

Introduction of MCF-7 breast cancer cells

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JNCI J Natl Cancer Inst (2015) 107(7): djv073

doi:10.1093/jnci/djv073

First published online March 31, 2015

Commentary

75TH ANNIVERSARY COMMENTARY

MCF-7 Cells—Changing the Course of Breast Cancer Research and Care for 45 Years

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- Generation of the MCF-7: Pleural effusion from a patient with metastatic breast cancer
- ER+ & PR+ & HER2-
- Most studied human breast cancer cell line: ~25,000 publications

- **MCF-7 and the Estrogen Receptor**
 - as one of a very few to express **substantial levels of ER** mimicking the majority of invasive human breast cancers that express ER
 - a stable cell line for understanding **intracellular binding constants**, **transport mechanisms**, and the mode of **nuclear uptake**
 - antibodies have been used in chromatin immunoprecipitation (**ChIP**) to define DNA binding sites of ER in target genes
 - also express androgen, progesterone, and glucocorticoid receptors
 - **steroid signaling pathways** & other pathways of **hormone response and resistance**
- **Estrogen stimulates MCF-7 cells to grow**
 - estrogen regulation of **growth factor signaling** and action; regulates the **cell cycle**
 - estrogen simultaneously **induces** and **represses** a large number of genes, indicating a complex **network** of changes that coordinate to alter growth
- **MCF-7 and HER2**
 - do **not** have amplification of the HER2 (ErbB2) oncogene
 - given potential cross-talk between ER and HER2, people generated MCF-7 cells that overexpress HER2
- **Genomics and Evolution of MCF-7 Cells**
 - disconcerting aspects of MCF-7 cells: ability to adapt and **evolve** over time
 - **Variants** of MCF-7: MCF-7L (Lippman), B (Benz), KO (Kent Osborne), and many more
 - behaved differently in biologic assays: gene expression and genomic profiles; karyotype differences; differences in genomic rearrangements
 - **heterogeneity** of MCF-7 in culture is indeed remarkable

Genetic variability in MCF-7 sublines: evidence of rapid genomic and RNA expression profile modifications

Mélanie Nugoli, Paul Chuchana, Julie Vendrell, Béatrice Orsetti, Lisa Ursule, Catherine Nguyen, Daniel Birnbaum, Emmanuel JP Douzery, Pascale Cohen and Charles Theillet ✉

BMC Cancer 2003 3:13 | DOI: 10.1186/1471-2407-3-13 | © Nugoli et al; licensee BioMed Central Ltd. 2003

Received: 6 December 2002 | Accepted: 24 April 2003 | Published: 24 April 2003

Table 1
Number of copy number alterations found in MCF-7 variants.

Variants	Gains	Losses	Total number of events
MCF-7-R	18	16	34
MCF-7-R-D4	17	22	39
MCF-7-R-G1	18	20	38
MCF-7-R-F3	17	22	39
MCF7-MVLN-sens	15	22	37
MCF7-MVLN-6ms7	16	24	40
MCF7-MVLN-6ms8	15	21	36
MCF-7-MF	12	23	35
MCF-7-O	14	20	34
MCF-7-MG	18	23	41
MCF-7-ATCC	11	17	28

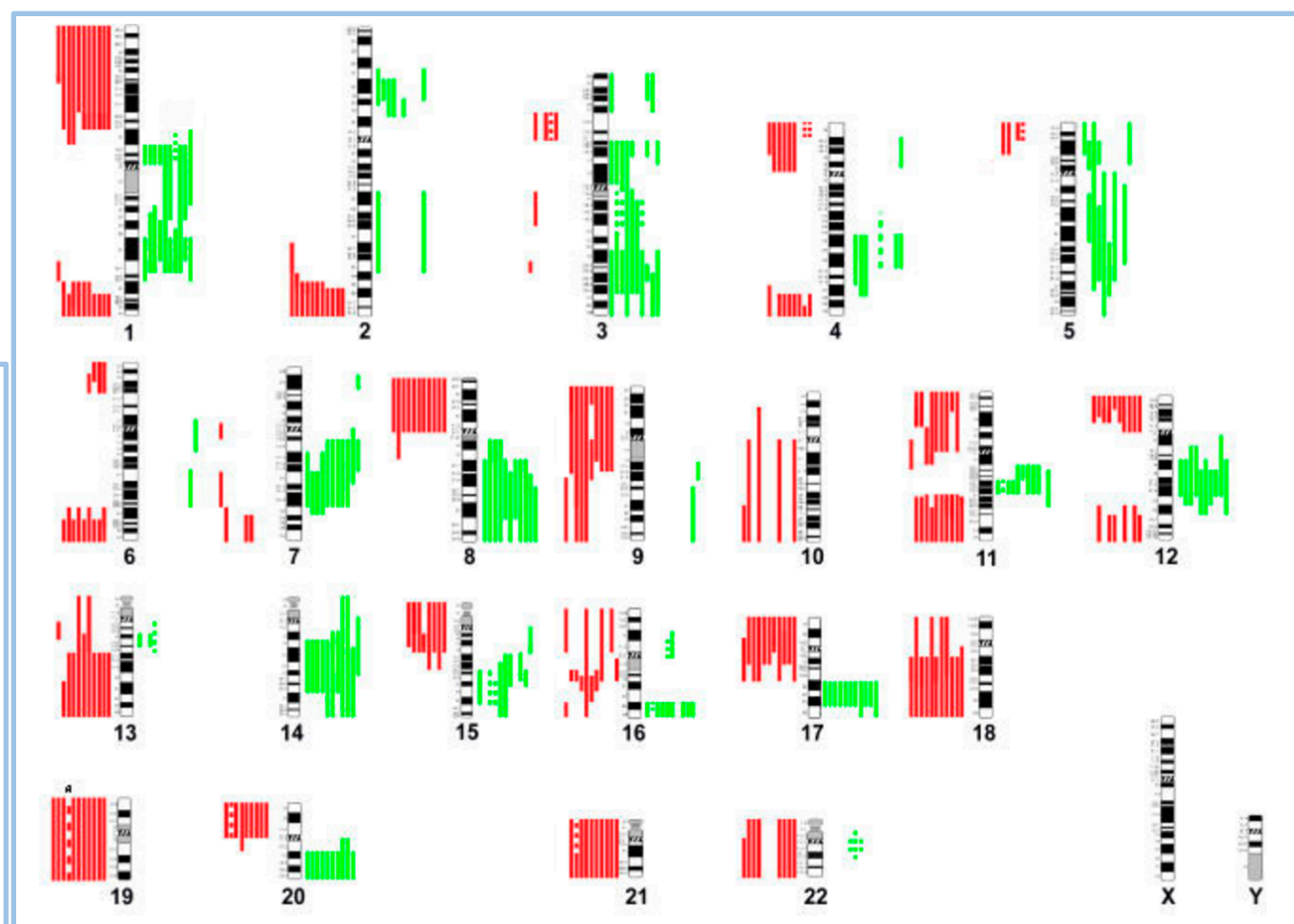
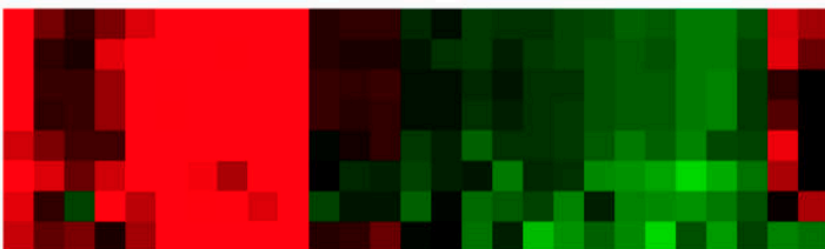
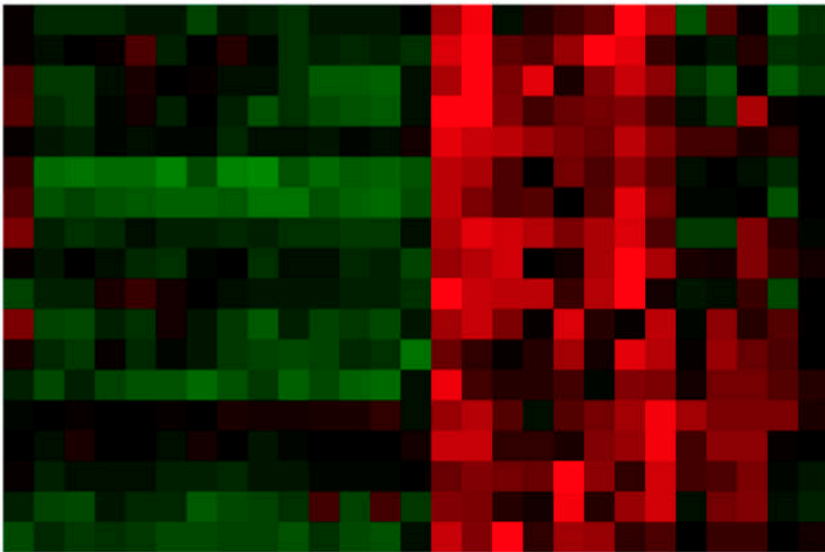
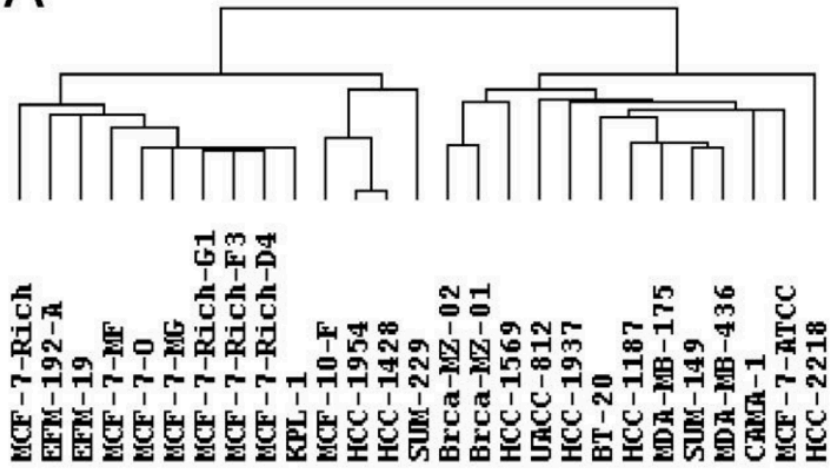


Figure 1

CGH profiles of 11 MCF-7 sublines. Copy number alterations are indicated as bars on each side of the chromosome ideograms, losses are shown by bars on the left, gains on the right. Each bar corresponds to an event observed in one subline. Events indicated by dotted lines corresponded to gains or losses reproducibly observed but whose fluorescence ratios did not reach the significance thresholds (1.3 or 0.75). Bars have been ordered from left to right for gains and from right to left for losses. The relative order was (1) MCF-7-R, (2) MCF-7-R-D4, (3) MCF-7-R-G1, (4) MCF-7-R-F3, (5) MCF-7-MVLN, (6) MCF-7-6ms7, (7) MCF-7-6ms8, (8) MCF-7-MF, (9) MCF-7-O, (10) MCF-7-MG, (11) MCF-7-ATCC.

A



B

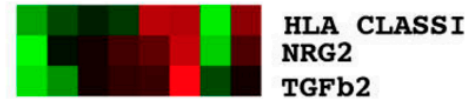
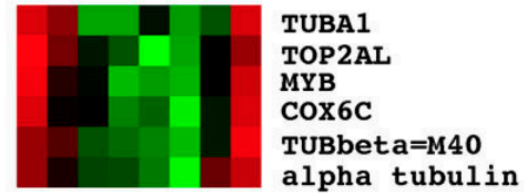
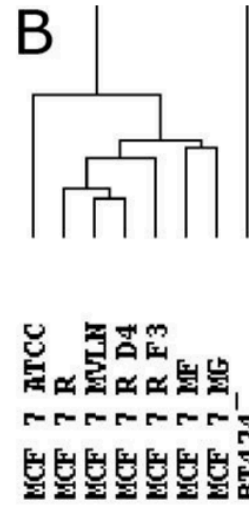
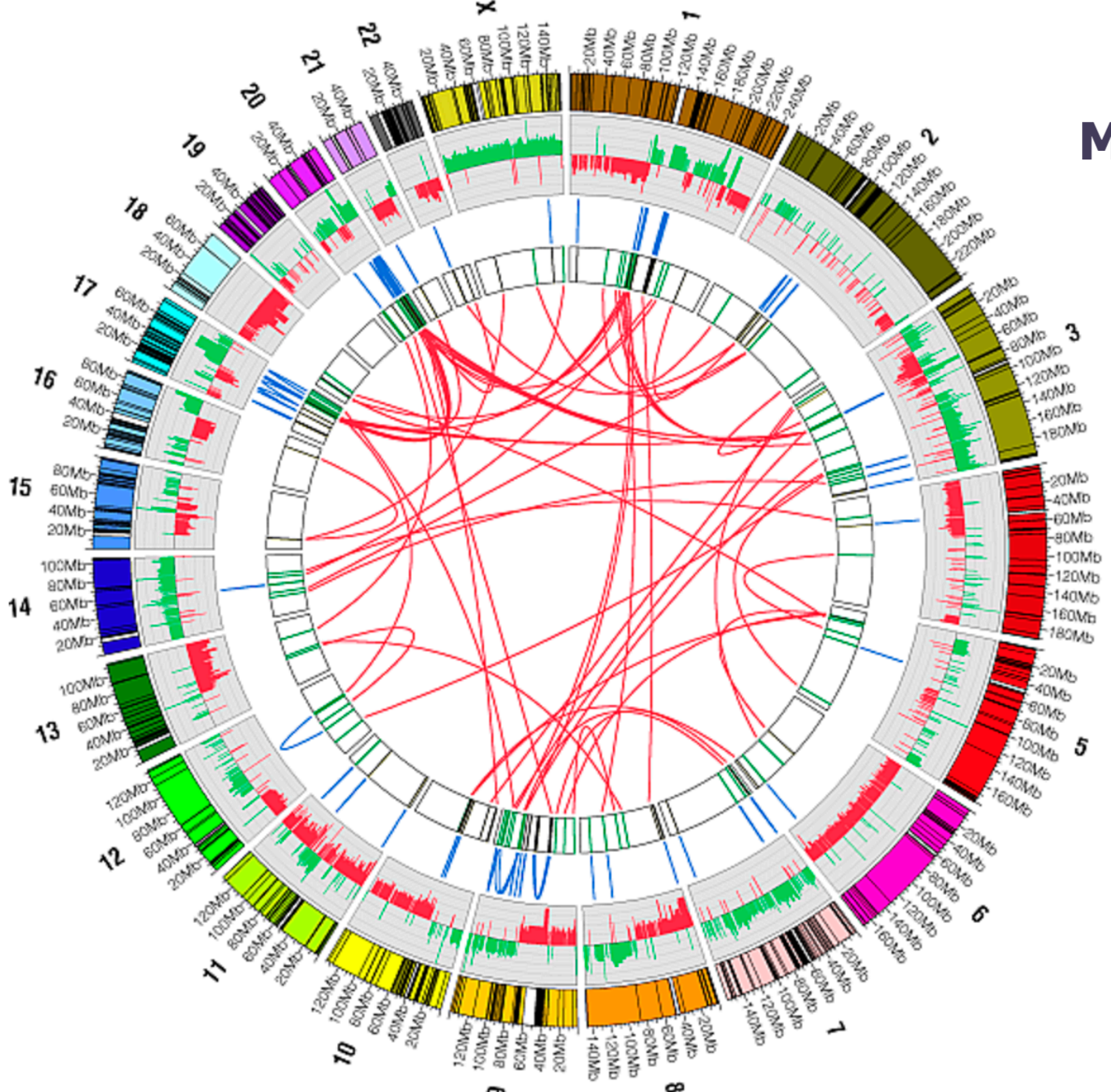


Figure 4 Hierarchical clustering of RNA expression profiles. Panel A clustering analysis of expression profiles of 8 MCF-7 sublines along with those of 19 breast cancer cell lines. Expression profiling was done using home made Nylon arrays comprising 721 cDNAs corresponding to identified genes localized on either chromosome 1q or 17q. Panel B clustering analysis of profiles of 7 MCF-7 sublines and the BT-474 breast cancer cell line. Nylon arrays comprised 1034 genes selected on the basis of their involvement in cancer.

MCF-7 Breast Cancer Genome Analysis



- Chromosomes are individually colored with centromeres in white and Low Copy Repeat (LCR) regions in black.
- MCF-7 BAC array Comparative Genome Hybridization data (Jonsson et al. 2007) is plotted with gains in green and losses in red using \log_2 ratio.
- The inner chromosome annotations depict 157 somatic MCF-7 breast tumor chromosomal rearrangements associated with LCRs (black) and breakpoints not associated with LCRs (green).
- Chromosomal rearrangements are depicted on each side of the MCF-7 breakpoints; intra-chromosomal rearrangements (blue) are located outside
- inter-chromosomal rearrangements (red) are located in the center of the circle.

Mutations from CCLE

Mutations in MCF7

Showing 1 to 50 of 52 entries

Gene	Protein Change	Chr	Start	End	Sample	NCBI Build	Variant Classification	Variant Type	Reference Allele	Tumor Allele 1	dbSNP ID
TRIM33		1	114940211	114940212	MCF7_BREAST	37	3'UTR	Ins	-	T	rs66490349
KRAS		1	153665919	153665920	MCF7_BREAST	37	3'UTR	Ins	-	C	rs66682713
CDK11B	p.PPLPGAGIPPP939del	1	240370914	240370946	MCF7_BREAST	37	In_Frame_Del	Del	GCCCC...	-	rs4997328;rs4997329
CACNB2		10	18828721	18828722	MCF7_BREAST	37	3'UTR	Ins	-	AA	rs3841459
ERCC6	p.V83I	10	50740764	50740764	MCF7_BREAST	37	Missense_Mutation	SNP	C	T	
CTBP2	p.K974fs	10	126678123	126678123	MCF7_BREAST	37	Frame_Shift_Del	Del	T	-	
TCERG1L	p.E435fs	10	132915153	132915153	MCF7_BREAST	37	Frame_Shift_Del	Del	T	-	
ILK		11	6630029	6630029	MCF7_BREAST	37	Intron	Del	C	-	
MAML2	p.604_607QQQQ>Q	11	95825375	95825383	MCF7_BREAST	37	In_Frame_Del	Del	TGCTG...	-	rs113349418

- **10 most significantly mutated genes from 800 WXS analysis in TCGA**
 - PIK3CA, TP53, MAP3K1, MAP2K4, GATA3, MLL3, CDH1, PTEN, PIK3R1, RUNX1
 - **Present:** PIK3CA, MAP3K1,
 - **Absent:** TP53, MAP2K4, GATA3, MLL3, CDH1, PTEN, PIK3R1, RUNX1