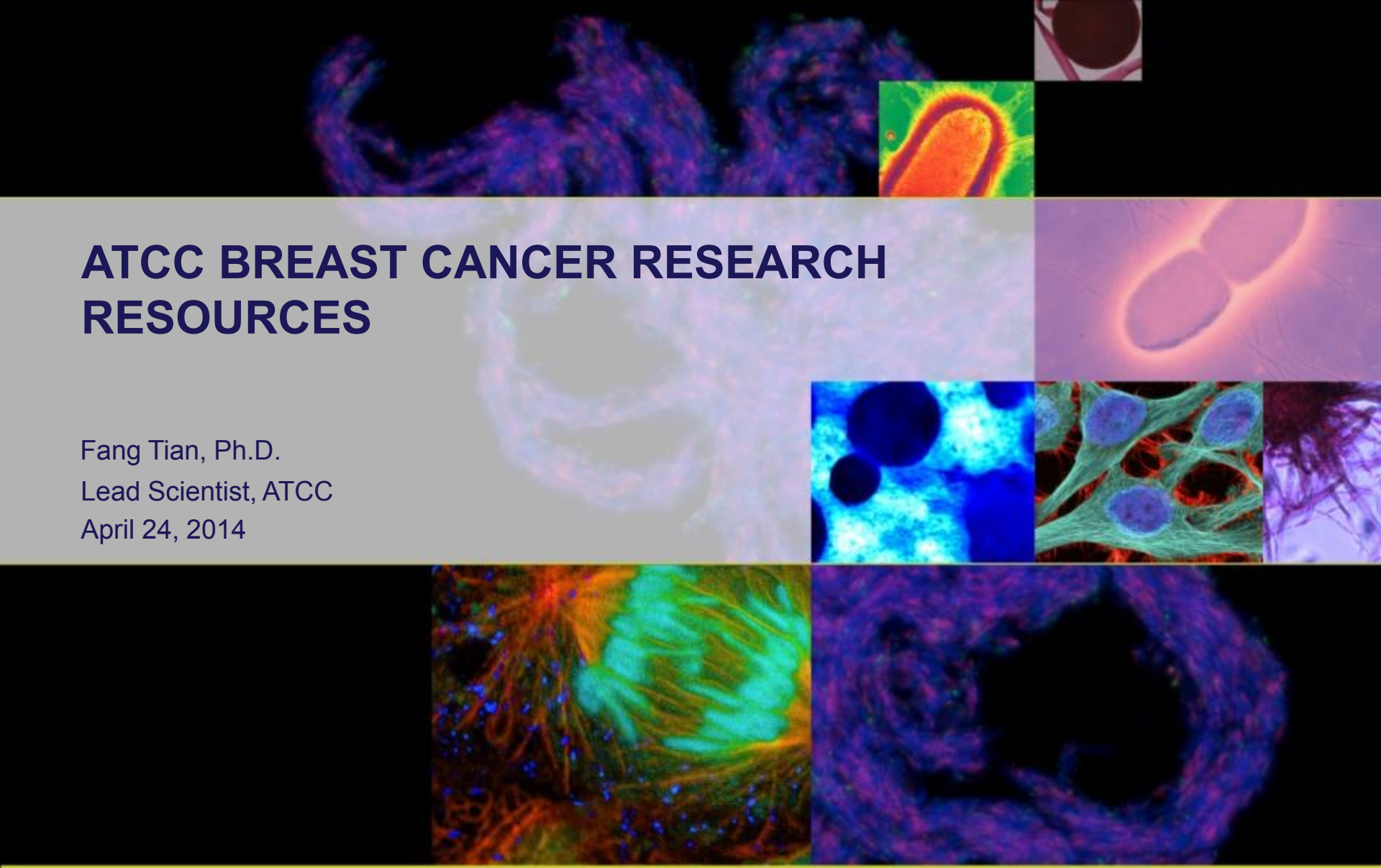
ATCC BREAST CANCER RESEARCH RESOURCES

Fang Tian, Ph.D.
Lead Scientist, ATCC
April 24, 2014



ATCC® THE ESSENTIALS OF LIFE SCIENCE RESEARCH GLOBALLY DELIVERED™

Who we are

- ATCC serves and supports the scientific community with industry-standard products and innovative solutions
- World's leading biological resource center and provider of biological standards
- Broad range of biological materials
  - Microorganisms
  - Cell lines
  - Derivatives
  - Bioproducts
- Founded in 1925, ATCC is a non-profit organization with headquarters in Manassas, VA

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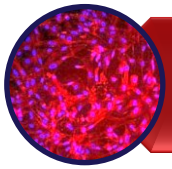
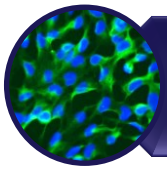
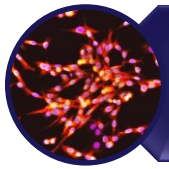
Outline



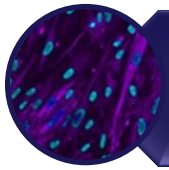
What do we know about breast cancer?



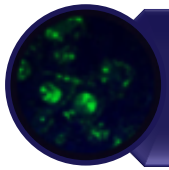
What's new in breast cancer research?



What's new about ATCC breast cancer cell lines?



ATCC breast cancer cells for animal models



ATCC primary breast cells and immortalized cells

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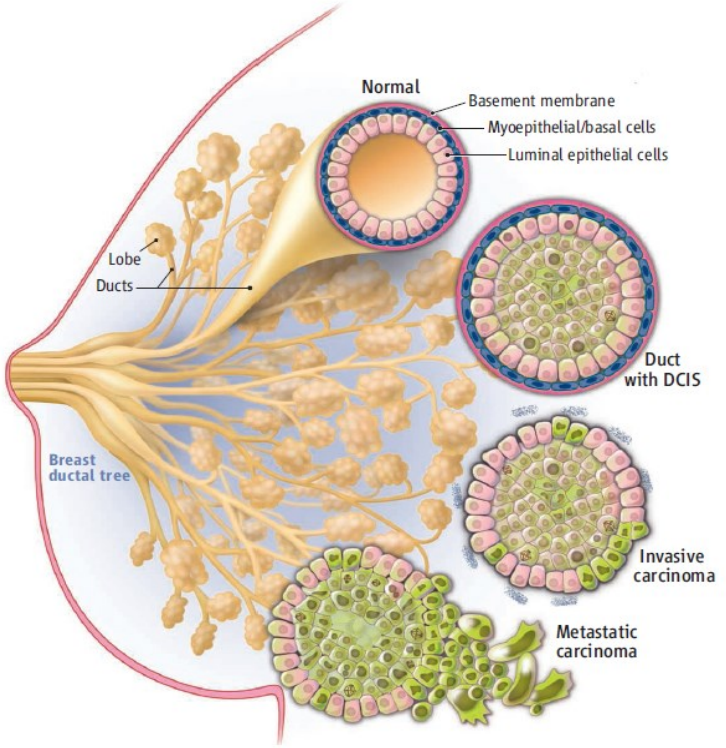
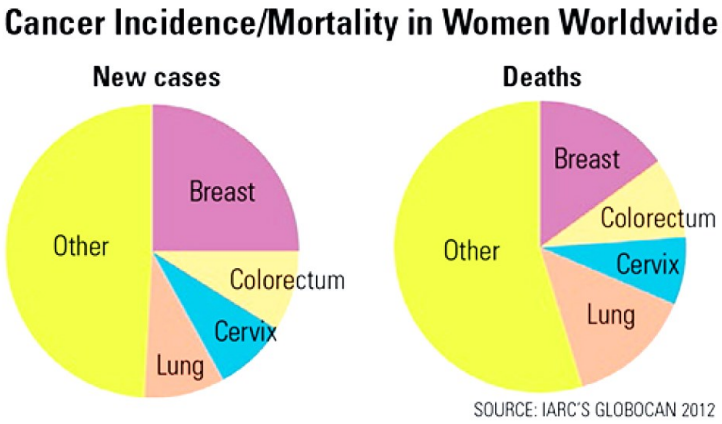
Breast cancer

- Breast cancer is a malignant form of cancer that develops in breast tissue.
- Estimated new cases and deaths in the United States in 2014:

	Female	Male
New Cases	232,670	2,360
Deaths	40,000	430



Science 343:1454, March 28, 2014



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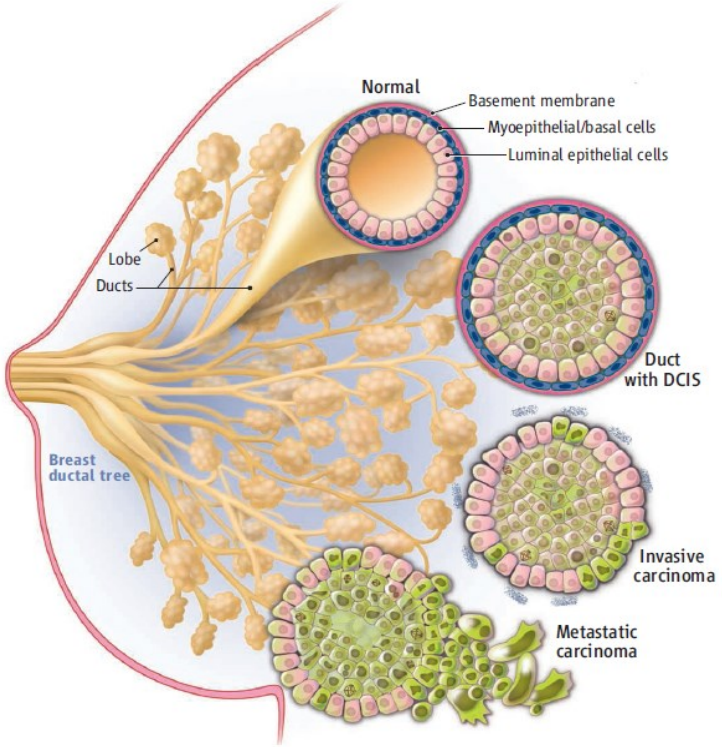
Breast cancer

- Pathology subtype
- Stage classification
- Risk factor
- Clinical diagnostics
- Anti-breast cancer therapeutics

Special Issue | 28 March 2014
Breast Cancer



Science 343:1454, March 28, 2014

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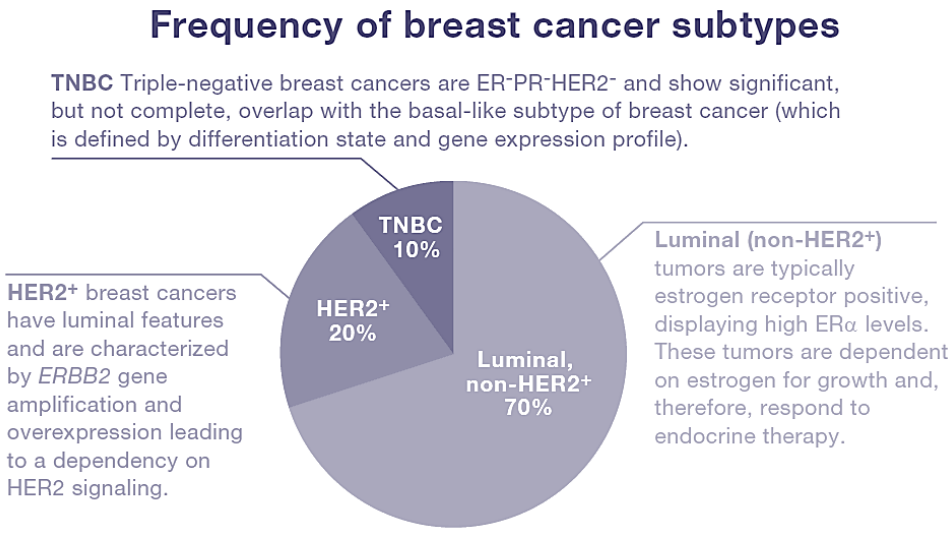
Molecular-based classification

- The categorization of breast tumors based on hormone receptor and HER2 status



Top 21 most commonly mutated genes in breast cancer			
Gene	**All (%)**	**Luminal (%)**	**TNBC (%)**
TP53	35	26	54
PIK3CA	34	44	8
GATA3	9	13	0
MAP3K1	8	11	0
MLL3	6	8	3
CDH1	6	8	2
USH2A	5	4	8
PTEN	3	3	3
RUNX1	3	4	0
MAP2K4	3	4	1
NCOR1	3	3	1
RB1	3	2	5
TBX3	2	3	1
PIK3R1	2	3	2
CTCF	2	2	1
NF1	2	2	1
SF3B1	2	2	0
AKT1	2	2	0
CBFB	1	2	1
FOXA1	1	1	1
CDKN1B	1	1	0

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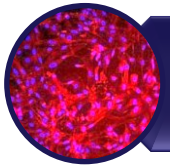
Polyak K, Filho OM. *Cancer Cell* 22(4):562, 2012.

Outline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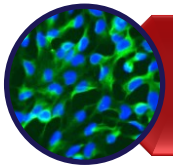
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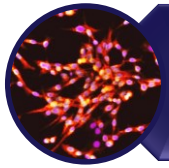
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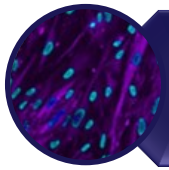
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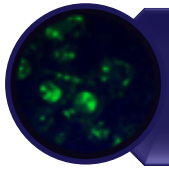
ATCC primary breast cells and immortalized cells

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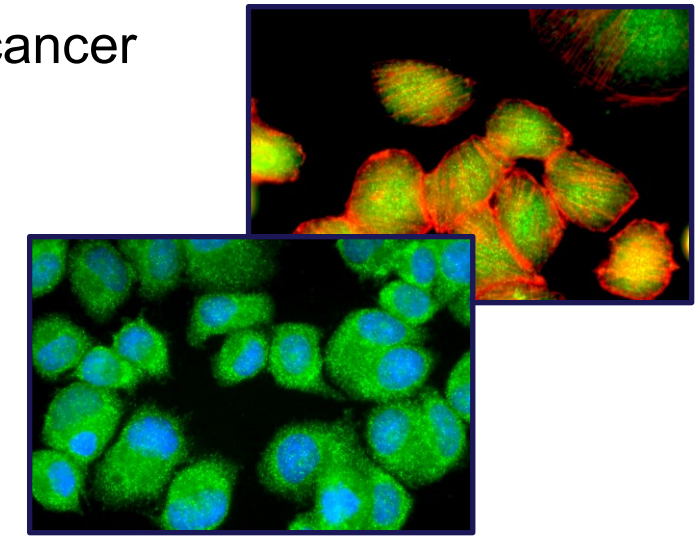
Large scale multicenter collaborative studies

Large scale initiatives

- The Cancer Genome Atlas (TCGA)
- International Cancer Genome Consortium (ICGC)
- Cancer Genome Project, Wellcome Trust Sanger Institute
- Collaborative Oncological Gene-environment Study (COGS)

Major outcomes

- Genetic landscape of breast cancer
- Genomic and clinical features of breast cancer
- New classification of breast cancer
- Genomic evolution of breast cancer



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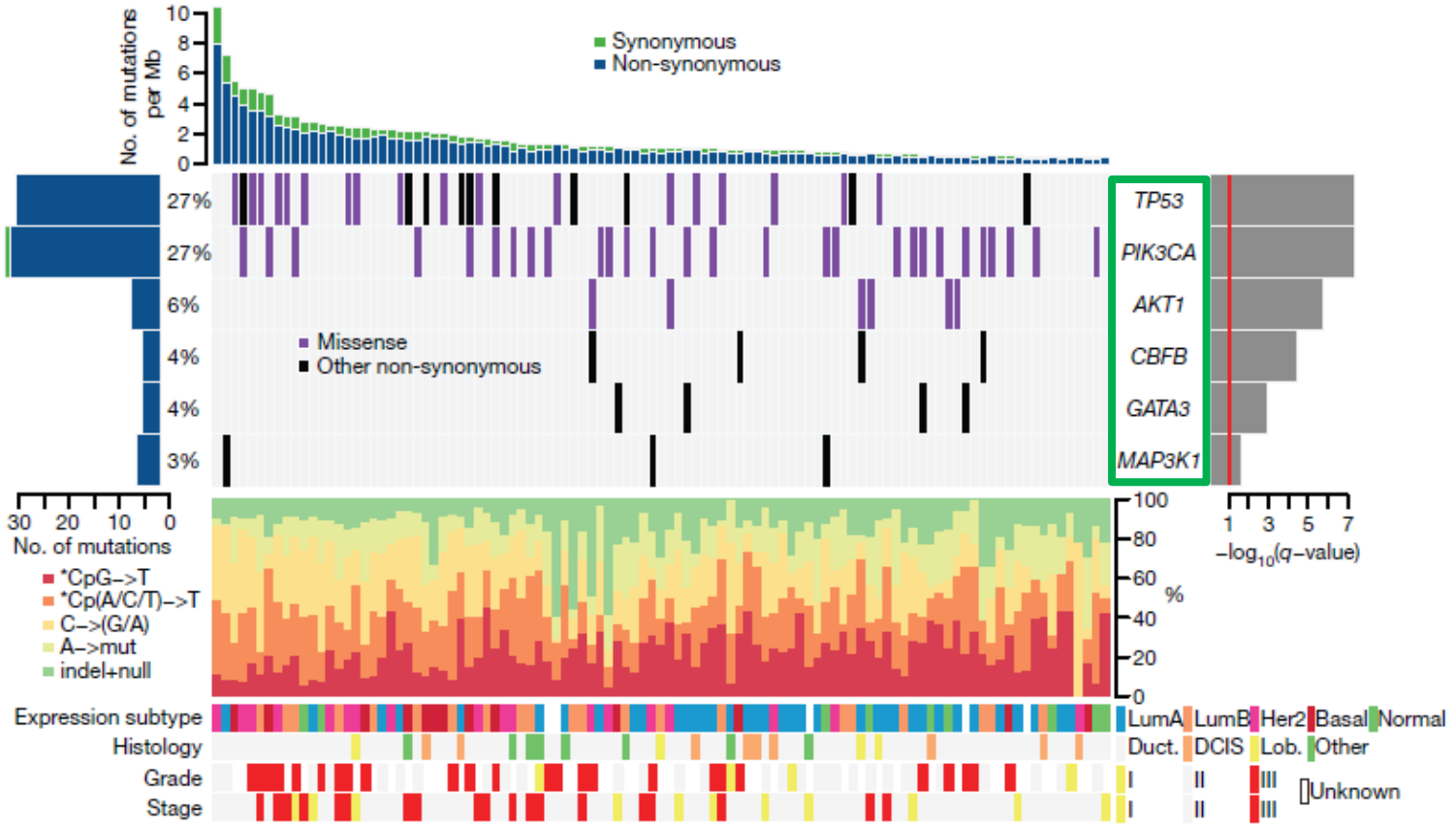
Analysis of mutations across breast cancer subtypes

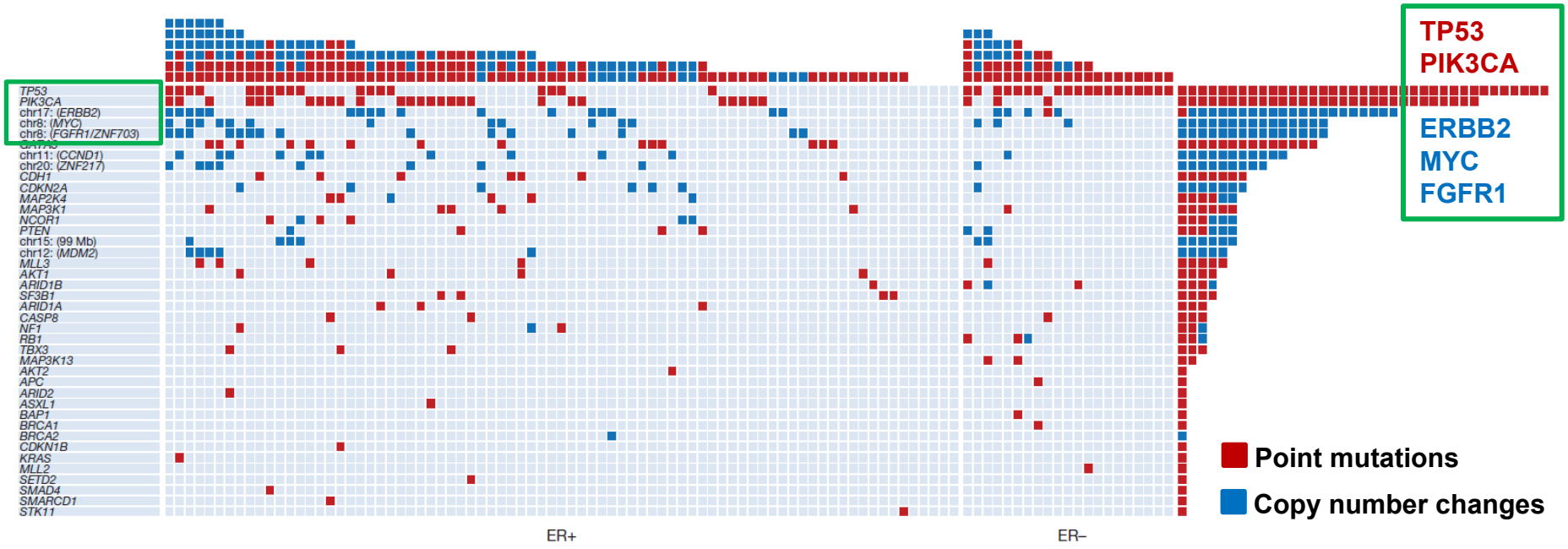
The most significantly mutated genes in breast cancer as determined by whole-exome sequencing



International Cancer Genome Consortium (ICGC). *Nature* 486: 405, June 21, 2012

Landscape of driver mutations in breast cancer

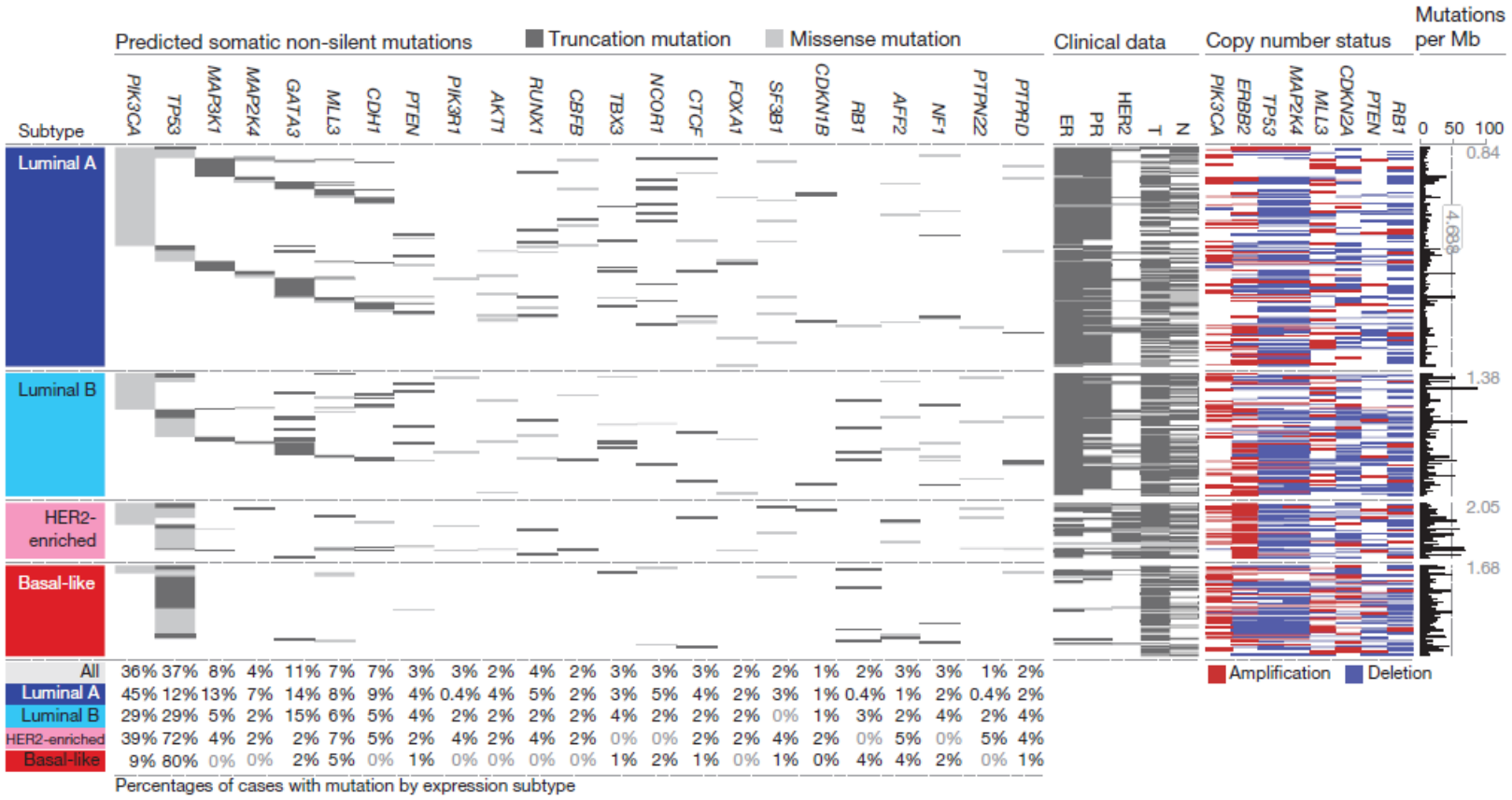
Each of the 40 cancer genes where a driver mutation or copy number change has been identified is listed down the left-hand side



Cancer Genome Project, Wellcome Trust Sanger Institute. *Nature* 486: 400, June 21, 2012

Comprehensive molecular portraits of breast cancer

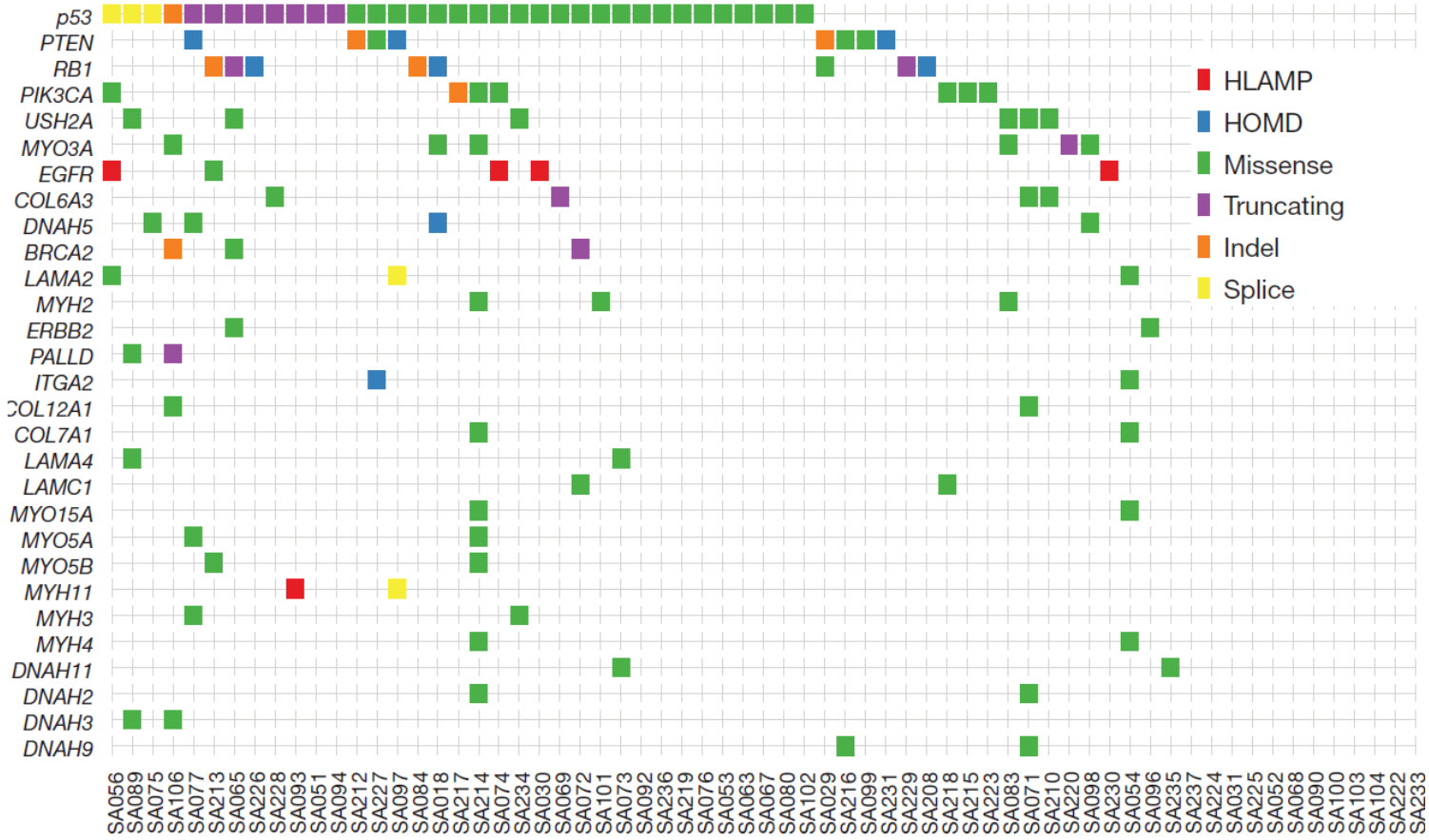
Significantly mutated genes and correlations with genomic and clinical features



The Cancer Genome Atlas Network. *Nature* 490: 61, October 4, 2012

Genomic evolution in triple-negative breast cancer

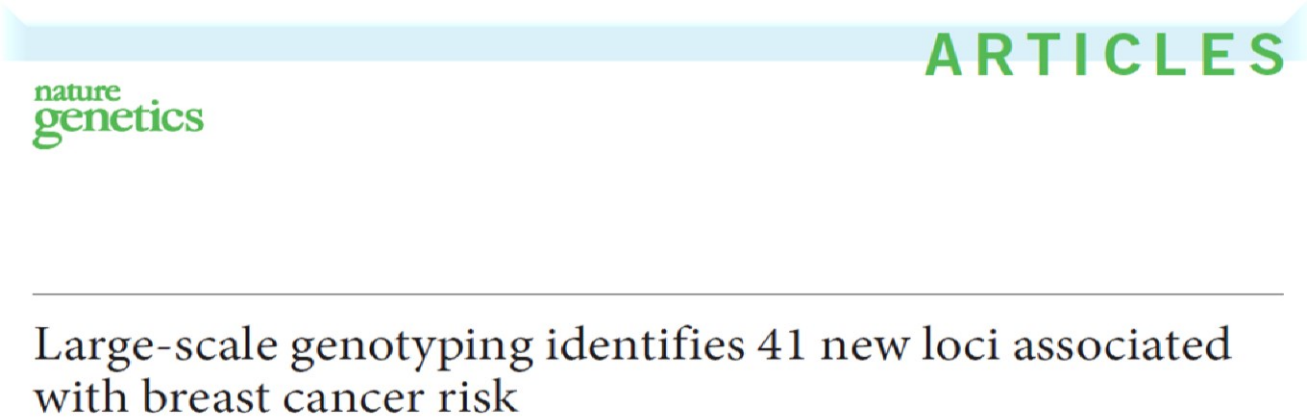
Population patterns of genomic aberrations in TNBC



Shah SP., et al. *Nature* 486: 395-399, June 21, 2012

Genomic studies identify breast cancer risk loci

Collaborative Oncological Gene-Environment Study (COGS). *Nature Genetics* 392: 45(4), April 2013



Collaborative Oncological Gene-Environment Study (COGS). *Nature Genetics* 353: 45(4), April 2013

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Proposed new subgroup classification

ARTICLE

doi:10.1038/nature10983

The genomic and transcriptomic architecture of 2,000 breast tumours reveals novel subgroups

Christina Curtis[1,2]†*, Sohrab P. Shah[3,4]*, Suet-Feung Chin[1,2]*, Gulisa Turashvili[3,4]*, Oscar M. Rueda[1,2], Mark J. Dunning[2], Doug Speed[2,5]†, Andy G. Lynch[1,2], Shamith Samarajiwa[1,2], Yinyin Yuan[1,2], Stefan Gräf[1,2], Gavin Ha[3], Gholamreza Haffari[3], Ali Bashashati[3], Roslin Russell[2], Steven McKinney[3,4], METABRIC Group‡, Anita Langerød[6], Andrew Green[7], Elena Provenzano[8], Gordon Wishart[8], Sarah Pinder[9], Peter Watson[3,4,10], Florian Markowetz[1,2], Leigh Murphy[10], Ian Ellis[7], Arnie Purushotham[9,11], Anne-Lise Børresen-Dale[6,12], James D. Brenton[2,13], Simon Tavaré[1,2,5,14], Carlos Caldas[1,2,8,13] & Samuel Aparicio[3,4]

The elucidation of breast cancer subgroups and their molecular drivers requires integrated views of the genome and transcriptome from representative numbers of patients. We present an integrated analysis of copy number and gene expression in a discovery and validation set of 997 and 995 primary breast tumours, respectively, with long-term clinical follow-up. Inherited variants (copy number variants and single nucleotide polymorphisms) and acquired somatic copy number aberrations (CNAs) were associated with expression in ~40% of genes, with the landscape dominated by ***cis***- and ***trans***-acting CNAs. By delineating expression outlier genes driven in ***cis*** by CNAs, we identified putative cancer genes, including deletions in *PPP2R2A*, *MTAP* and *MAP2K4*. Unsupervised analysis of paired DNA–RNA profiles revealed novel subgroups with distinct clinical outcomes, which reproduced in the validation cohort. These include a high-risk, oestrogen-receptor-positive 11q13/14 ***cis***-acting subgroup and a favourable prognosis subgroup devoid of CNAs. ***Trans***-acting aberration hotspots were found to modulate subgroup-specific gene networks, including a TCR deletion-mediated adaptive immune response in the 'CNA-devoid' subgroup and a basal-specific chromosome 5 deletion-associated mitotic network. Our results provide a novel molecular stratification of the breast cancer population, derived from the impact of somatic CNAs on the transcriptome.

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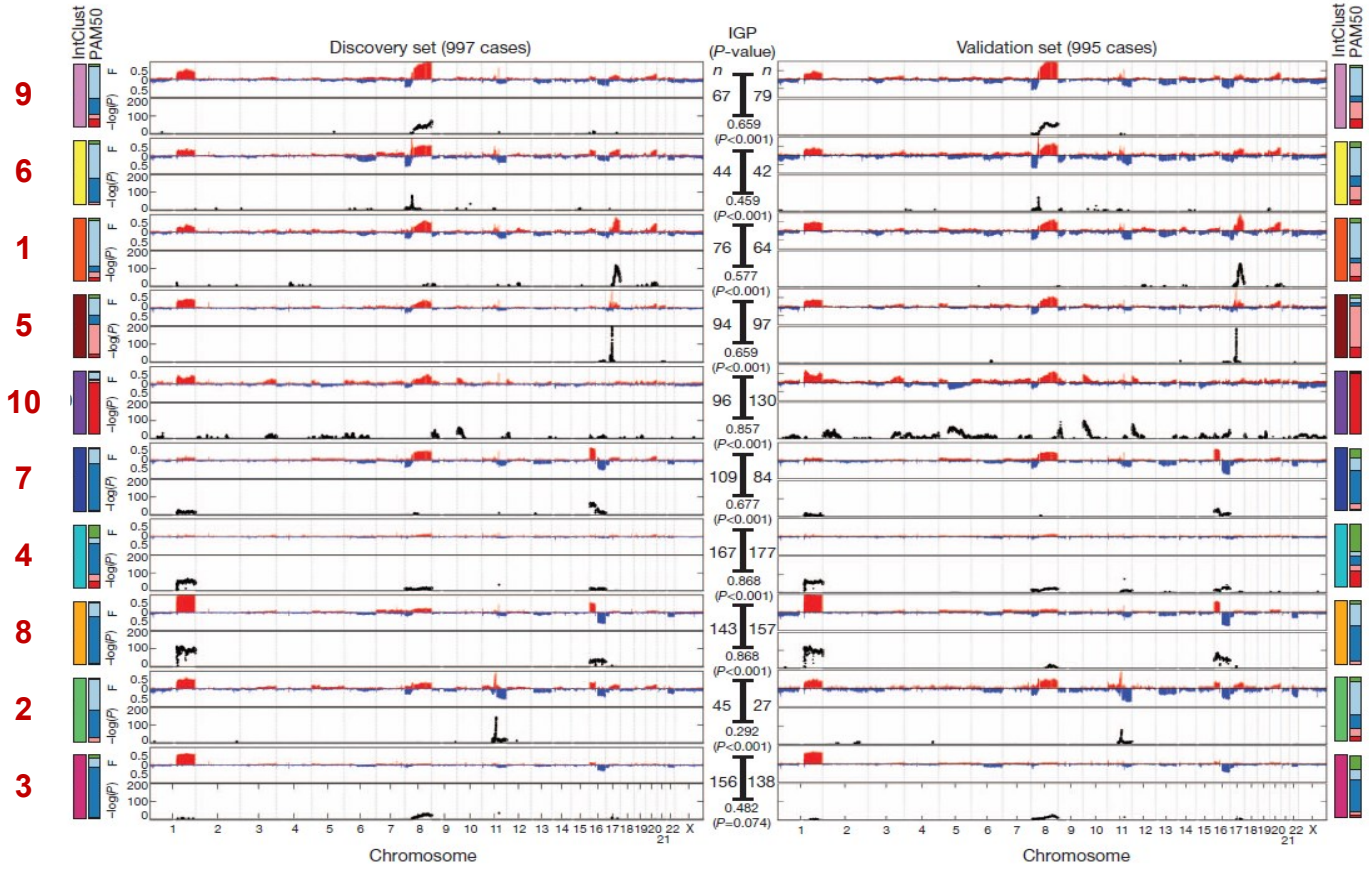
Curtis C, et al.. *Nature* 486: 346-352, June 21, 2012

Elucidation of novel breast cancer subgroups

Identification of 10 integrative subgroups with distinct copy number profiles



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Elucidation of novel breast cancer subgroups

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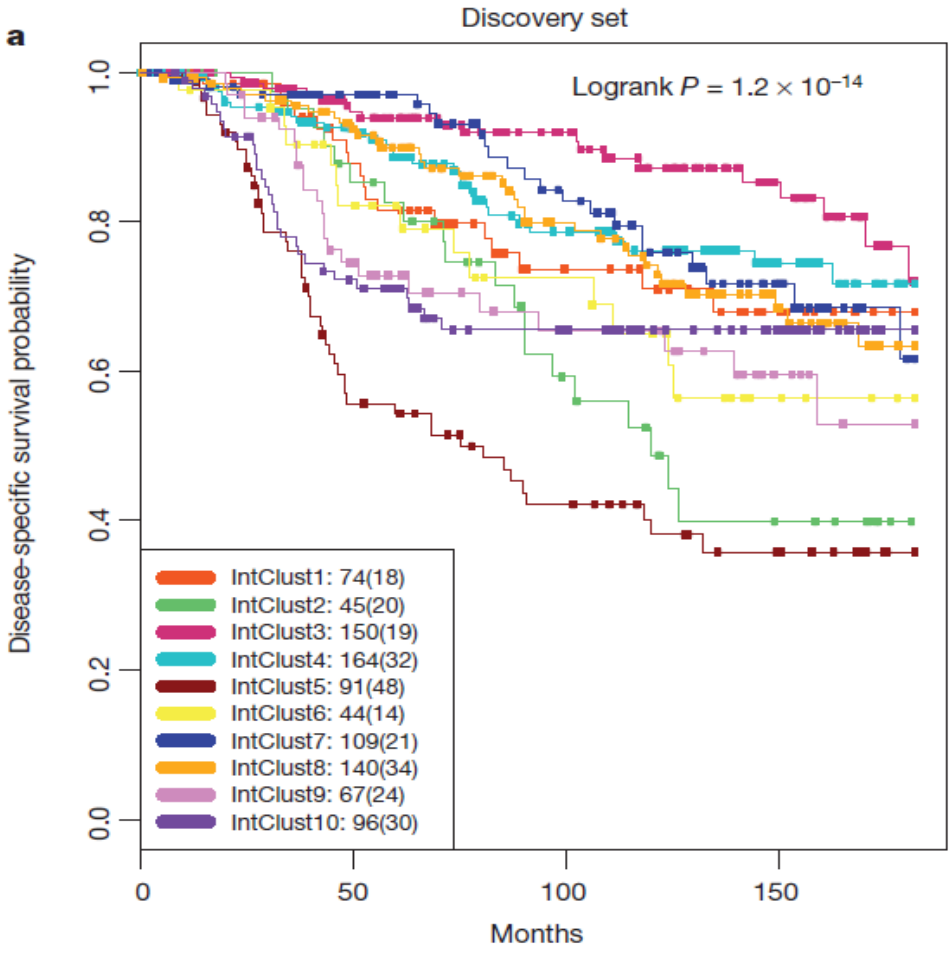
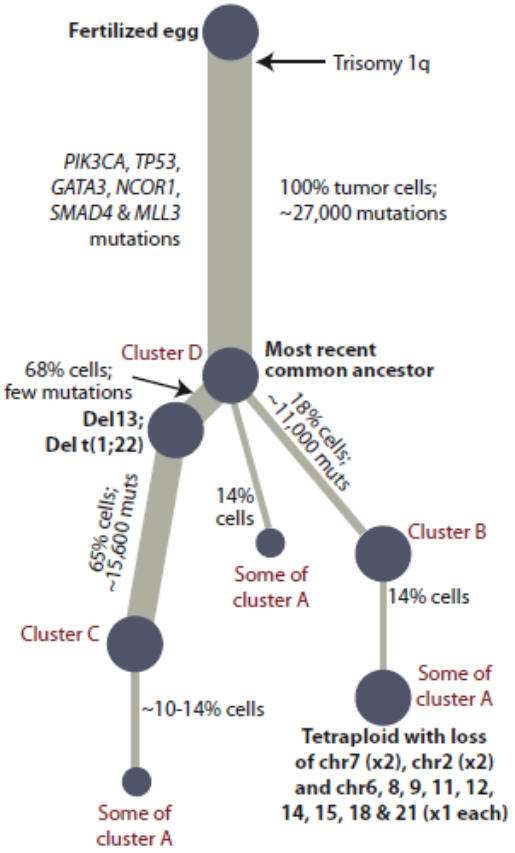


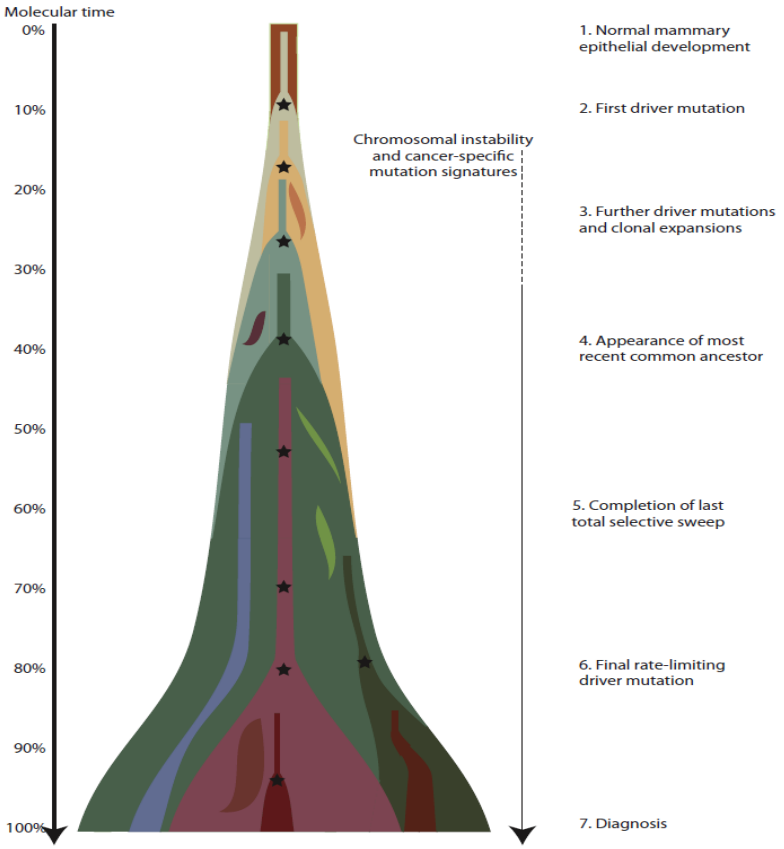
Curtis C, et al.. *Nature* 486: 346-352, June 21, 2012

The life history of 21 breast cancer

Reconstruction of the phylogenetic tree



A model for breast cancer development over molecular time



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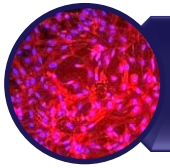
Nik-Zainal S, et al. *Cell* 149, 994–1007, May 25, 2012

Outline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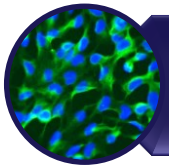
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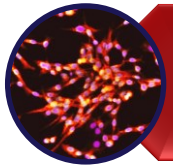
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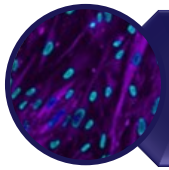
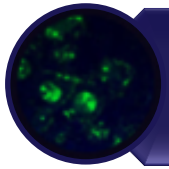

ATCC breast cancer cells for animal models


ATCC primary breast cells and immortalized cells

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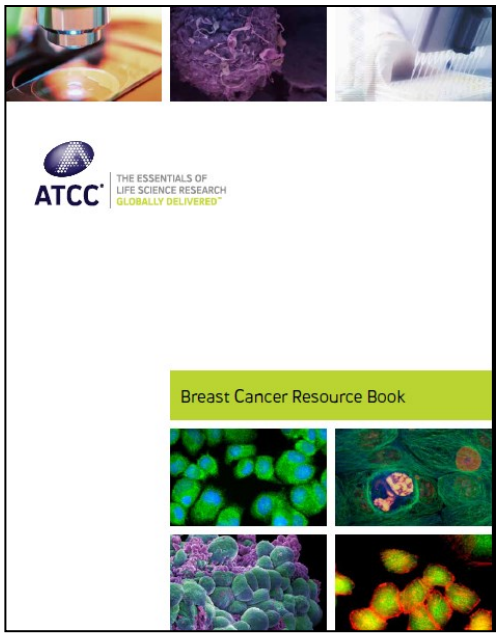
ATCC breast cancer resource

- Complete list of ATCC breast cancer cell lines
  - Human, mouse, rat, monkey, dog
- Breast cancer line by gene
- Variety of tumor cell panels
  - By tissue
  - By genetic alteration
  - By *in vivo* model
- Paired tumor/normal cell lines
- Primary mammary epithelial cells
- hTERT immortalized mammary epithelial cells
- Mammary epithelial cell culture media



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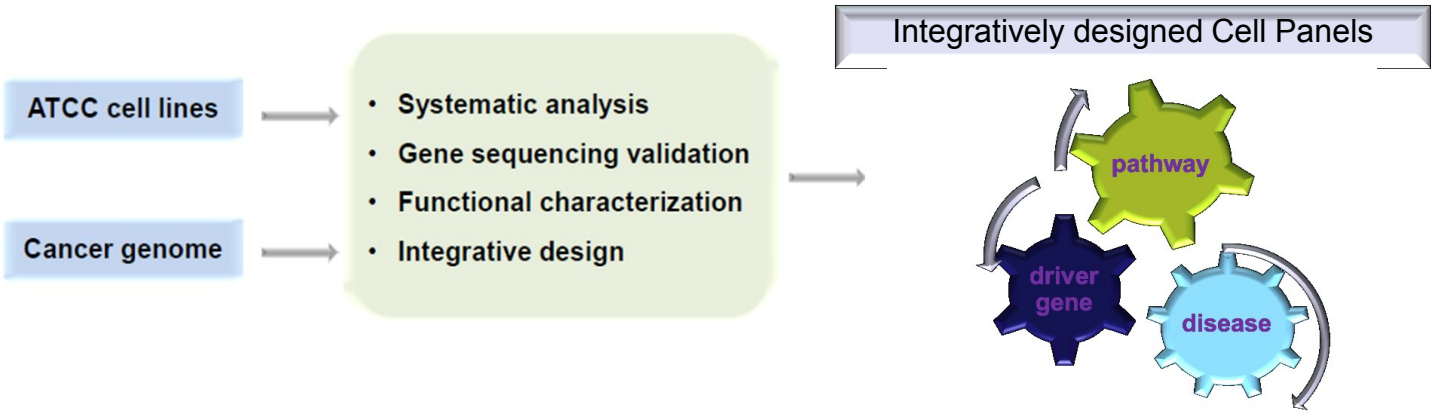
ATCC breast cancer cell lines



- Various tools
- Authenticated & high quality
- Convenience
- Value added
- Scientifically relevant

Basic information, traditional grouping

additional information, applications, focused areas

	Species	Tissue	Cell type	Disease	Genetic alternation	biomarkers	Signaling pathway	Drug discovery
ATCC	●	●	●	●	●	●	●	●
RIKEN	●	●	●	●				
DSMZ	●	●	●	●				
ECACC	●	●	●	●				
JCRB	●	●	●	●				

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ATCC Breast Cancer Cell Panels

If you are interested in	Supportive materials
Using a large number of cell lines to identify other rare or novel mutations/targets	• Breast Cancer Cell Panel (ATCC® 30-4500K™) • 45 breast cancer cell lines
Basic or translational research focused on triple-negative breast cancer	• Triple-Negative Breast Cancer Cell Panels (ATCC® TCP-1001™, TCP-1002™, TCP-1003™)
Patient therapeutic treatment history or biomarker expression	• Breast Cancer Biomarkers Cell Line Panel 1 (ATCC® TCP-1004™)
Breast cancer metastasis, *in vivo* mouse models of breast cancer, or the EGFR-MEK signaling pathways	• Breast Cancer Mouse Model Cell Panel (ATCC® TCP-1005™)
p53 hotspot mutations, or characterization and validation data	• Breast Cancer p53 Hotspot Mutation Cell Panel (ATCC® TCP-2010™)
Significantly mutated genes, copy number changes, characterizations, and validation data	• Genetic Alteration Cell Panels (ATCC® TCP-1027™ to TCP-1036™)

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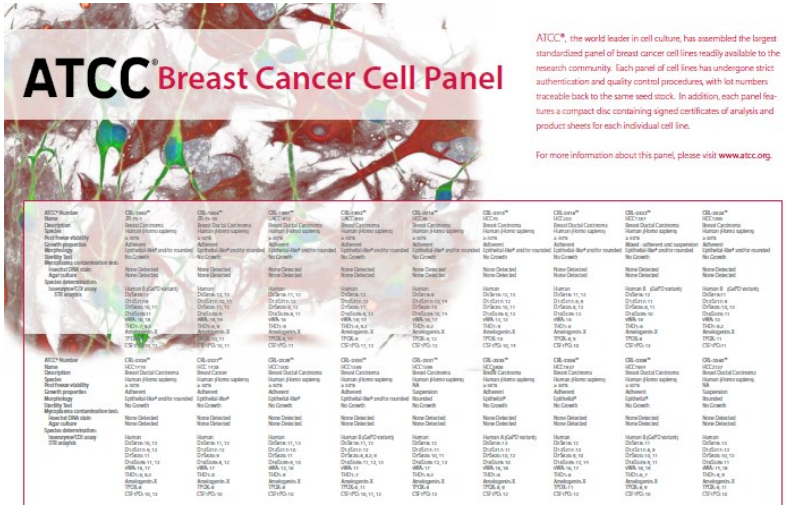
Comprehensive Breast Cancer Cell Panel (ATCC® 30-4500K™)

- 45 breast cancer cell lines
- Authenticated, high quality
- Cell line lot numbers traceable back to the same seed stock
- Includes commonly cited breast cancer cell lines
- Can be used in anti-breast cancer drug screening
- Can be used to identify rare or novel mutations/targets
- Provided with a CD containing signed certificates of analysis and product sheets



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Triple-negative Breast Cancer Cell Panels

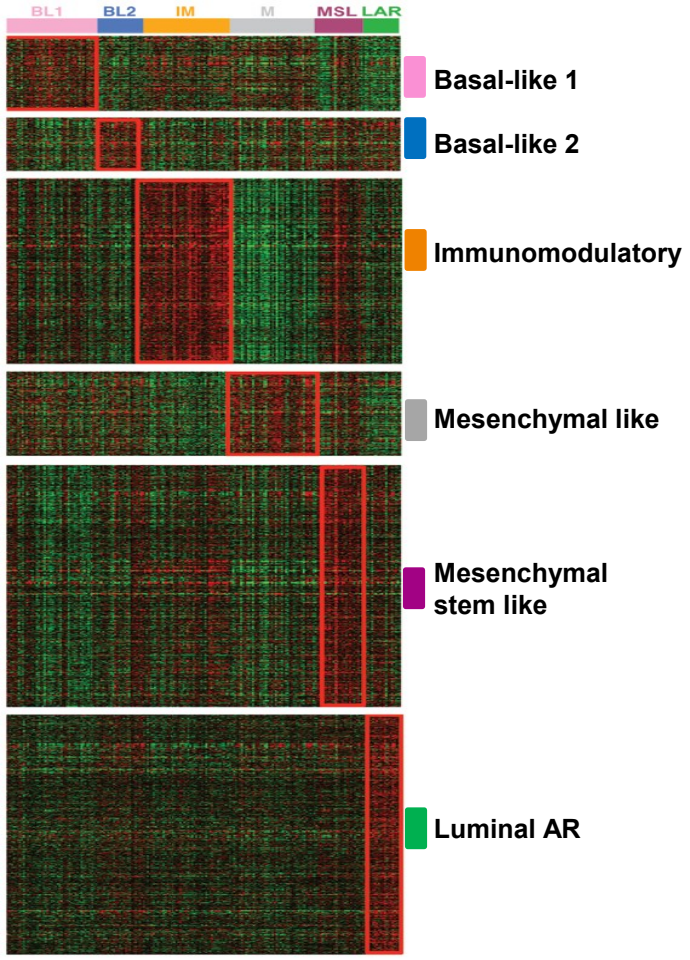
Background

Identification of human triple-negative breast cancer subtypes and preclinical models for selection of targeted therapies

Brian D. Lehmann,[1] Joshua A. Bauer,[1] Xi Chen,[2] Melinda E. Sanders,[3] A. Bapsi Chakravarthy,[4] Yu Shyr,[2] and Jennifer A. Pietenpol[1]

[1]Department of Biochemistry, [2]Department of Biostatistics, [3]Department of Pathology, and [4]Department of Radiation Oncology, Vanderbilt-Ingram Cancer Center, Vanderbilt University School of Medicine, Nashville, Tennessee, USA.

- Analyzed the gene expression profiles from 21 breast cancer data sets and identified 587 TNBC cases
- Identified 6 TNBC subtypes with unique gene expression profiles and ontologies
- Assigned TNBC cell lines to subtypes



ATCC Triple-Negative Breast Cancer Cell Panels

Panel 1: Basal-like morphology
Panel 2: Mesenchymal & luminal
Panel 3: All 18 triple-negative breast cancer cell lines

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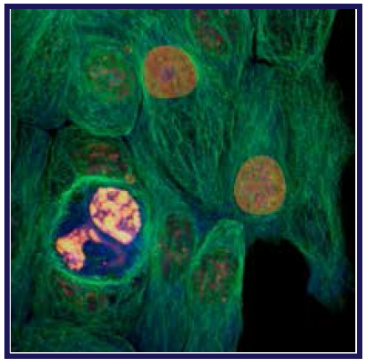
Lehmann BD, et al. *J Clin Invest* 121(7): 2750-2767, 2011.

Example of triple-negative breast cancer cell lines

ATCC® No.	Name	Subtype	Tissue	Tumor Source	Histology	Mutant Gene	Zygosity	Gene Sequence	Protein Sequence
HTB-132™	MDA-MB-468	BL1	Breast	Metastasis; pleural	Adenocarcinoma	PTEN RB1 SMAD4 TP53	Homozygous Homozygous Homozygous Homozygous	c. 253+1G>T c.265_2787del2523 c.1_1659del1659 c.818G>A	p.? p.? p.0? p.R273H
CRL-2315™	HCC70	BL2	Breast	Primary	Ductal carcinoma	PTEN TP53	Homozygous Homozygous	c.270delT c.743G>A	p.F90fs*9 p.R248Q
CRL-2322™	HCC1187	IM	Breast	Primary	Ductal carcinoma	TP53	Homozygous	c.322_324delGGT	p.G108del
HTB-122™	BT-549	M	Breast	Ductal carcinoma	Ductal carcinoma	PTEN RB1 TP53	Homozygous Homozygous Homozygous	c.823delG c.265_607del343 c.747G>C	p.V275fs*1 p.? p.R249S
HTB-26™	MDA-MB-231	MSL	Breast	Adenocarcinoma	Adenocarcinoma	BRAF CDKN2A KRAS NF2 TP53	Heterozygous Homozygous Heterozygous Homozygous Homozygous	c.1391G>T c.1_471del471 c.38G>A c.691G>T c.839G>A	p.G464V p.0? p.G13D p.E231* p.R280K
HTB-131™	MDA-MB-453	LAR	Breast	Carcinoma	Carcinoma	CDH1 PIK3CA	Homozygous Heterozygous	c.1913G>A c.3140A>G	p.W638* p.H1047R

- Three triple-negative breast cancer cell panels
- Total of 18 cell lines
- Represent 6 identified subtypes
- Annotated with mutation data



ATCC®

Breast Cancer Biomarkers Cell Line Panel (ATCC® TCP-1004™)

ATCC® No.	Name	Tumor Source	Pathology	Age	Positive markers	Negative markers	Other Significant Features	Patient Treatment
CRL-1897™	UACC-812	Primary	Infiltrating ductal carcinoma	43	HER-2/neu	ER, PR, EGFR, P-glycoprotein	-	Vinblastine, Adriamycin, Cytoxan, Cyclophosphamide, Methotrexate, 5-fluorouracil
CRL-1902™	UACC-893	Primary	Infiltrating ductal carcinoma	57	HER-2/neu	ER, PR, EGFR, P-glycoprotein, MASPIN	MASPIN promoter methylation has been reported for this line	None
CRL-2983™	UACC-3199	Metastasis; axillary nodes	Infiltrating ductal carcinoma	58	EGFR	ER, PR, HER-2/Neu	Methylated BRCA-1 promoter	Cytoxan, Adriamycin, 5-fluorouracil, Tamoxifen, Mitoxantrone, Vinblastine
CRL-2988™	UACC-3133	Metastasis; pleural effusion	Ductal carcinoma	63	HER-2/neu, BMP-3	ER (very low), PR, EGFR, MASPIN, DSC3, BMP-2	MASPIN promoter methylation has been reported for this line	Surgery only
CRL-3127™	UACC-1179	Metastasis; pleural effusion	Adenocarcinoma	62	HER-2/neu	ER, PR, EGFR, MASPIN, DSC3	P53 R213X mutation and MASPIN promoter methylation have been reported for this line	Adriamycin, Cytoxan, Methotrexate, Tamoxifen
CRL-3166™	UACC-732	Metastasis; pleural effusion	Adenocarcinoma	35	HER-2/neu, PR	ER, EGFR	Drug resistant cell line to cyclin D kinase 4/6 inhibitor and HER-2 inhibitors	Vinblastine, Adriamycin, Cytoxan
CRL-3180™	UACC-2087	Metastasis; pleural effusion	Adenocarcinoma	53	EGFR	ER, PR, HER-2/Neu, vimentin, MASPIN, DSC3	P53 V216M mutation has been reported in this cell line. It has also been reported that the MASPIN promoter is not methylated.	Cyclophosphamide, Methotrexate, 5-flurouracil, Thymidine phophorylase, Tamoxifen

Seven breast cancer cell lines isolated from variety of primary and metastatic sites. Each cell line was annotated with pre-operative therapeutics treatment and published biomarkers.

ATCC®

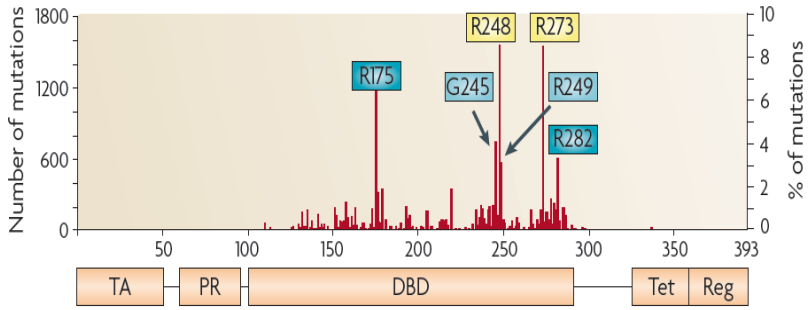
New tools relevant to recent studies

Top genes reported in breast cancer	ATCC molecular signature cell panels	Features
TP53	p53 hotspot mutation cell panel (TCP-2010™)	TP53 hotspot mutations
PIK3CA	PI3K genetic alteration cell panel (TCP-1028™)	PIK3CA hotspot mutations
PTEN	PTEN genetic alteration cell panel (TCP-1030™)	PTEN mutations and deletions
EGFR	EGFR genetic alteration cell panel (TCP-1027™)	EGFR mutations and amplification
ERBB2	EGFR genetic alteration cell panel (TCP-1027™)	ERBB2 amplification
MYC	MYC genetic alteration cell panel (TCP-1035™)	MYC mutations and amplification
FGFR1	FGFR genetic alteration cell panel (TCP-1034™)	FGFR1, FGFR2 amplification

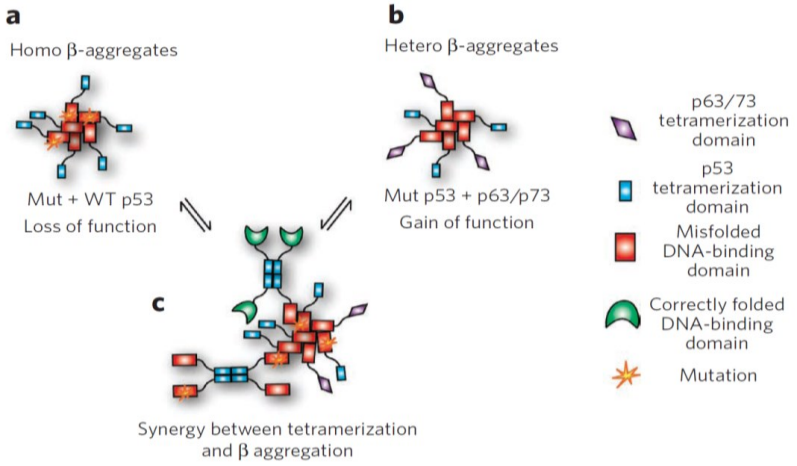
ATCC®

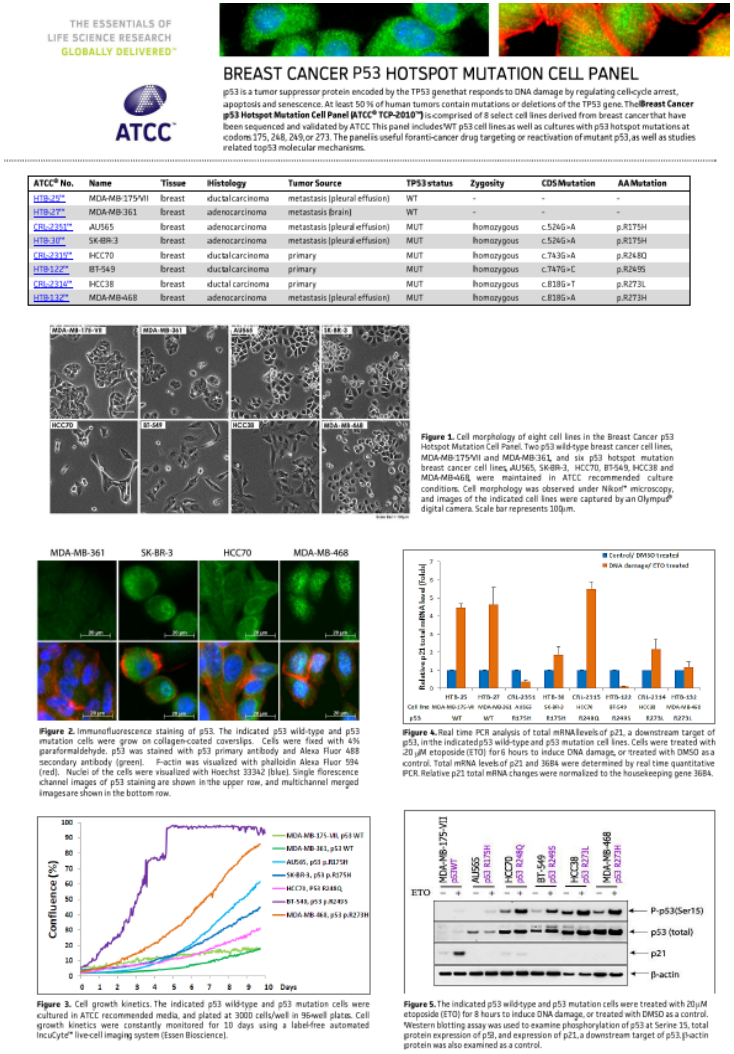
Breast cancer p53 hotspot mutation cell panel

p53, guardian of the genome



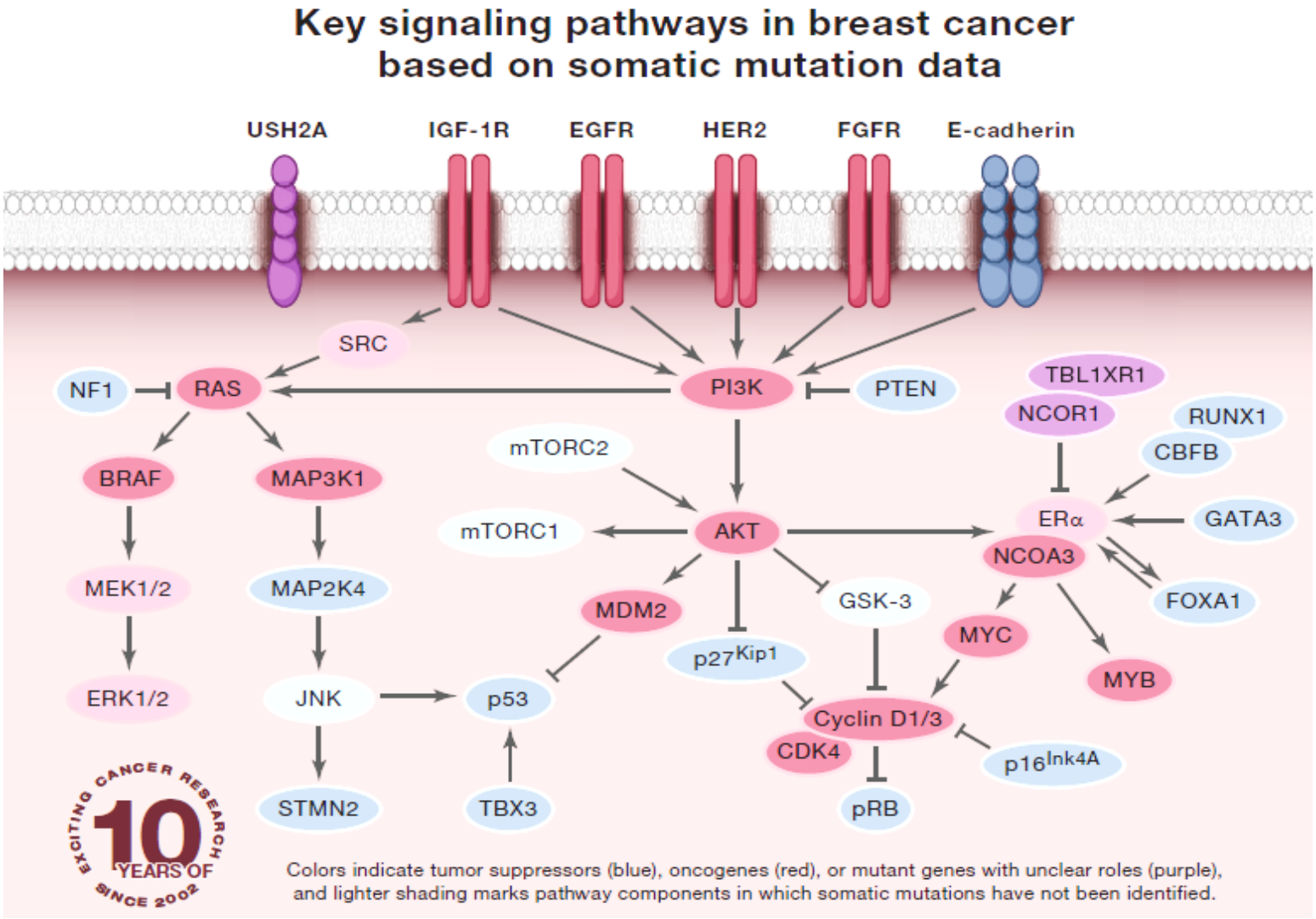
p53 gain of function mutation





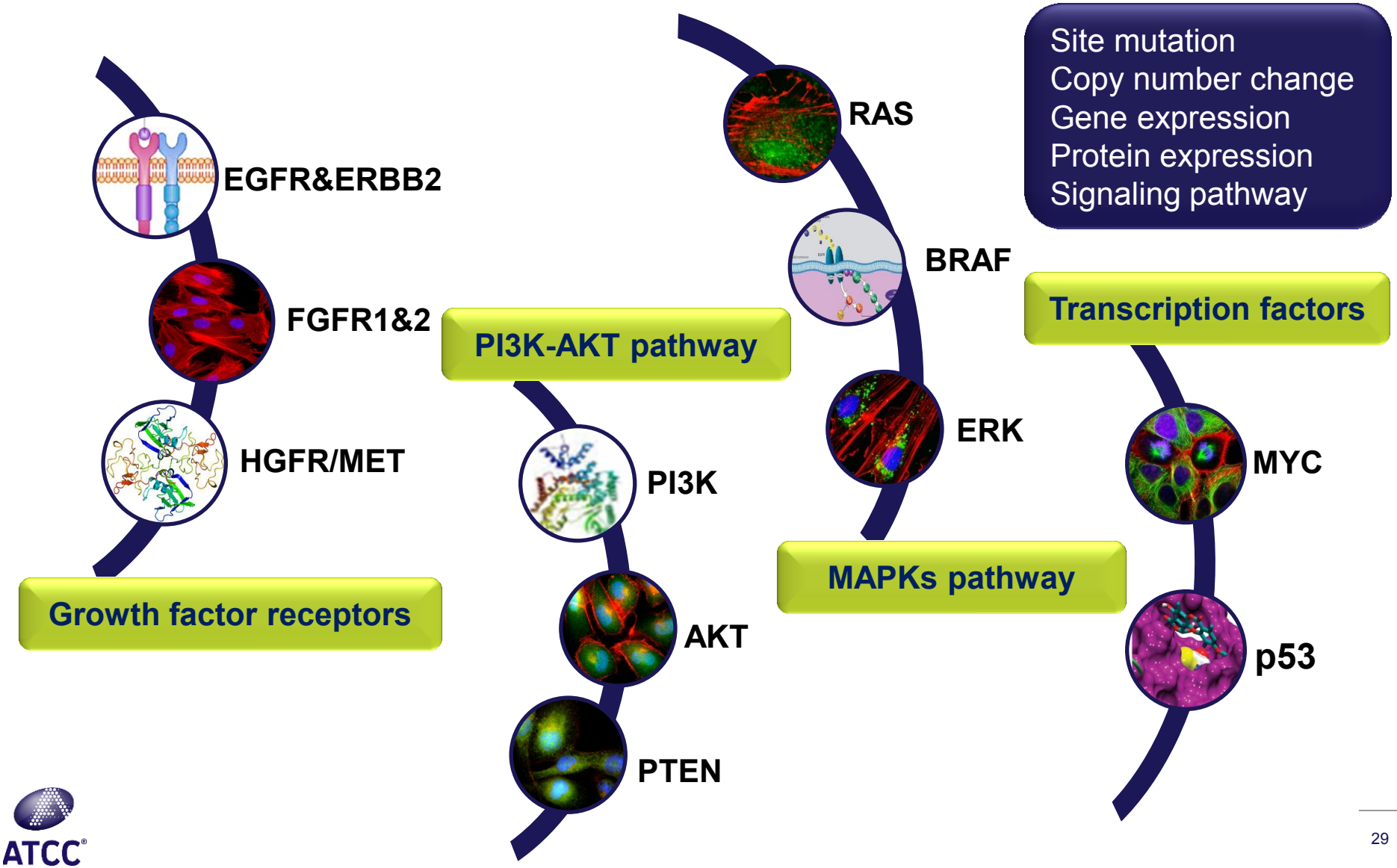
Jie Xu et al., *Nature Chemical Biology* 7: 285-295, 2011

Molecular mechanisms of breast cancer



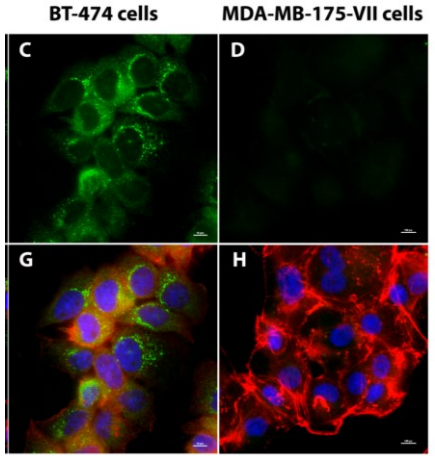
Polyak K, Filho OM. *Cancer Cell* 22(4):562, 2012.

Molecular Signature Cell Panels

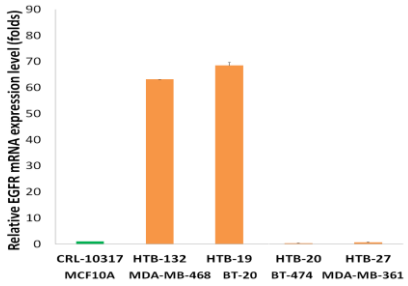


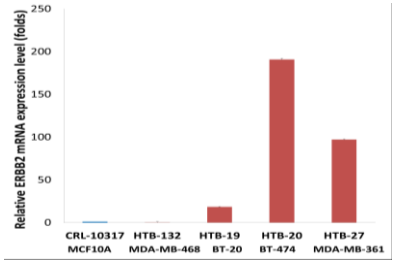
Breast cancer cell lines in EGFR cell panel

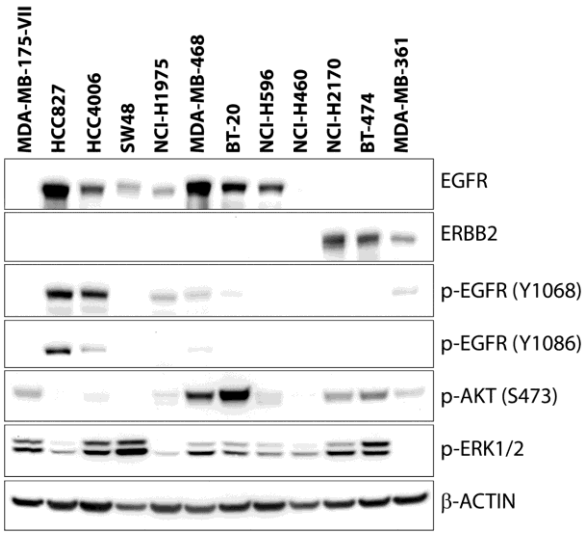
ATCC® number	Cell line name	gene	EGFR copy number variation	ERBB2 copy number variation	Tumor source	Histology
HTB-132™	MDA-MB-468	EGFR	Amplification	–	Breast	Adenocarcinoma
HTB-19™	BT-20	EGFR	Amplification	–	Breast	Carcinoma
HTB-20™	BT-474	ERBB2	–	Amplification	Breast	Ductal carcinoma
HTB-27™	MDA-MB-361	ERBB2	–	Amplification	Breast	Adenocarcinoma
HTB-25™	MDA-MB -175 VII		WT control cell line		Breast	Ductal carcinoma
CRL-10317™	MCF10A		WT control cell line		Normal breast	Normal



C-D: ERBB2, G-H, merged with F-actin/ Hoechst



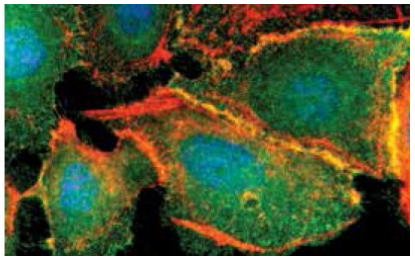




Breast cancer cell lines in EGFR cell panel

ATCC® number	Cell line name	Gene	EGFR copy number variation	ERBB2 copy number variation	Tumor source	Histology	Other mutations in related signaling pathway
HTB-132™	MDA-MB-468	EGFR	Amplification	–	Breast	Adenocarcinoma	
HTB-19™	BT-20	EGFR	Amplification	–	Breast	Carcinoma	MAPK1 H61Q
HTB-20™	BT-474	ERBB2	–	Amplification	Breast	Ductal carcinoma	PIK3CA H1047R
HTB-27™	MDA-MB-361	ERBB2	–	Amplification	Breast	Adenocarcinoma	PIK3CA E545K; PIK3CA K567R;
HTB-25™	MDA-MB -175 VII	WT control cell line			Breast	Ductal carcinoma	
CRL-10317™	MCF10A	WT control cell line			Normal breast	Normal	

- Captured the key molecular features in breast cancer
- Verified mutation status, gene expression, and protein expression
- Represented the genetic complexity observed in clinical patients



ATCC®

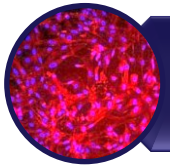
Paired tumor/ normal cell lines

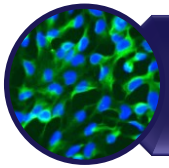
Tumor-derived cell lines matched to normal cell lines obtained from the same patient

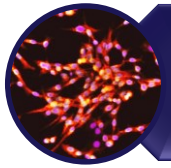
Tumor cell lines tumor source	Pathology	Name	ATCC® No	Normal pairing tissue source	Pathology	Name	ATCC® No.
Metastasis: lymph node	Ductal carcinoma	HCC10008	CRL-2320™	B lymphoblast	Normal	HCC1007 BL	CRL-2319™
Mammary gland	Ductal carcinoma	Hs574.T	CRL-7345™	Skin	Normal	Hs574.Sk	CRL-7346™
Mammary gland	Ductal carcinoma	Hs578T	HTB-126™	Mammary gland	Normal	Hs578Bst	HTB-125™
Mammary gland	Ductal carcinoma	HCC1954	CRL-2338™	B lymphoblast	Normal	HCC1954 BL	CRL-2339™
Mammary gland	Ductal carcinoma	HCC38	CRL-2314™	B lymphoblast	Normal	HCC38 BL	CRL-2346™
Mammary gland	Ductal carcinoma	HCC1143	CRL-2321™	B lymphoblast	Normal	HC1143 BL	CRL-2362™
Mammary gland	Ductal carcinoma	HCC1187	CRL-2322™	B lymphoblast	Normal	HCC1187 BL	CRL-2323™
Mammary gland	Ductal carcinoma	HCC1395	CRL-2324™	B lymphoblast	Normal	HCC1395 BL	CRL-2325™
Mammary gland	Ductal carcinoma	HCC1599	CRL-2331™	B lymphoblast	Normal	HCC1599 BL	CRL-2332™
Mammary gland	Ductal carcinoma	HCC1937	CRL-2336™	B lymphoblast	Normal	HCC1937 BL	CRL-2337™
Mammary gland	Ductal carcinoma	HCC2218	CRL-2343™	B lymphoblast	Normal	HCC2218 BL	CRL-2363™

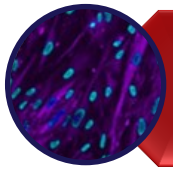
ATCC®

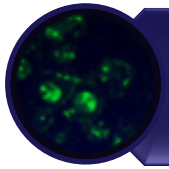
Outline


What do we know about breast cancer?


What's new in breast cancer research?


What's new about ATCC breast cancer cell lines?


ATCC breast cancer cells for animal models


ATCC primary breast cells and immortalized cells

ATCC®

Breast cancer cell line in vivo models

Commonly used human breast cancer line xenografts

Subcutaneous models

- HTB-30™ SK-BR-3
- HTB-132™ MDA-MB-468

Orthotopic models

- HTB-20™ BT474
- HTB-26™ MDA-MB-231
- HTB-22™ MCF-7
- HTB-130™ MDA-MB-436
- HTB-131™ MDA-MB-453

Commonly used murine breast cancer model

- CRL-2539™ 4T1

ATCC®

Revisit mouse breast cancer cell lines

Cancer immunotherapy-

Scientific breakthroughs from 2013

- New hope of antibody therapy
  - Anti CTLA-4
  - Anti PD-1
- Combination therapy
  - Immunotherapy + molecular targeted therapy
- Need for appropriate *in vivo* models
  - Immunocompetent mouse model

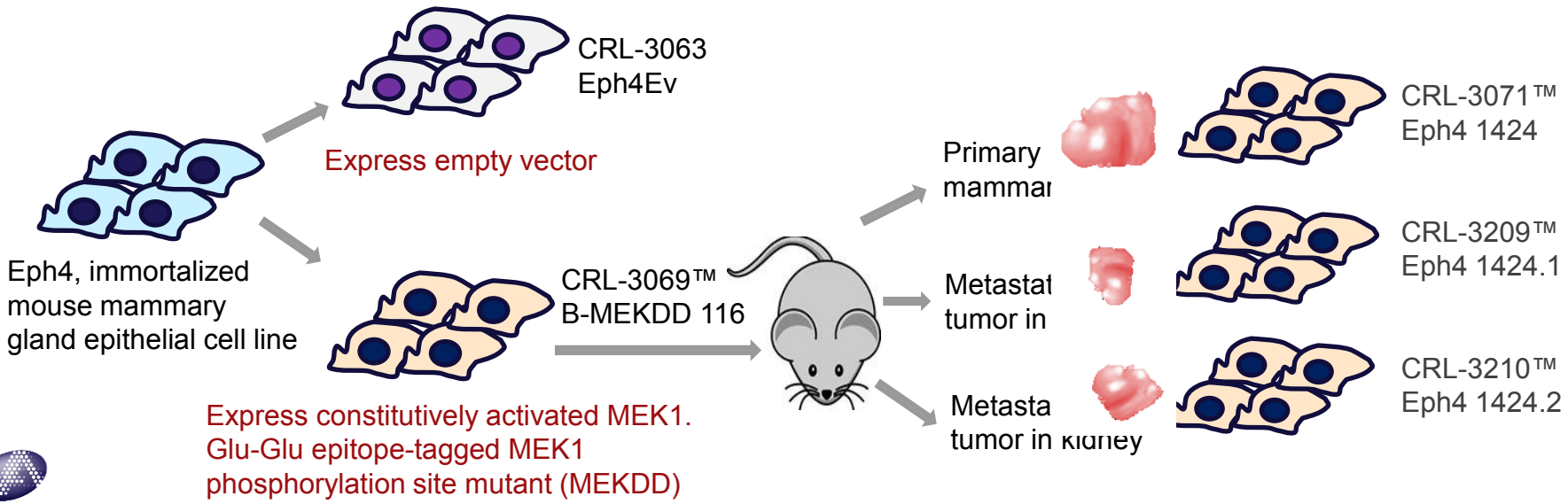
ATCC®

Breast Cancer Mouse Model Cell Panel (ATCC® TCP-1005™)

- Mouse mammary cell lines
- MEK mutation
- EGFR pathway
- Oncogenes in cell transformation

ATCC® No.	Designation
CRL-3063™	Eph4Ev
CRL-3069™	B-MEKDD 116
CRL-3071™	Eph4 1424
CRL-3209™	Eph4 1424.1
CRL-3210™	Eph4 1424.2
CRL-3086™	M158
CRL-3090™	NF639
CRL-3092™	Ac 711

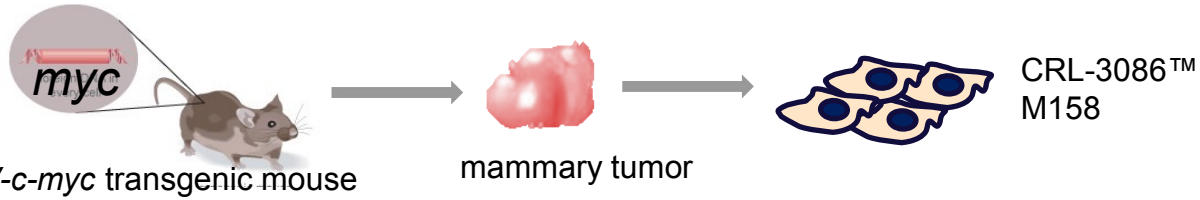
Dr. Philip Leder
Nat Rev Mol Cell Biol.
Nov 2008



ATCC®

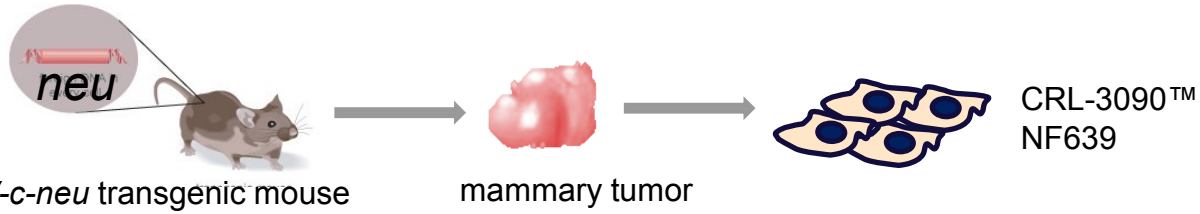
Breast Cancer Mouse Model Cell Panel (ATCC® TCP-1005™)

Myc



MMTV-c-myc transgenic mouse → mammary tumor → CRL-3086™ M158

EGFR2



MMTV-c-neu transgenic mouse → mammary tumor → CRL-3090™ NF639

Ha-Ras

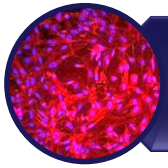
Zeta-Glovin-v-Ha-*ras* transgenic mouse → mammary tumor → CRL-3092™ Ac 711

Transgenic mouse models and cell lines have been used in signal pathway studies and drug discovery

ATCC®

Cancer Cell 2: 29-42, 2001; *Oncogene* 16: 737 – 746, 1998

Outline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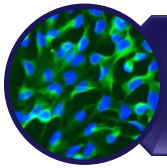
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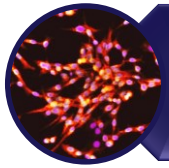
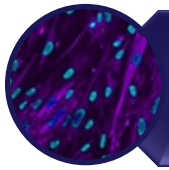
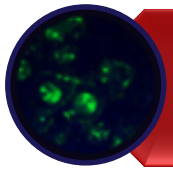

What's new about ATCC breast cancer cell lines?


ATCC breast cancer cells for animal models


ATCC primary breast cells and immortalized cells

ATCC®

Primary Cells – weighing the pros and cons

- Prepared directly from tissue
- Physiologically-relevant
- Low risk for phenotypic or genotypic drift

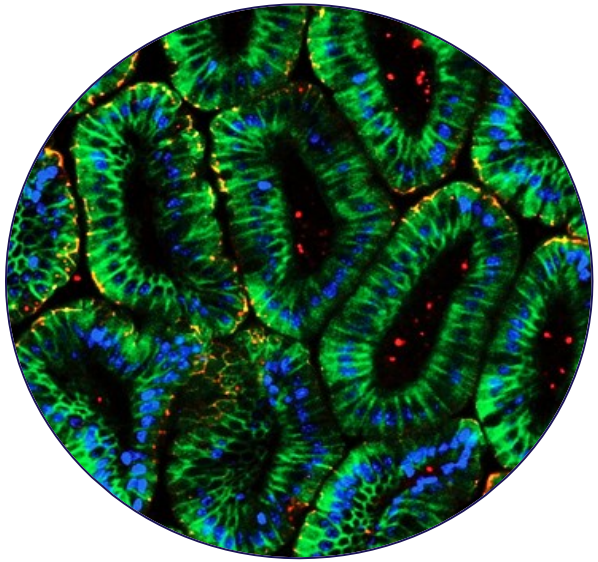
- Sourcing of tissue may be difficult and expensive to establish
- Isolation conditions may be difficult and expensive to establish
- Small yield
- Limited culture life

ATCC®

Normal human primary cells from ATCC

Epithelial Tissue

- Corneal Epithelial Cells
- Prostate Epithelial Cells
- Small Airway Epithelial Cells
- Bronchial/Tracheal Epithelial Cells
- Renal Proximal Tubule Epithelial Cells
- Renal Cortical Epithelial Cells
- Renal Mixed Epithelial Cells
- Keratinocytes
  - Neonatal Foreskin Epidermal Keratinocytes
  - Adult Epidermal Keratinocytes
- Melanocytes
  - Neonatal Foreskin Epidermal Melanocytes
  - Adult Epidermal Melanocytes

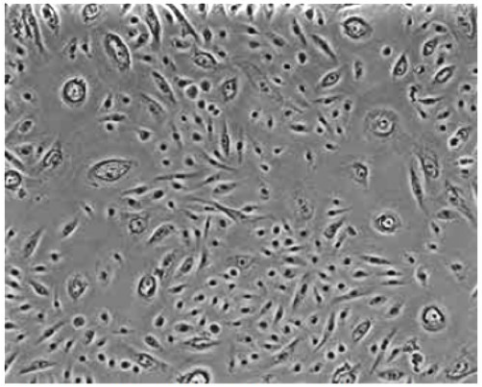


ATCC®

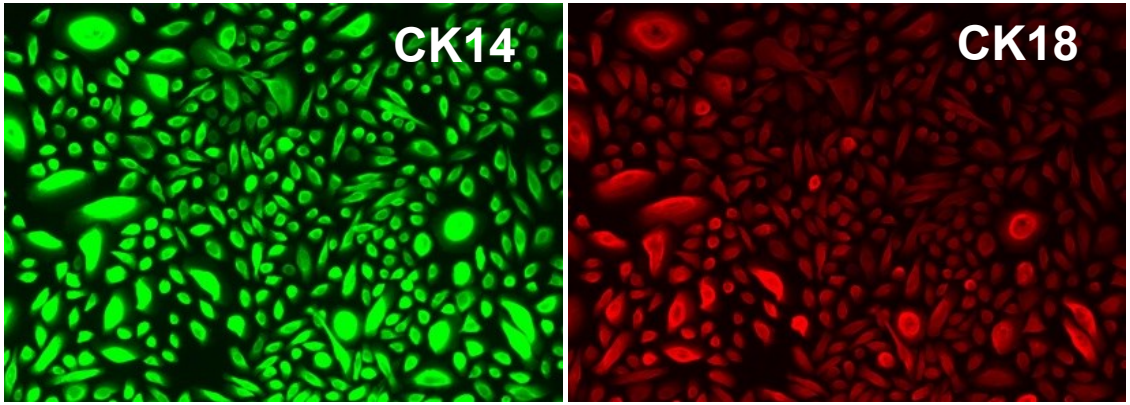
Primary Mammary Epithelial Cells (ATCC® PCS-600-010)

Cell Specifications:

- Cryopreserved at low passage (P2)
- Tested for:
  - High post-thaw viability
  - Growth to ≥ 15 PDL
  - Free from microbial contamination.



ATCC® PCS-600-010 Normal, Human Primary Mammary Epithelial Cells



myoepithelial **luminal**

Primary Mammary epithelial cells display CK14-positive (myoepithelial marker) and CK18-positive (luminal marker).

ATCC®

Roads to cell immortalization

↗ Telomerase
hTERT
HPV-16 E6
Myc T58A

↘ p53/p21
SV40T
HPV-16 E6

↘ p16/pRB
HPV-16 E7
CDK4
Bmi-1

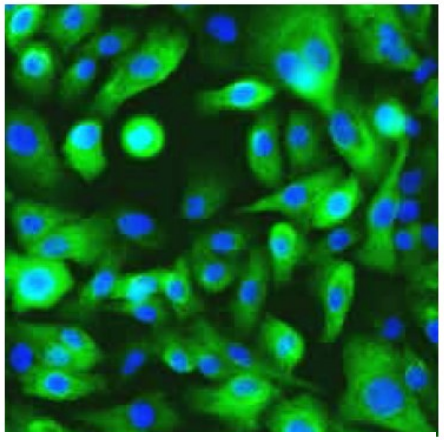
Other Methods
Feeder culture (3T3)
Rho-associated kinase inhibitor (Y-27632)
Physiological Oxygen (2-5%)

Plasmids and Reagents	ATCC® No.
hTERT	MBA-141™
SV40-T	VRMC-3™
HPV-16 E6/E7	CRL-2203™, 45113D™
CDK4	MGC-19704™, MGC-4678™, MGC-3719™
Bmi-1	81582D™, MGC-12685™
3T3 Feeder Cells	CCL-92™, 48-X™
ROCK Inhibitor Y-27632	ACS-3030™

ATCC®

hTERT-HME1 [ME16C] (ATCC® CRL-4010™)

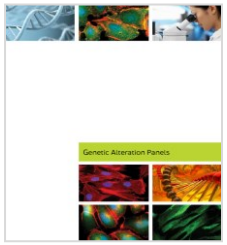
- The human mammary epithelium hTERT-HME1 [ME16C] (ATCC® CRL-4010™) cell line was derived from normal primary mammary epithelial cells.
- Human telomerase reverse transcriptase (hTERT) immortalized cell lines combine the *in vivo* nature of primary cells with the traditional cell line's ability to survive continuously *in vitro*.
- hTERT-HME1 cells have served as normal controls in several studies that sought to unravel the molecular mechanism of breast cancer pathogenesis.



ATCC® CRL-4010™
stained with pancytokeratin mAb
(green) and Hoechst dye (blue)

Summary

- Breast cancer is the leading cause of cancer-related mortality in women.
- New disease classifications, relevant signaling pathways, and genetic regulators of breast cancer have been identified over the past decade.
- To continue facilitating progress in basic research and drug discovery, ATCC provides comprehensive breast cancer research resources including a large number of breast cancer cell lines, various tumor cell panels with in-depth genetic alteration and molecular profiles, useful cell lines for developing *in vivo* animal model, as well as primary cells and immortalized mammary epithelial cells. These tools can be used to address the newest identified genomic and clinical features of breast cancer subtypes.



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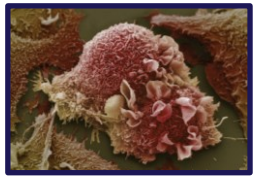
Thank you!

Register for more webinars in the ATCC "*Excellence in Research*" webinar series at www.atcc.org/webinars.

May 8, 2014
10:00 AM, 3:00 PM EST
Liz Kerrigan will discuss the importance of molecular standards, and how their use can contribute to improvements in assay reproducibility and reliability.



June 5, 2014
10:00 AM, 3:00 PM EST
Dr. Doug Storts and Dr. Yvonne Reid will discuss the recent advances in STR profiling technologies and how the Standard STR protocol is transforming scientific practices.

Thank you for joining today!
Please send additional questions to tech@atcc.org

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