

WuXi Biology Cancer Cell Panel Service

The right solution for accelerating
cancer drug development

Contact

Declan Ryan (US)
Vice President, Business Development
declan.ryan@wuxiapptec.com

Dave Madge (Europe)
Vice President, Business Development
rosie.hutchings@wuxiapptec.com

Longji Xu (China)
Director, Business Development
xu_longji@wuxiapptec.com

www.wuxiapptec.com



WuXi Research Service Division

The WuXi AppTec Research Service Division (RSD) aims at providing superior support to our partners and promoting efficiency and collaboration between WuXi's business units. RSD combines WuXi's capability and technology platform in chemistry, biology, oncology, and immunology to provide open access and integrated service for drug discovery and research. The services include in the new RSD are the International Discovery Service Unit (IDSU), the Chemistry Service Unit (CSU), the Oncology-Immunology Unit, the Core Analytical Services Unit (CAS), the Biology Unit (which includes HTS, *in vitro* screening, infectious diseases, neurosciences, fibrosis, cardiovascular

and metabolic diseases), Crelux and newly acquired HD Biosciences (HDB). This new integration will provide closer points of contacts for our partners and discovery teams, streamline the exceptional services offered across our platform, and enhance efficiency and productivity to drug discovery. We will focus on boosting our scientific capabilities and leading technology development to maintain WuXi's industry leading position in technology and research service. We aim to provide outstanding service to our existing partners and to our broader discovery community!

Steve Yang, Ph.D.
Chief Business Officer
Chief Strategy Officer
EVP & Head of RSD

International Discovery Service Unit (IDSU)

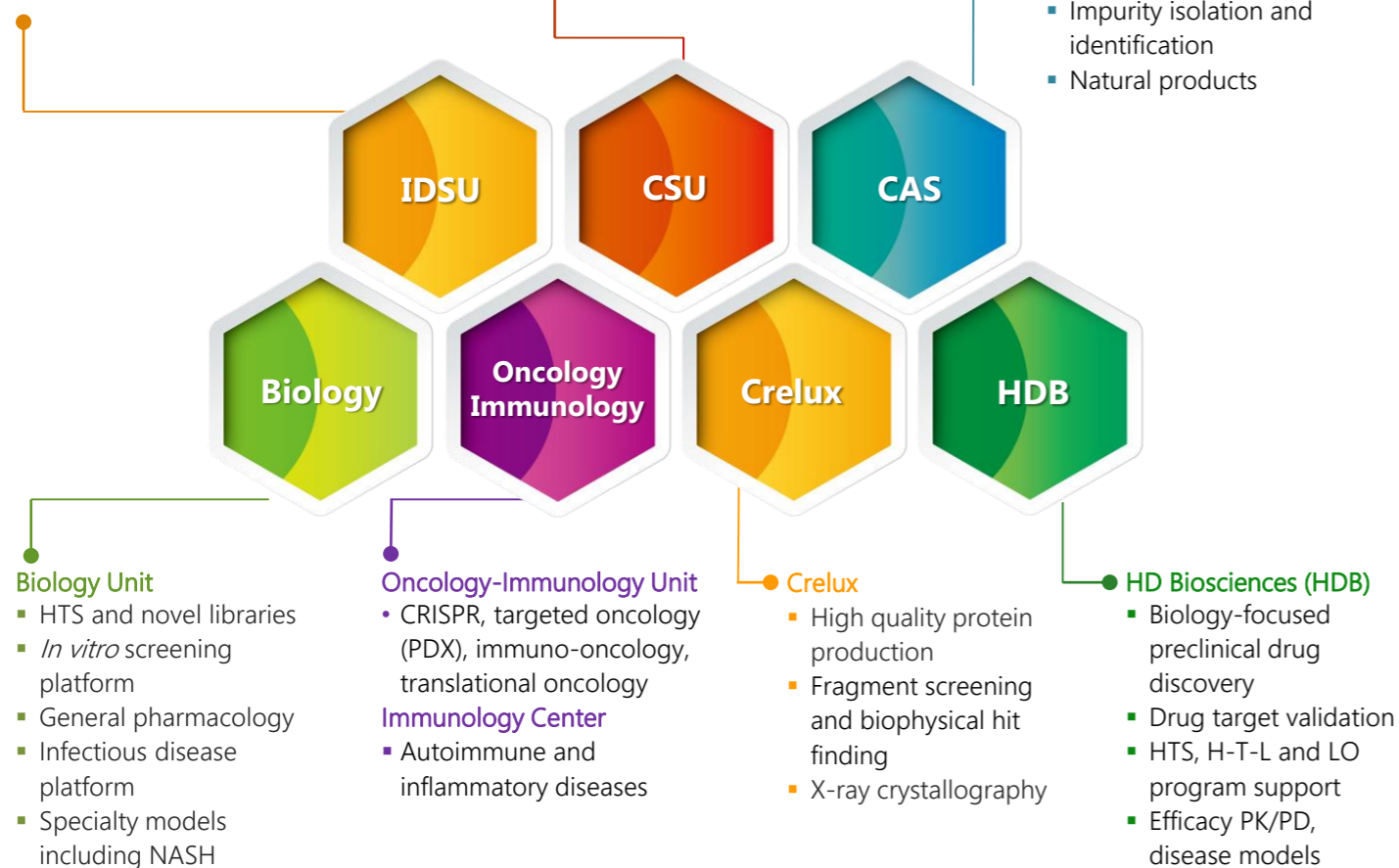
- Med. Chem. design
- Project management
- Deliver preclinical candidates

Chemistry Service Unit (CSU)

- Speed and quality syntheses
- Shorten synthesis cycle time

Core Analytical Services Unit (CAS)

- Analytical testing and release
- High throughput purification
- SFC large scale chiral separation
- Impurity isolation and identification
- Natural products



WuXi Biology Cancer Cell Panel

The Biology Unit offers a diverse *in vitro* screening panel of over 378 authenticated, well-validated human cancer cell lines across 21 organs/tissues. The cancer cell panel provides powerful tools for cancer research and drug discovery. Key features of WuXi cancer cell panel include:

- High quality cell banking system: mycoplasma-proof and STR verified
- 353 validated and well-characterized human cancer cell lines for oncology drug discovery programs
- Compound screening for potency (% inhibition & IC50) and synergy (combination study)
- Professional design with stringent quality control of study results
- Fast study turnaround
- A comprehensive range of functional assays

Large Scale Human Cancer Cell Lines for Cell Panel Services

A wide range of 378 human cancer cell lines is available for oncology drug discovery programs. The cell banking system is a two-tiered banking system with mycoplasma testing and STR validation. Established cell growth data and standard of care profiling enhance the quality of study. The table shows the distribution of 378 human cancer cell lines, sorted by the origins of derived organs/tissues.

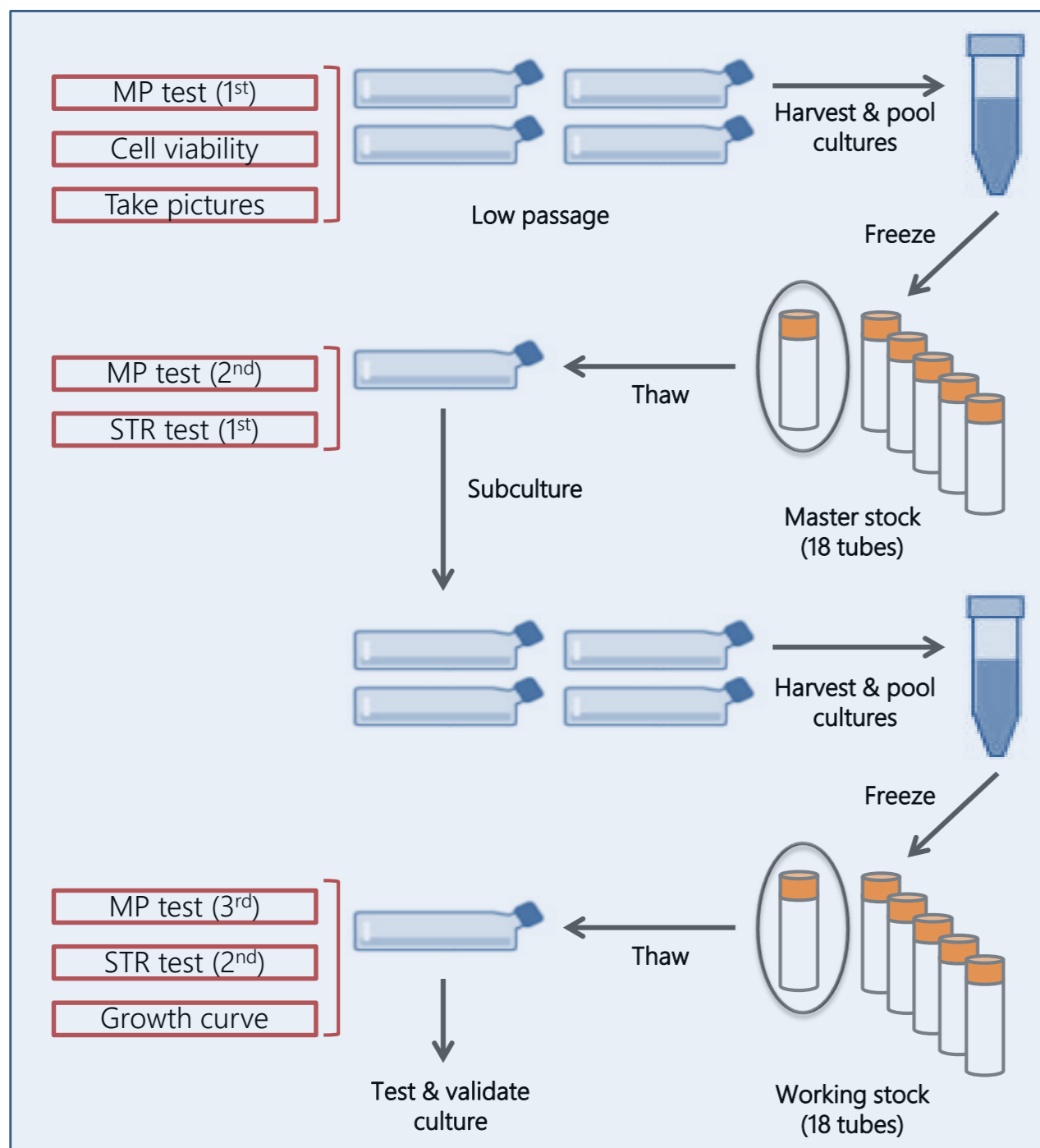
Cancer Cell Line	Number of Cell Lines	% of Total
Lung	120	31.7
Breast	66	17.5
Hematopoietic/lymphoid tissue	44	11.6
Large intestine	35	9.3
Liver	15	4.0
Skin	11	2.9
Connective/soft tissue	11	2.9
Stomach	9	2.4
Pancreas	9	2.4
Brain	9	2.4
Kidney	8	2.1
Bone	7	1.8
Upper aerodigestive tract	7	1.8
Bladder	6	1.6
Ovary	6	1.6
Prostate	5	1.3
Thyroid	3	0.8
Uterus	3	0.8
Cervix	2	0.5
Small intestine	1	0.3
Adrenal gland	1	0.3

378 Human Cancer Cell Line Resources

353	of 378 cell lines are banked with quality control: mycoplasma-proof and STR verified
231	of 345 banked cell lines have 7-day growth curve data generated with IncuCyte® or CellTiter-Glo® assay
289	of 345 banked cell lines have been successfully applied for compound profiling in the past

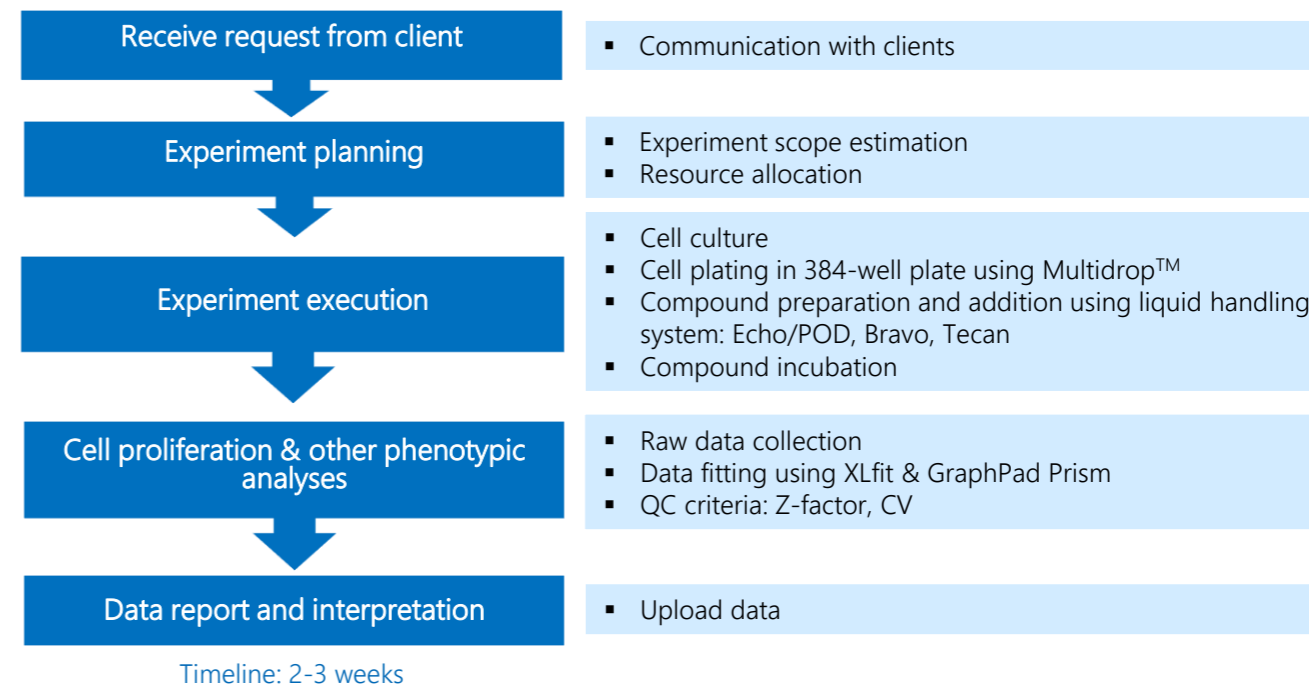
High Quality Cell Bank: Two-tiered Banking System

- Bank at early passage: P2-P10
- Mycoplasma negative: MycoAlert™ Mycoplasma Detection Kit (Lonza-LT07-318)
- Cell line identity validation: Short Tandem Repeat (STR) profiling
- Viability assay: CellTiter-Glo® Luminescent Cell Viability Assay (Promega)
- Important cell line characteristics: optional
- Well documented with good tracking record



Professional Study Design to Ensure High Quality Data for the Report Generation

Cell Panel Screening Flowchart: rapid compound screening, data analysis, and report generation with average turnaround time of 2-3 weeks for cytotoxicity screening.



Experimental Design

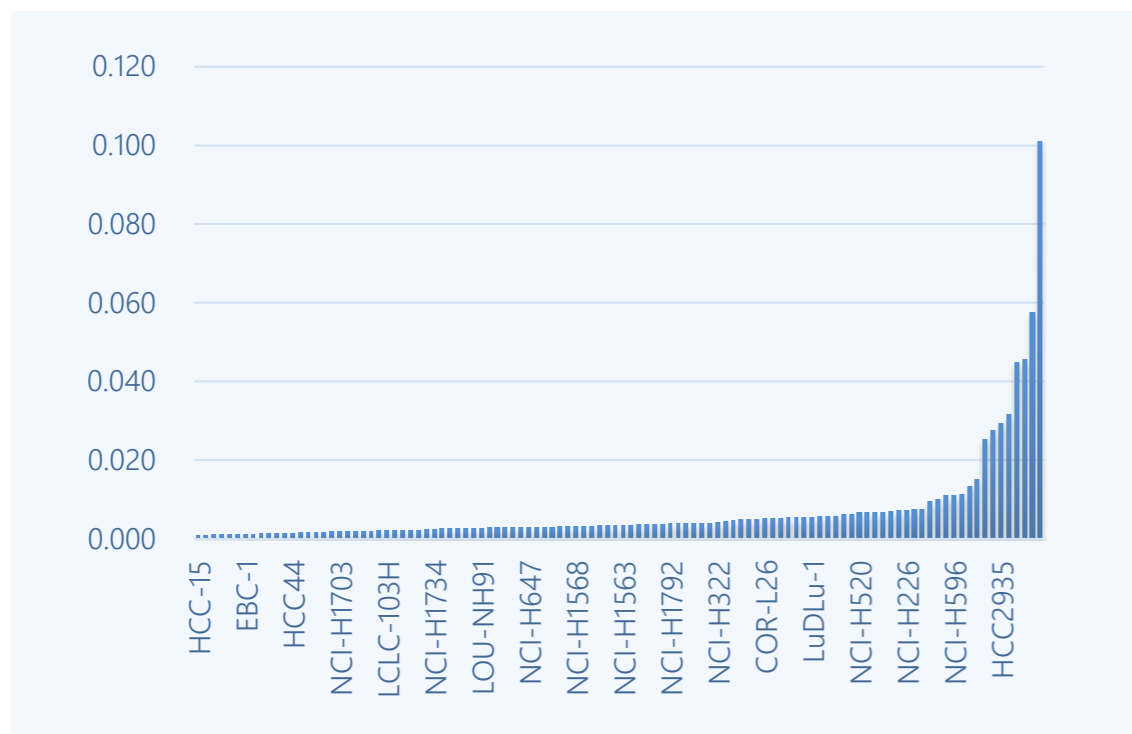
- Design with empty wells
- Set up multiple controls: reference compound, medium control, no inhibition (ZPE), 100% inhibition (HPE)
- Available screen formats: 384-well plate, 96-well plate, customized format
- Data QC: cross-day and cross-plate tests of EC/IC50; Z factor & CV

384-well Plate Map: 14 Compounds/Plate, 9 Test Concentrations/Compound, Duplicate/Concentration

Row	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24		
A	Empty	Media control	Compound 1 (starting conc. 1:3 dilution, 9 doses)									HPE	Compound 8													
B			Compound 2										HPE	Compound 9												
C			Compound 3											HPE	Compound 10											
D			Compound 4												HPE	Compound 11										
E			Compound 5													HPE	Compound 12									
F			Compound 6														HPE	Compound 13								
G			Compound 7															HPE	Compound 14							
H	Empty	Media control	Compound 1									ZPE	Compound 8													
I			Compound 2										ZPE	Compound 9												
J			Compound 3											ZPE	Compound 10											
K			Compound 4												ZPE	Compound 11										
L			Compound 5													ZPE	Compound 12									
M			Compound 6														ZPE	Compound 13								
N			Compound 7															ZPE	Compound 14							
O	Empty	Media control	Compound 1									HPE	Compound 8													
P			Compound 2										HPE	Compound 9												

The cytotoxicity assay using Promega CellTiter-Glo® Luminescent Cell Viability Assay kit is applied to determine the potency of compounds in cancer cell lines with IC₅₀ calculation. As shown in the plate map of 384-well format, 9 doses of testing compounds are applied with 1:3 dilution (n=2 per data point). DMSO and Paclitaxel are included as negative and positive controls. The dose range of compounds, the duration of compound treatment, and reference compounds can be defined by clients. Customized template designs are available.

SoC Profiling of Cancer Cells

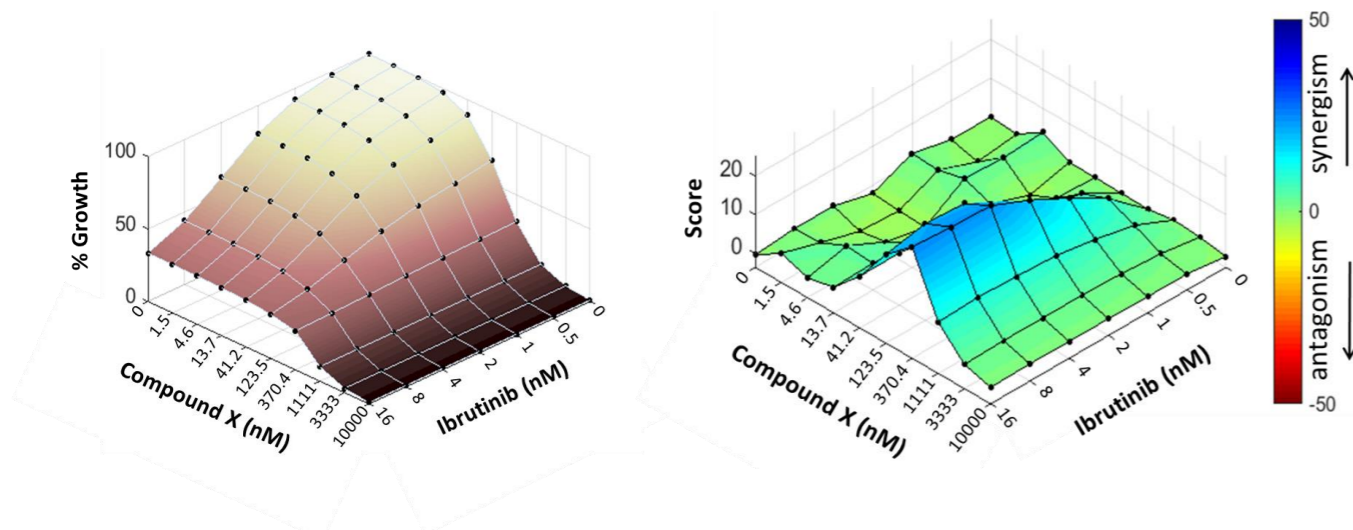
IC₅₀ of Compound P on 108 NSCLC Cell Lines

IC₅₀ of SoC Compound P on 108 NSCLC cancer cell lines with 7-day incubation. The IC₅₀ values were determined using Promega CellTiter-Glo® Luminescent Cell Viability Assay.

Custom Drug Combination Study

- Study combination drug responses to identify synergistic and antagonistic interactions with Combination Index (CI) calculation
- Flexibility in assay formats, dose range, and treatment times

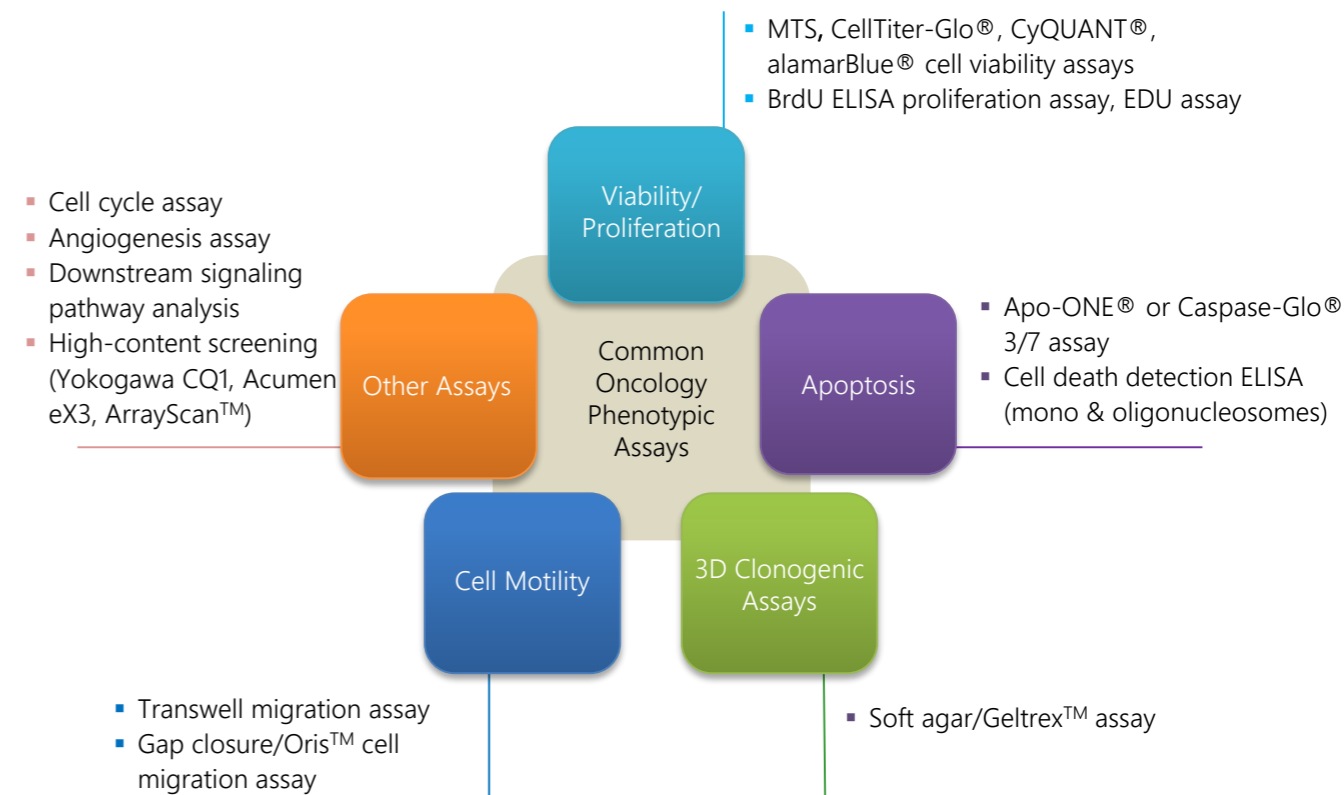
Synergistic effects of Compound X with Ibrutinib in TMD-8 Cells



Pairing of two compounds at various doses showed synergistic toxicity of Compound X and ibrutinib combination in TMD-8 cells.

A Comprehensive Range of *In Vitro* Functional Assays

WuXi provides diverse cell-based functional assays for oncology drug discovery program, including cell viability, proliferation, apoptosis, 3D clonogenic assay, cell migration/invasion, and cell cycle assays.



Facilities and Instruments

Various automated systems operated by experienced scientists to ensure both efficiency and accuracy of study

Facilities

- BSL1 and BSL2 cell culture laboratories

Partial list of available instruments

- Liquid handling systems
 - JANUS™ (2)
 - Bravo (2)
 - Echo® 555 (3) / POD
 - Tecan HP D300
- Reagent addition
 - Multidrop™ (several)
- Plate washers
 - ELx405™, EL406™
- Plate reader
 - EnVision® (3)
- Cell counters
 - Cedex and Countess®
 - Z2 and Vi-CELL®
 - IncuCyte®
- High-content screening system
 - Yokogawa CQ1
 - Acumen eX3
 - ArrayScan™

Confocal Quantitative Image Cytometer
YokogawaHP D300 Digital Dispenser
TecanEcho® 555 Liquid Handler
Labcyte, Inc.Bravo Automated Liquid Handling Platform
Agilent TechnologiesIncuCyte® ZOOM Live-Cell Imaging System
Essen BioScience