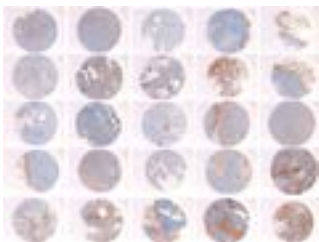


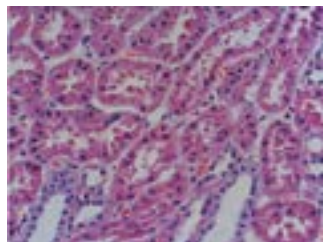
Translational Oncology

- Biomarker discovery
- Mouse clinical trial
- 61 PDX-derived primary cancer cell lines
- Drug-resistant xenograft models
- Combination therapy platform including radiation
- World leading genome sequencing and bioinformatics capability

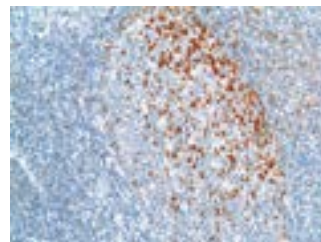
Tissue based biomarker capability



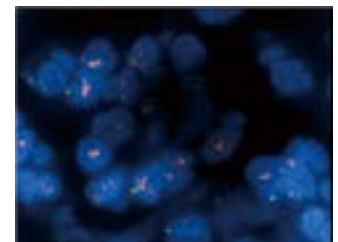
Tissue microarray enables high-throughput biomarker analysis



H&E staining



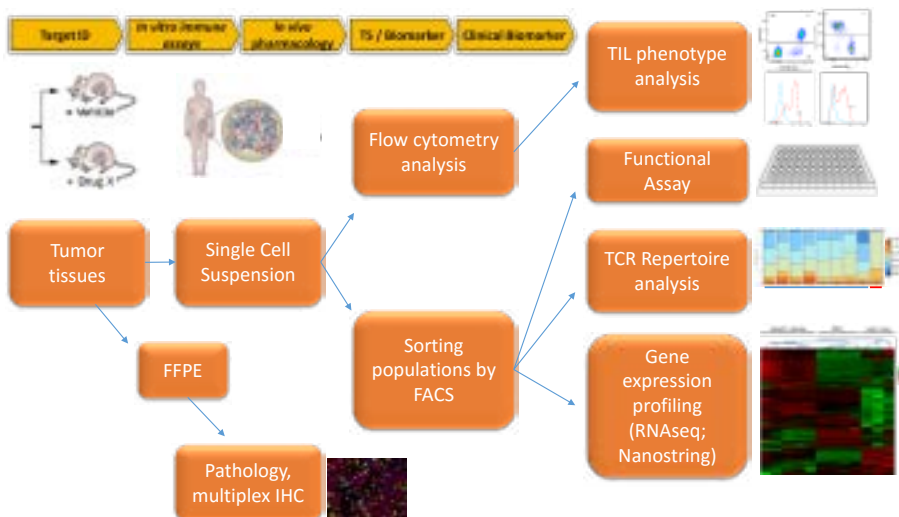
PD-1 expression detected by IHC



HER-2/CEP-17 detected by FISH

Discovery & clinical biomarker services

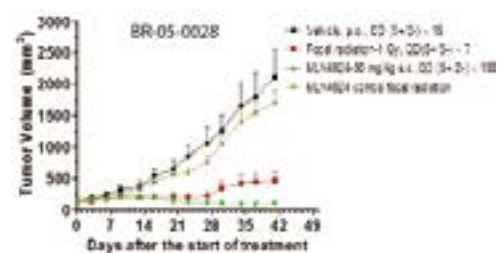
- Pathology capabilities, Flow-cytometry, Next generation sequencing, LIMS system for project & sample management, GCP compliance and CAP accreditation.



<http://onco.wuxiapptec.com/login>

Combination therapy platform including radiation

- Breast cancer model: BR-05-0028
- MLN4924, a NAE inhibitor, showed synergetic effect with focal radiation.



PDX derived human cancer cell lines (PCC)

- 61 human cancer cell lines generated from PDX models
 - » With matched PDX models
 - » Cancer stem cell (CSC) features
 - » 58/61 form xenografts in mice which recapitulate pathology of the original patient tumor
 - » Genomic profiling data available
- List of human cancer lines from PDX

Cancer type	Primary cells	Tumorigenesis in mice
Lung	14	13
Gastric	11	11
Liver	2	2
Colorectal	11	10
Esophagus	5	5
Pancreatic	17	16
Melanoma	1	1
Total	61	58

Drug-resistant xenograft models

- Resistance was induced by repeated treatment
- Genomic profiling data available for erlotinib and crizotinib resistant NSCLC models

Xenograft models resistant to Standard-of-Care

Acquired

de novo

Erlotinib/Osimertinib Resistant NSCLC

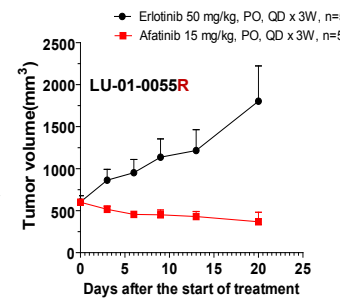
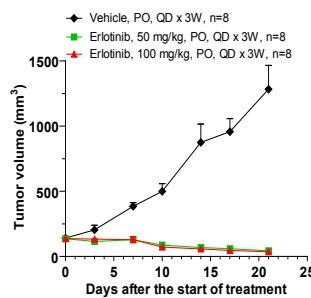
Crizotinib Resistant NSCLC (ALK fusion)

Tamoxifen-resistant MCF-7 model

PARPi Resistant Cell-lines

Chemotherapy (5-FU, Cisplatin, Oxaliplatin, Docetaxel, Paclitaxel, Irinotecan) Resistant PDX models

Erlotinib resistant Lung cancer PDX harboring EGFR^{L858R}



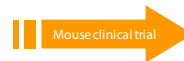
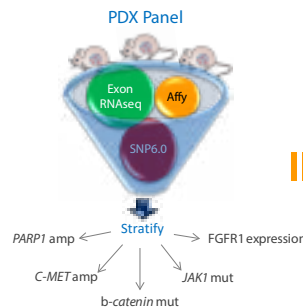
- LU-01-0055 PDX harboring EGFR^{L858R}
- Sensitive to erlotinib

- Erlotinib resistant LU-01-0055R
- Afatinib overcame the erlotinib resistance

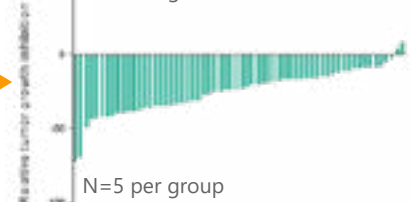
Mouse trial in PDX models

WuXi Oncology & Immunology has conducted multiple mouse trials in the following two categories, which will serve as proof-of-concept for preclinical pharmacology studies.

Types of mouse trial	Typical study size
All comers in certain cancer types	20-60 PDX models, 2-4 groups, n=3-10
Selected models based on genomic profiling	20-60 PDX models, 2-8 groups, n=5-10



Case study example: Squamous lung PDXs (62) treated with an agent



Mouse genetically engineered cell-line models

Target	Model ID	Target	Model ID
EGFR	Ba/F3 EGFR exon 19 del/T790M	TRK	Ba/F3 ETV6-NTRK3 fusion plus G623R mutation
	Ba/F3 EGFR exon 19 del/T790M/C797S		Ba/F3 ETV6-NTRK3 fusion plus G696A mutation
	Ba/F3 EGFR exon 19 del/C797S		Ba/F3 ETV6-NTRK3 fusion only
	Ba/F3 EGFR L858R/T790M/C797S		Ba/F3 TPM3-NTRK1 fusion plus G595R mutation
	PC9 EGFR exon 19 del/T790M/C797S		Ba/F3 TPM3-NTRK1 fusion plus G667C mutation
	H1975 EGFR exon 19 del/T790M/C797S		Ba/F3 TPM3-NTRK1 fusion
	H1975 EGFR L858R/T790M/C797S		Ba/F3 LMNA-NTRK1 fusion plus G595R mutation
			Ba/F3 LMNA-NTRK1 fusion plus G667C mutation
			Ba/F3 LMNA-NTRK1 fusion
ALK	Ba/F3 EML4-ALK-WT	RET	Ba/F3 CCDC6-RET
	Ba/F3 EML4-ALK-L1196M		Ba/F3 CCDC6-RET+V804M
	Ba/F3 EML4-ALK-C1156Y		Ba/F3 CCDC6-RET+V804L
	Ba/F3 EML4-ALK-G1202R/L1196M		
	Ba/F3 EML4-ALK-G1202R		

