

1 Introduction

High Content Screening (HCS) combines automated imaging and advanced analysis to provide detailed, single-cell data, accelerating disease research and drug discovery

Revvity offers a comprehensive portfolio of cellular imaging solutions and Preclinical Services featuring OncoSignature™ Cell Panel, Drug Combination, Functional Genomic and Immune Cell screening workflows.

Here we introduce our Preclinical high content imaging services, which integrate our expertise in both screening and imaging to support your drug discovery pipelines.

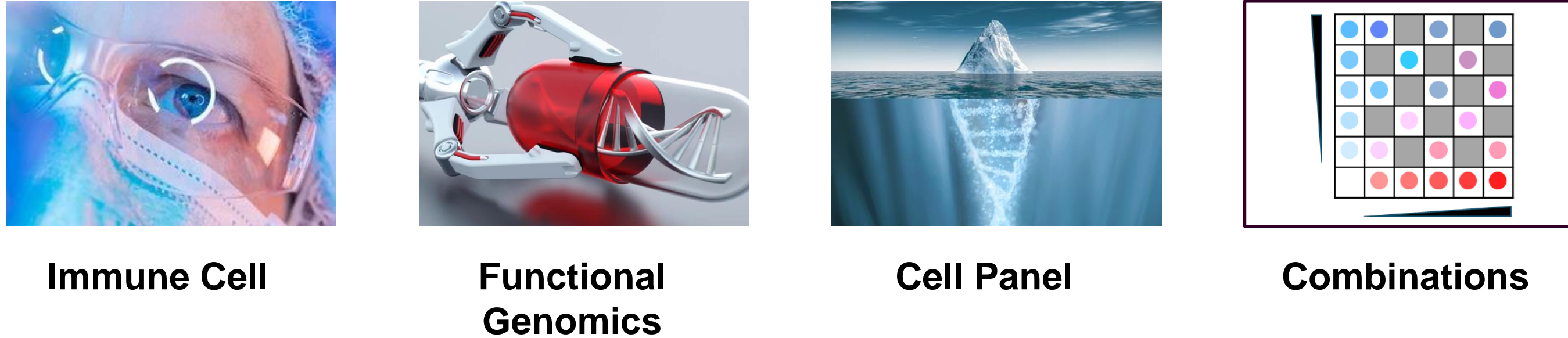


Figure 1. Revvity Preclinical Services Screening Platforms amenable to HCS.

2 HCS Workflow

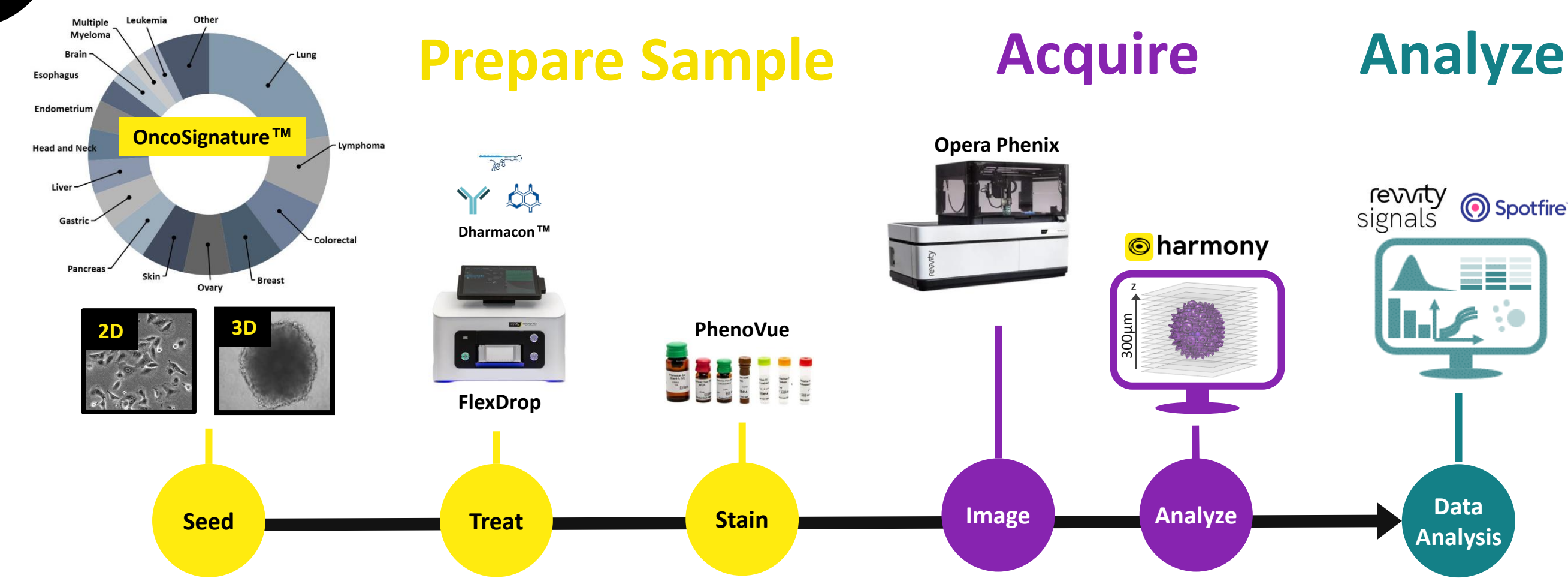


Figure 2. Utilizing Revvity's proven technologies. Opera Phenix™ Plus confocal imager, Harmony™ image analysis software and Signals™ data analysis and visualisation software, PhenoVue™ reagents and Dharmacon™ functional genomic reagents.

3 Universal Assays: Cell health, activity and MOA

Cell Cycle

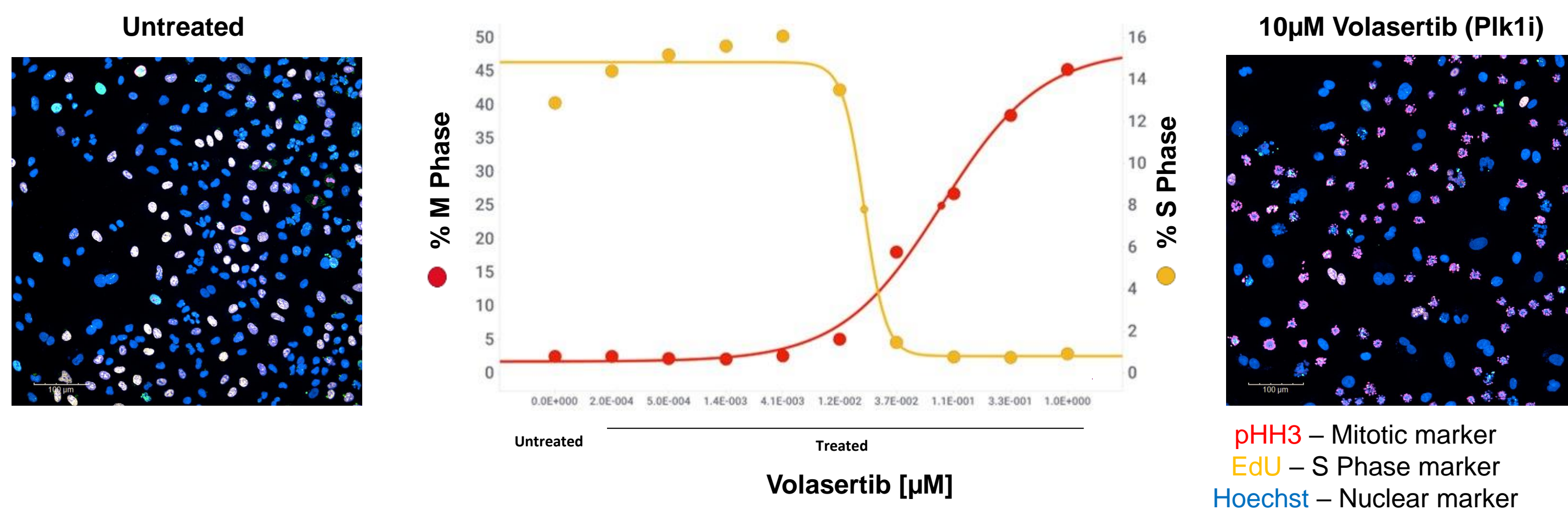


Figure 3. Cell Cycle Assay. A549 cells were treated with a reference inducer of mitotic arrest (Volasertib; Plk1 inhibitor) for 24h with EdU (a marker of cells actively transiting through S-phase) added to the medium in the final 1 hour of treatment. Cells were then fixed and stained for Phospho-Histone H3, a marker of mitotic cells, and imaged on the Opera Phenix Plus.

Autophagy

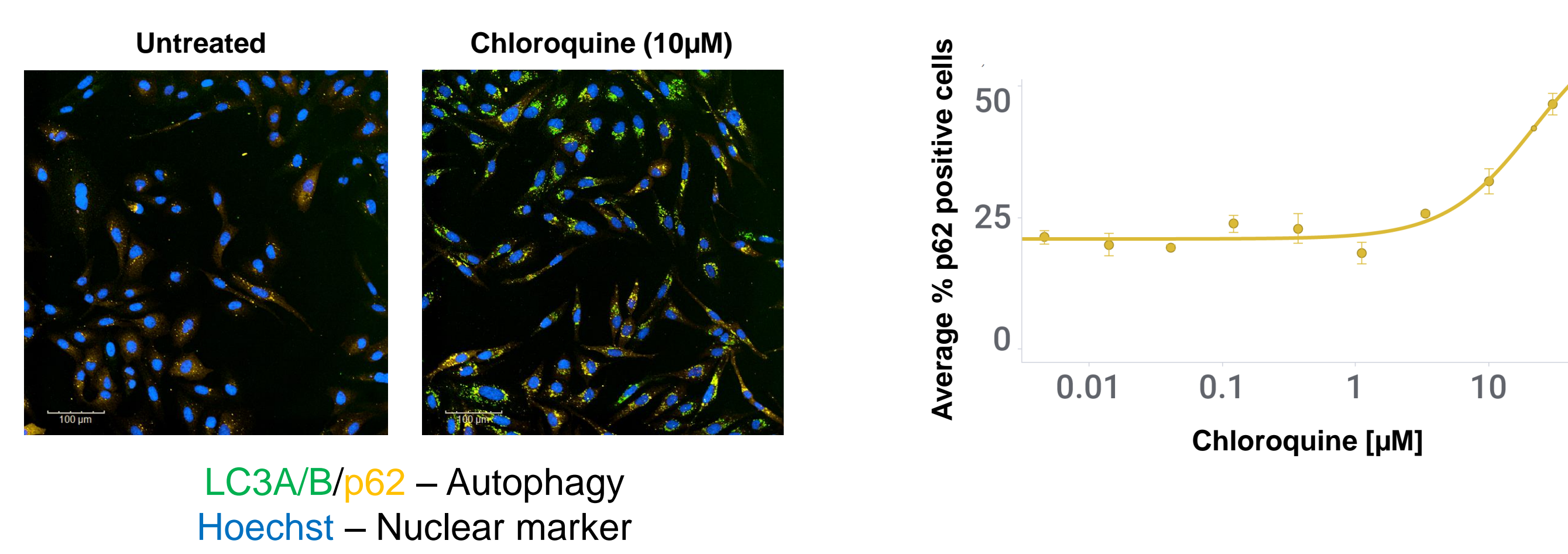


Figure 4. Autophagy Assay. U2OS cells were treated with Chloroquine, a reference inhibitor of autophagic flux, for 24h. The cells were then fixed, stained for LC3A/B and p62 – markers that accumulate when autophagy is inhibited - and imaged using the Opera Phenix Plus.

Apoptosis

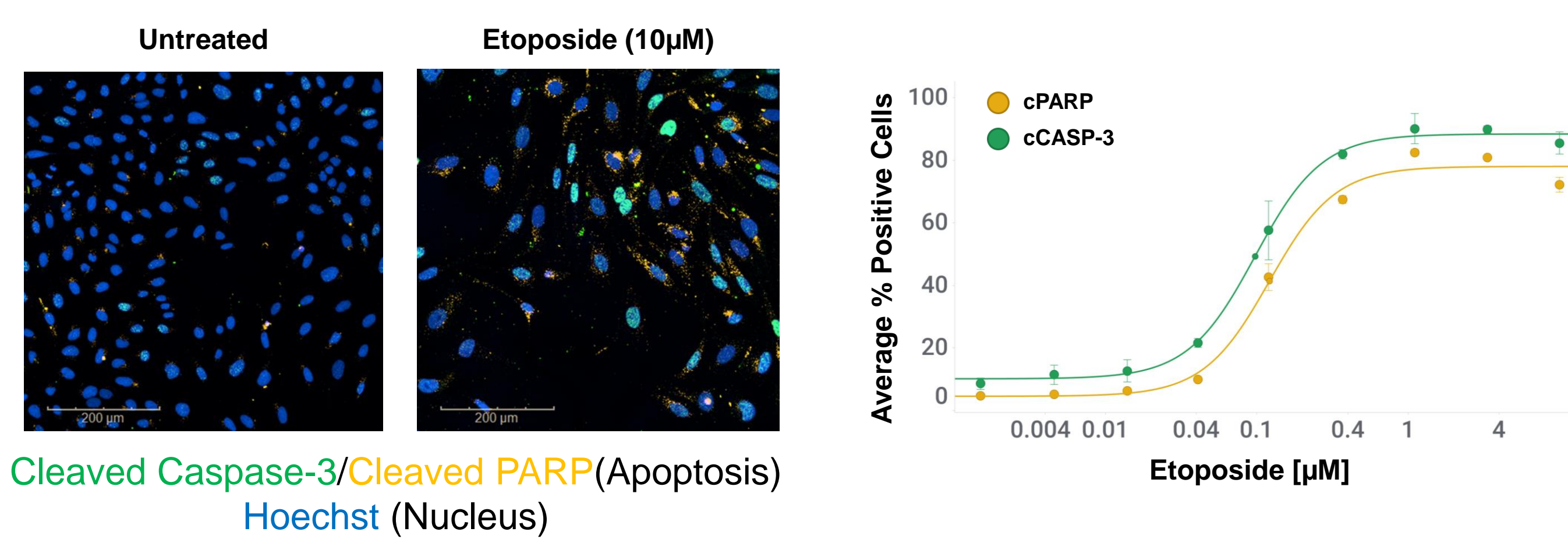


Figure 5. Apoptosis Assay. U2OS cells were treated with Etoposide, a reference topoisomerase inhibitor and apoptosis inducer, for 48h. The cells were then fixed, immuno-stained for cleaved-caspase-3 and cleaved-PARP – markers of apoptosis - and imaged using the Opera Phenix Plus.

DNA Damage

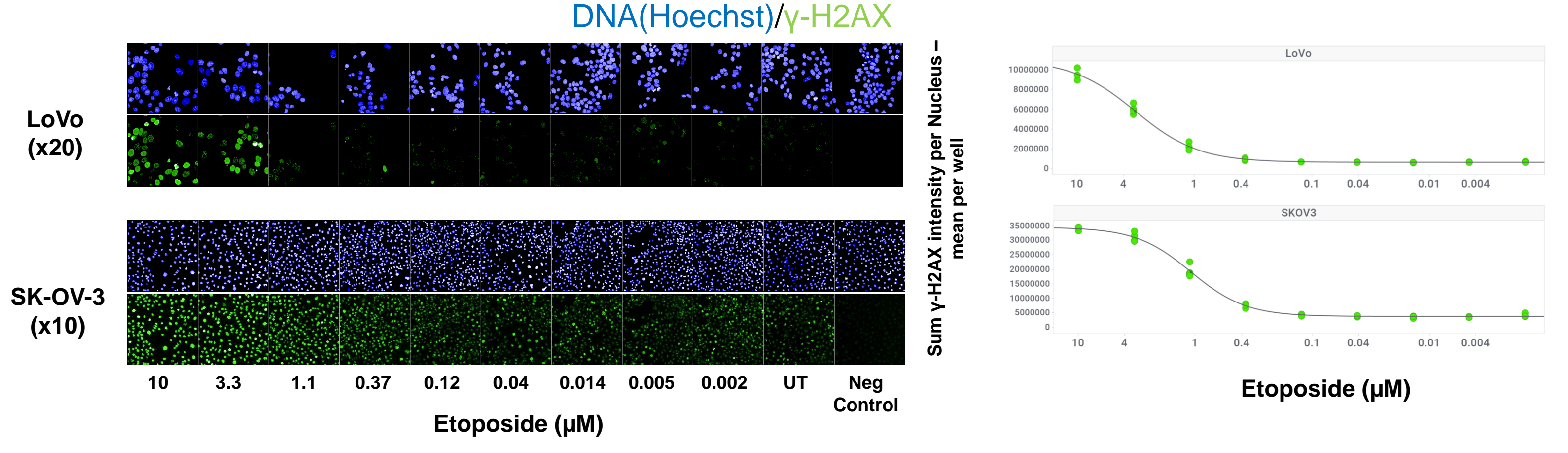


Figure 6. DNA Damage Assay. Cells were treated with a reference inducer of DNA damage, Etoposide (topoisomerase inhibitor), for 24h, fixed and DNA damage assessed by γ -H2AX immunostaining and imaging on the Opera Phenix Plus system.

4 Customized Assays

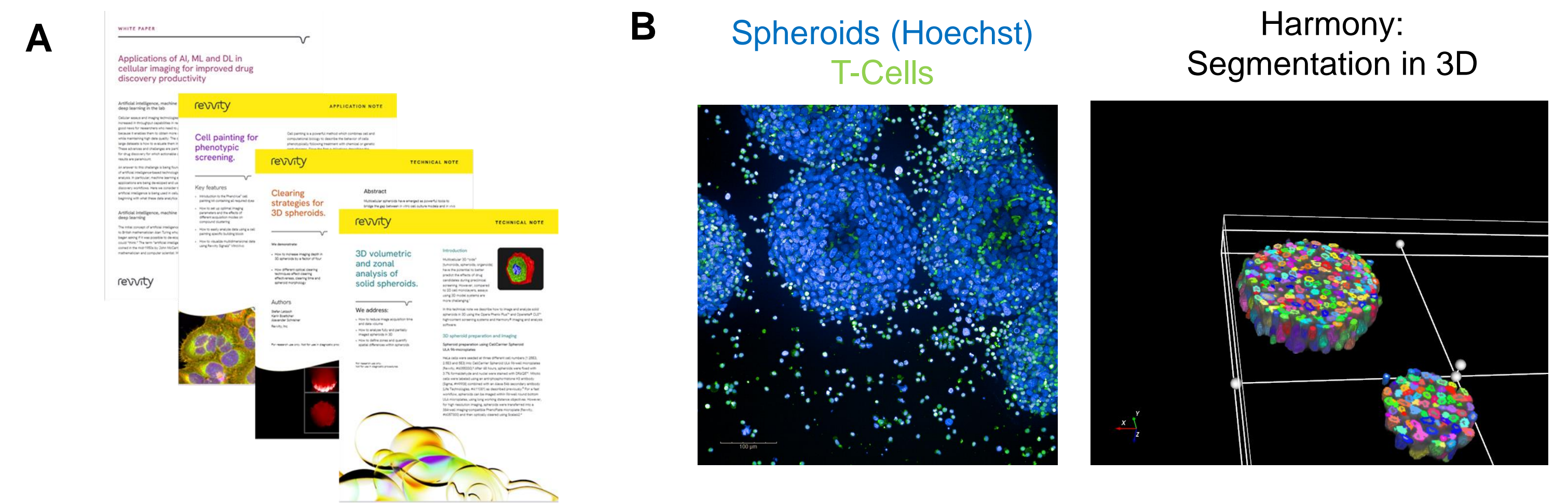


Figure 7. Leverage Revvity's Expertise for Custom Assays. A, Example applications, technical notes, and white papers showcasing our extensive expertise. B, Example images from a custom assay of T-cell infiltration into spheroids. Images were acquired on the Opera Phenix Plus; spheroids and individual cells were segmented in 3D using Harmony software.

5 OncoSignature™ Cell Panel Screening: Stratifying by Sensitivity and Response

Integrating Universal and Custom Assays into Large Cell Panel Screens

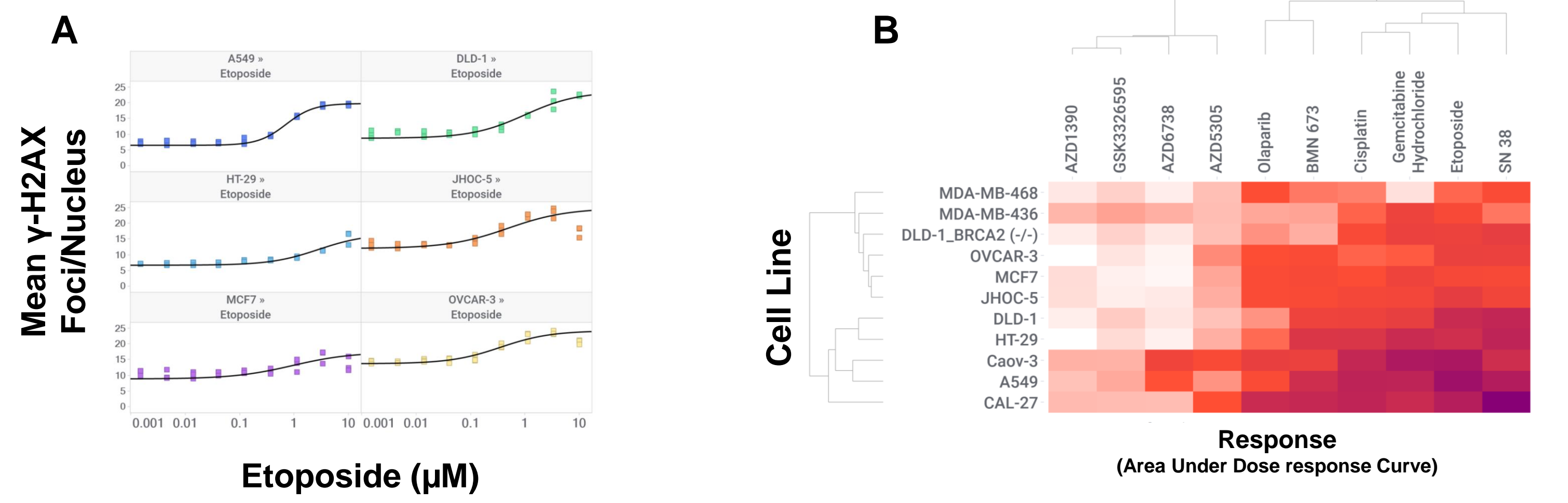


Figure 8. Cell Panel Screening Reveals Unique DNA Damage Responses. Example screen of a focused library of reference DNA damage compounds. Cells were treated for 24h, fixed and DNA damage assessed by γ -H2AX immunostaining and imaging on the Opera Phenix Plus system. A, Example dose response curves illustrating data robustness. B, Hierarchical clustering to reveal patterns in single agent response patterns across the panel (darker red indicates greater response).

6 Cell Painting: Phenotypic Profiling

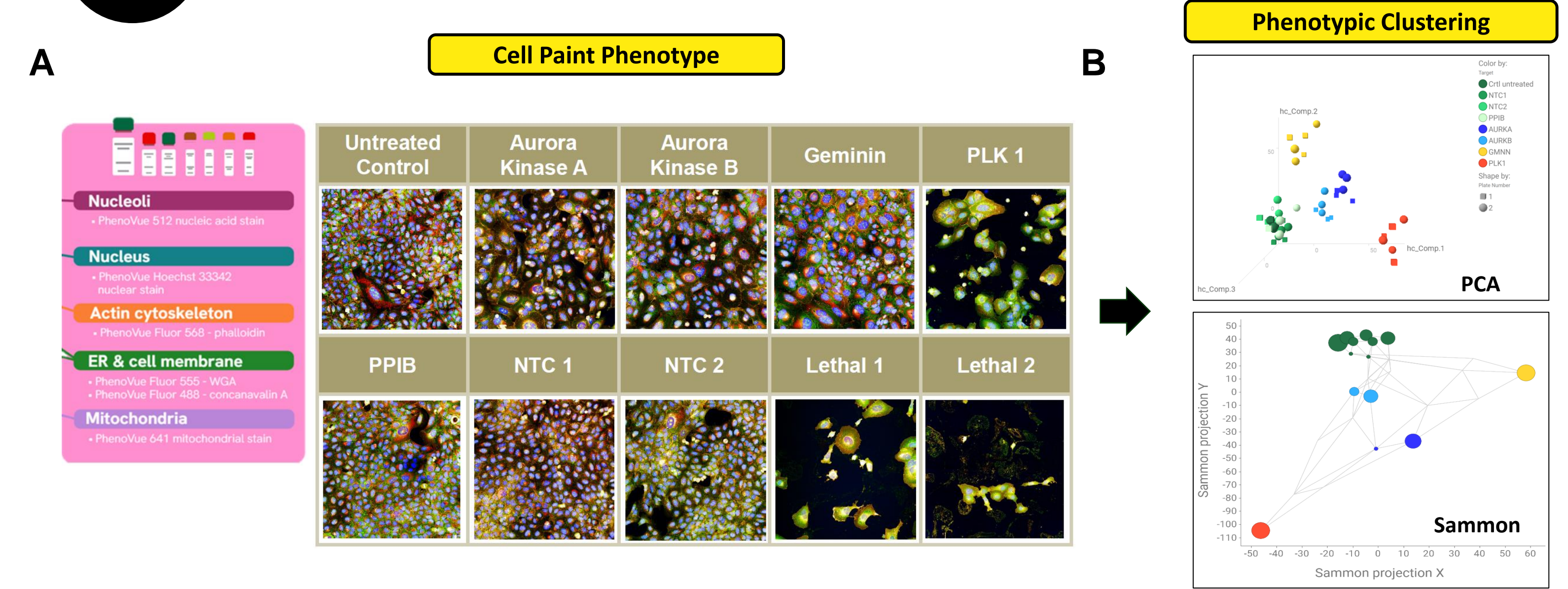


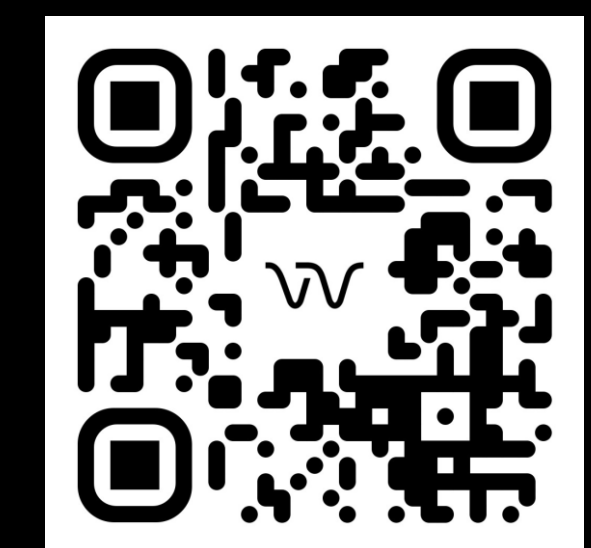
Figure 9. Phenotypic analysis of CRISPR-Cas9 cell cycle knockouts. Cas9-expressing U2OS cells were treated with Dharmacon™ Edit-R™ synthetic sgRNAs, labelled with the PhenoVue™ Cell Painting Jump kit and imaged on the Operetta CLS. A, Cell painting reveals distinct phenotypic changes. B, Phenotypic clustering in Signals clearly separated knockout and control-specific clusters.

7 Summary

Revvity offers preclinical high content imaging services that can be included as part of our OncoSignature™ Cell Panel, Drug Combination, Functional Genomic and Immune Cell screens to support your drug discovery pipelines.

Assay options include:

1. 'Universal' assays
2. Customized assays
3. Cell painting



These assays can be integrated into both small- or large-scale screening campaigns and as part of large cell panel screens.