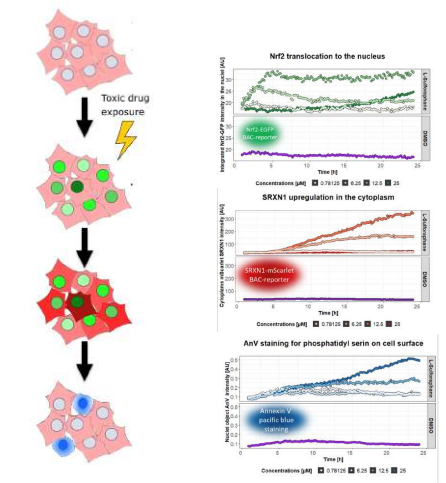
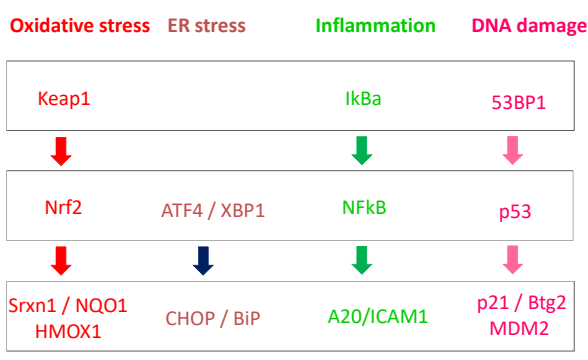
- Mechanism-based chemical safety assessment requires cost-effective and high-throughput test systems
- Mechanisms should represent AOP MIE and KE for fit-for-purpose regulatory translation
- High-throughput test systems should preferably qualify and quantify modulation of MIEs and activation of KEs
- EU-ToxRisk has used the CALUX reporter system to detect MIE and KE activation
- EU-ToxRisk has used the cellular stress response reporters with imaging to detect KE activation
- EU-ToxRisk has established novel iPSC fluorescent protein reporters based on CRISPR genome engineering technology

MIE and KE CALUX reporter system



High content imaging platform for AOP KEs

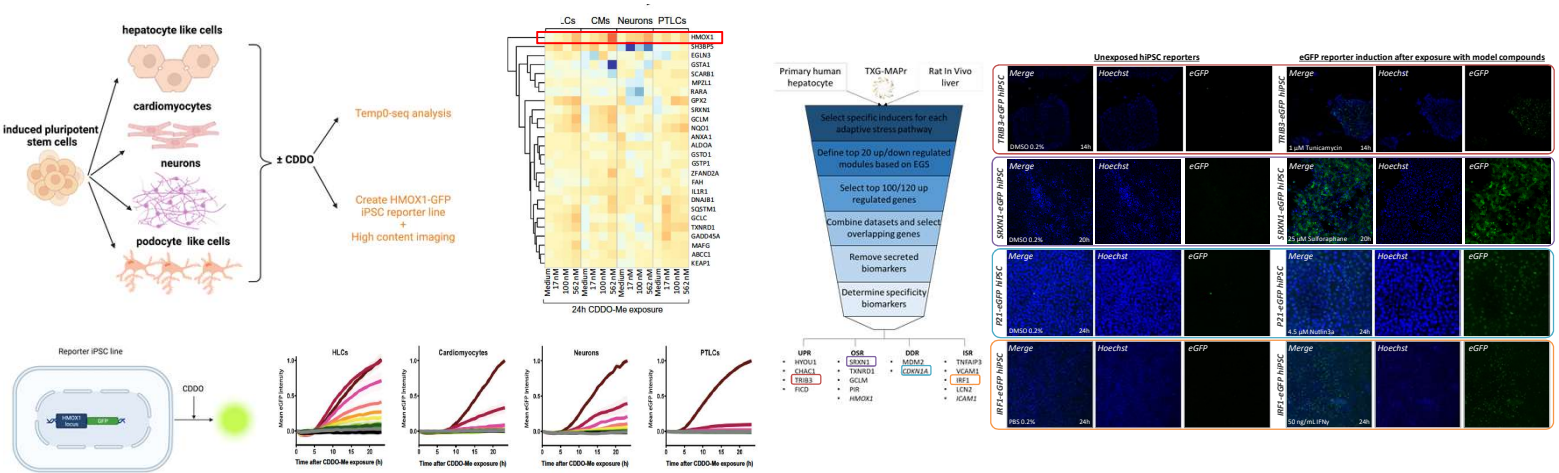
- Reporter panel**
- Oxidative stress reporters
 - Unfolded protein response reporters
 - Inflammatory response reporters
 - DNA damage reporters
 - Mitochondrial morphological reporter
 - ER morphological reporter
 - ... and more



Cellular stress response reporter platform for AOP KE activation quantification

Multiplexed fluorescent cellular stress response reporters

iPSC-based cellular stress response reporters based on CRISPR genome engineering



TXG-MAPr based identification of stress pathway target genes to be fluorescently tagged for HCI analysis based toxicity screens in iPSC progeny

iPSC HMOX1-GFP reporter and differential activation in liver hepatocyte, cardiomyocyte, neuronal and renal proximal tubular cell progeny (Snijders et al. Arch Toxicol. 2021)

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