Tumor Cell Panels: New Tools in Genomic Era

*Chris White, Lysa-Anne Volpe, Luping Chen, Anupreet Bal, Michael Jackson, John Foulke, Fang Tian**

American Type Culture Collection (ATCC), Manassas, VA 20110

ATCC™ THE ESSENTIALS OF LIFE SCIENCE RESEARCH GLOBALLY DELIVERED™

Abstract

Increased understanding of cancer genome is affecting every corner of cancer research. Although human tumor cell lines have been used as essential tools for decades, there are only a few cell line panels have been developed for the drug screening. There is a gap between the new knowledge of cancer genome and the cell line based platforms for both basic and translational research.

Here, we show that new generation tumor cell panels are filling the gap. The panels were generated by selecting authenticated cell lines derived from variant cancer types, and annotated with genetic alteration information generated by large scale sequencing projects such as the Catalog of Somatic Mutations in Cancer (COSMIC) and the Cancer Cell Line Encyclopedia (CCLE). To capture the genetic diversity of cancer, each panel includes cell lines with varying gene mutation complexity. To further facilitate targeted drug discovery, the molecular signature tumor cell line panels focus on individual driver genes, critical protein kinases, transcription factors and cell signaling pathways. Those panels have been analyzed to verify gene mutation, gene expression, protein expression and bio-functions.

Introduction

ATCC tumor cell panels program initiative

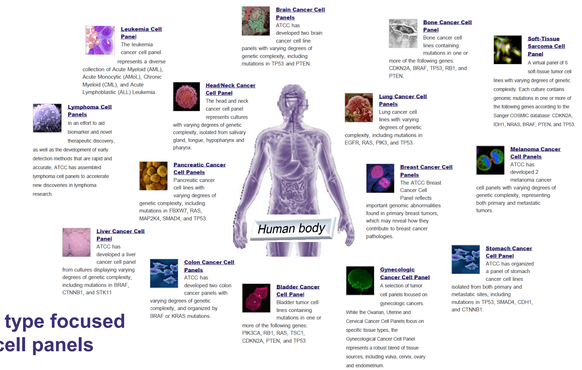
ATCC cell lines

Cancer genome

- Systematic analysis
- Gene sequencing validation
- Functional characterization
- Integrative design

Next generation tumor cell panels

Cancer type focused tumor cell panels

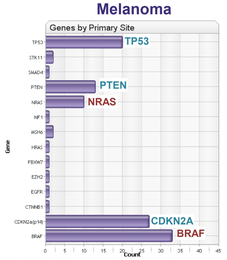


The mutation data was obtained from the Sanger Institute Catalogue Of Somatic Mutations In Cancer database

Results

Bioinformatics analysis and clustering of ATCC cell lines

Diseased focused clustering



Mutation frequencies in melanoma cell lines

Gene focused clustering

PIK3CA mutation	frequency
p.E545K	28%
p.E545D	3%
p.H1047R	28%
p.H1047L	3%
p.E542K	5%
p.R88Q	5%
p.K111E	3%
p.K111N	3%
p.K111R	3%
p.P539R	3%
p.Q546R	3%
p.D549N	3%
p.E453K	3%
p.G118D	3%
p.P124L	3%
p.P449T	3%
p.G106_R108del	3%

Tissue source

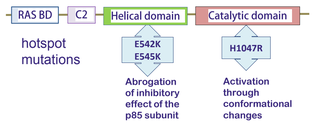
Breast
Caecum
Cervix
Colon
Lung
Lymphoid
Ovary
Pharynx
Prostate
Stomach
Urinary bladder
Uterus

Cell lines: 36

Metastatic melanoma cancer cell panel

Item No.	Name	Mutant	Zygosity	DNA Sequence	AA Sequence
HTB-69	SK-MEL-3	BRAF	heterozygous	c.1799T>A	p.V600E
		TP53	homozygous	c.799C>T	p.R267W
CRL-7724	SH-4	BRAF	homozygous	c.1799T>A	p.V600E
		CDKN2A	homozygous	c.1_471del471	p.0?
HTB-71	SK-MEL-24	BRAF	heterozygous	c.1799T>A	p.V600E
		CDKN2A	homozygous	c.1_471del471	p.0?
		PTEN	homozygous	c.80_164del85	p.?
HTB-66	RPMI-7951	BRAF	homozygous	c.1799T>A	p.V600E
		CDKN2A	homozygous	c.47T>G	p.L16R
		PTEN	homozygous	c.1_79del79	p.?
		TP53	homozygous	c.497C>A	p.S166*

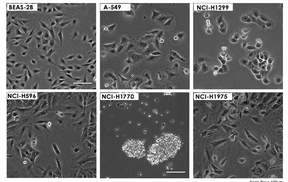
PIK3CA somatic mutation

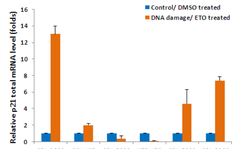


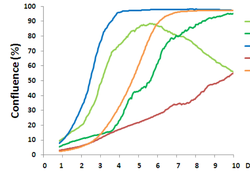
Molecular signature tumor cell panels

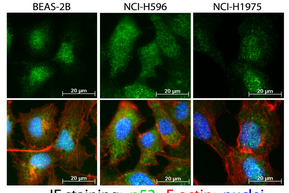
Non-small cell lung cancer p53 hotspot mutation tumor cell lines

ATCC® No.	Name	Tissue	Histology	Tumor Source	TP53 status	Zygosity	CDS mutation	AA mutation
CRL-9609™	BEAS-2B	lung	normal tissue,SV-40 immortalized	NA	WT	-	-	-
CCL-185™	A549	lung	non-small cell lung carcinoma	primary	WT	-	-	-
CRL-5803™	NCI-H1299	lung	non-small cell lung carcinoma	metastasis (lymph node)	NULL	homozygous	c.(del)	-
HTB-178™	NCI-H596	lung	adenosquamous carcinoma	primary	MUT	homozygous	c.733G>T	p.G245C
CRL-5893™	NCI-H1770	lung	non-small cell lung carcinoma	metastasis (lymph node)	MUT	homozygous	c.741 742CC>TT	p.R248W
CRL-5908™	NCI-H1975	lung	adenocarcinoma	primary	MUT	homozygous	c.818G>A	p.R273H

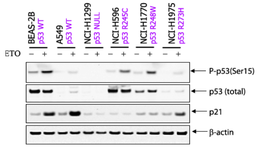








IF staining: p53; F-actin; nuclei



Seven p53 hotspot mutation panels include cell lines

- p53 wild type — Breast cancer cells, Colon cancer cells
- p53 null — NSCLC cells
- p53 hotspot codon 175 mutation — SCLC cells
- p53 hotspot codon 248 mutation — Pancreatic cancer cells
- p53 hotspot codon 273 mutation — Leukemia cells
- p53 hotspot codon 282 mutation — Lymphoma cells
- Other p53 hotspot: codon 220, 249

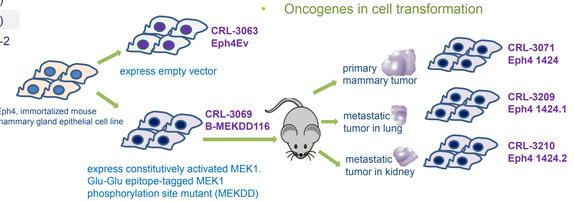
Cell death pathway BCL-2 family cell panels

Item No.	Cell line name	Expressing /Signature
CRL-2898	Neo Jurkat	empty vector
CRL-2899	BCL2 Jurkat	Bcl-2
CRL-2900	BCL2 (S70A) Jurkat	phosphorylation deficient mutants of Bcl-2 (S70A)
CRL-2901	BCL2 (S87A) Jurkat	phosphorylation deficient mutants of Bcl-2 (S78A)
CRL-2902	BCL2 (AAA) Jurkat	multi-site T69A/S70A/S87A (AAA) mutants of Bcl-2

Item No.	Cell line name	Derived from
CRL-2907	WT SV40 MEF	WT mouse
CRL-2908	Bcl2 KO SV40 MEF	Bcl2 KO mouse
CRL-2909	Bad KO SV40 MEF	Bad KO mouse
CRL-2910	Bax KO SV40 MEF	Bax KO mouse
CRL-2911	Bid KO SV40 MEF	Bid KO mouse
CRL-2912	Bak KO SV40 MEF	Bak KO mouse
CRL-2913	Bax Bak DKO SV40 MEF	Bax and Bak double KO mouse

Breast cancer mouse model cell panel

- MEK mutation
- EGFR pathway
- Oncogenes in cell transformation



Summary

- ATCC is harnessing the combined forces of genomic data and our highly reliable, authenticated cell lines to generate useful tools for cancer research
- Focused on disease, driver genes and signaling pathways, various cancer cell panels and normal cell controls facilitate both basic and translational research

Reference

Cancer Cell (2002) 2, 29-42
Oncogene (1998) 16, 737 – 746
Science (2001) 292, 727-730
Nature reviews drug discovery (2009) 8, 627-644
Nature (2010) 463, 899-905
Nature reviews Cancer (2010) 10, 241-253

ATCC 10801 University Boulevard, Manassas, Virginia 20110-2209 phone: 800.638.6597 email: ftian@atcc.org www.atcc.org