Cell Line Identity Update

Based on data from projects supported by the DTP Molecular Targets program, our classification of several cell lines has changed.

MDA-MB-435 and MDA-N are Melanoma cell lines, not breast cancer cell lines.

MDA-MB-435, a member of the NCI-DTP panel of 60 human tumor cell lines, has been used for decades as a model of metastatic human breast cancer. This cell line was derived at M.D. Anderson in 1976 from a pleural effusion from a 31-year old woman with a history of breast cancer (Cailleau R, Olive M, Cruciger QV. Long-term human breast carcinoma cell lines of metastatic origin: preliminary characterization. In Vitro. 1978 Nov;14(11):911-5.; Brinkley BR, Beall PT, Wible LJ, Mace ML, Turner DS, Cailleau RM. Variations in cell form and cytoskeleton in human breast carcinoma cells in vitro. Cancer Res. 1980 Sep;40(9):3118-29.) Further background information on this cell line may be found at the M.D. Anderson Breast Cancer Cell Line Database.

Recent advances in gene expression analysis allow the opportunity to more fully characterize tumor cell lines. Analysis of MDA-MB-435, in conjunction with the rest of the NCI60 panel, revealed that the pattern of gene expression for MDA-MB-435 more closely resembled that of melanoma cell lines than of other breast tumor lines (Ross et al. Systematic variation in gene expression patterns in human cancer cell lines. Nat Genet 2000 Mar;24(3):227-3.)

These findings prompted Ellison et al. to undertake a more detailed study of the characteristics of MDA-MB-435 (Ellison G, Klinowska T, Westwood RF, Docter E, French T, Fox JC. Further evidence to support the melanocytic origin of MDA-MB-435. Mol Pathol. 2002 Oct;55(5):294-9.). They measured expression of several breast-specific genes and several melanoma-specific genes in MDA-MB-435 (obtained from the American Type Culture Collection), as well as in other breast tumor cell lines, melanoma cell lines and normal breast. Breast-specific genes were not detectably expressed in MDA-MB-435 or in the melanoma lines, but were detected in most of the breast tumor cell lines as well as normal breast. However, melanocyte-specific genes were expressed in MDA-MB-435, as well as in most of the melanoma lines, but were not detectable in the other breast tumor cell lines. Additionally, xenografts of MDA-MB-435 implanted into mammary fat pads of female SCID mice showed immunohistochemical staining consistent with melanocytic origin.

More recently single nucleotide polymorphism (SNP) array analysis revealed that MDA-MB-435 is derived from the same individual as the melanoma cell line M14 (Garraway LA, et al. Integrative genomic analyses identify MITF as a lineage survival oncogene amplified in malignant melanoma. Nature. 2005 Jul 7;436(7047):117-22.; http://www.sanger.ac.uk/genetics/CGP/NCI60/).

The NCI Developmental Therapeutics Program obtained MDA-MB-435 from Dr. Patricia Steeg (NCI) — Dr. Steeg obtained the line from M.D. Anderson. The DTP has obtained DNA fingerprinting analysis of the MDA-MB-435 in the DTP repository, as well as MDA-MB-435 from the ATCC (which obtained their sample from M.D. Anderson). DNA fingerprinting on all MDA-MB-435 samples are consistent with their derivation from the same

individual. Thus the mix-up with the melanoma cell line M14 likely happened early in the history of the cell line.

Note added 8/5/2009: The panel designation for this cell line continues to be a topic for discussion, as seen in a recent publication by Chambers. (MDA-MB-435 and M14 cell lines: identical but not M14 melanoma? Cancer Res. 2009 Jul 1;69(13):5292-3.)

Note added 8/2007: A recent publication by Rae et al. used karyotype, CGH, and microsatalite polymorphism analyses, combined with bioinformatics analysis of gene expression and SNP data and concluded that "All currently available stocks of MDA-MB-435 cells are derived from the M14 melanoma cell line." (Rae JM et al. MDA-MB-435 cells are derived from M14 Melanoma cells — a loss for breast cancer, but a boon for melanoma research. Breast Cancer Res Treat. 2007 Jul;104(1):13-9.)

Note added 8/2011: Identifiler DNA profiling confirms that MDA-N is derived from MDA-MB-435, and we therefore consider MDA-N to be a melanoma cell line.

CNS cell lines SNB-19 and U251 are derived from the same individual.

Single nucleotide polymorphism (SNP) array analysis has demonstrated that the SNB-19 and U251 lines are derived from the same individual. (Garraway LA, et al. Integrative genomic analyses identify MITF as a lineage survival oncogene amplified in malignant melanoma. Nature. 2005 Jul 7;436(7047):117-22. ;).

Cell Line NCI/ADR-RES is an Ovarian tumor cell line, not a Breast line.

In 1986 Batist et al. (1) developed an adriamycin-resistant cell line, termed MCF-7/ADR-RES intended to be derived from the breast tumor cell line MCF-7. This cell line expresses high levels of MDR1 and P-glcyoprotein (2, 3), and given it's utility in identifying compounds subject to multi-drug resistance, was introduced into the NCI 60 human tumor cell line anti-cancer drug screen. However, in 1998, Scudiero et al (4) reported that DNA fingerprinting of MCF-7 and MCF-7/ADR-RES lines were inconsistent with these two lines having been derived from the same individual. Thus MCF-7/ADR-RES was renamed NCI/ADR-RES.

New data sheds light on the origin of the NCI/ADR-RES line. Spectral karyotyping of the 59 cell lines currently in the drug screen panel demonstrates that the Ovarian tumor cell line OVCAR-8 shares a large number of karyotypic abnormalities with the NCI/ADR-RES line (5). These abnormalities include many complex chromosomal rearrangements involving multiple chromosomes. These rearrangements are not shared by any of the other cell lines in the panel. Both of these cell lines exhibit profound chromosomal instability, thus even though they share many rearrangements, there are also considerable differences in their karyotypes. To see images of the karyotypes, click here. Ideograms for all 59 cell lines can be viewed at the NCBI SKY database at: http://www.ncbi.nlm.nih.gov/sky/.

In support of the karyotypic analysis, NCI obtained DNA fingerprinting analysis on these cell lines. Orchid Cellmark analyzed short tandem repeats by PCR at 14 loci. OVCAR-8 and NCI/ADR-RES are identical at 13/14 loci. Data from the remaining locus are consistent with loss of heterozygosity in NCI/ADR-RES. In contrast,

MCF-7 fingerprinting demonstrated it was unrelated to OVCAR-8 or NCI/ADR-RES. Thus DNA fingerprinting support OVCAR-8 and NCI/ADR-RES as being derived from the same individual.

Furthermore, gene expression patterns indicate very similar patterns of gene expression, apart from the high levels of MDR1 and Pgp seen in NCI/ADR-RES. Cluster analysis of microarray expression data showed OVCAR-8 and NCI/ADR-RES clustering tightly with one another (6).
More recently single nucleotide polymorphism (SNP) array analysis confirmed that the NCI/ADR-RES line is derived from the same individual as the ovarian line OVCAR-8 (Garraway LA, et al. Integrative genomic analyses identify MITF as a lineage survival oncogene amplified in malignant melanoma. Nature. 2005 Jul 7;436(7047):117-22.; http://www.sanger.ac.uk/genetics/CGP/NCI60/).
The conclusion that must be drawn is that the NCI/ADR-RES line is in fact derived from the ovarian cell line OVCAR-8.

References

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