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Comment Re: MDA-MB-435 and M14 Cell Lines: Identical but not M14 Melanoma?

To the Editor:

In support of the recent article by Chambers (1), we wish to share our data on the origin of the MDA-MB-435 and M14 cell lines. Chambers claims that it is most plausible that both cell lines represent MDA-MB-435 based on two X chromosomes in the MDA-MB-435 karyotype, whereas M14 had been derived from a man (1). However, karyotyping does not discriminate between paternal and maternal alleles and thus does not exclude loss of the Y chromosome combined with reduplication of the X chromosome. We previously reported an allelotype on human breast cancer cell lines, including MDA-MB-435 (2). Our analyses did not detect Y chromosome sequences and revealed heterozygosity of polymorphic microsatellite markers at Xp, implying that MDA-MB-435 had indeed been derived from a woman. Our MDA-MB-435 cell line was obtained directly from American Type Culture Collection at passage 239 and M14 from its originator at passage 10 (3). We confirmed that the cell lines were identical by microsatellite analysis, in concordance with Rae and colleagues (4), and we also identified unique mutations in the *p53* and *p16* genes in both cell lines (3). Altogether, it can be concluded conclusively that MDA-MB-435 and M14 are breast cancer cell lines.

The melanocytic phenotype of MDA-MB-435 may be explained by our recent molecular characterization of MDA-MB-435 and 40 other human breast cancer cell lines (3). Microarray gene expression profiling had revealed two major subgroups among the breast cancer cell lines: luminal type and basal type. As anticipated, MDA-MB-435 was basal type, along with 14 other cell lines, and unsupervised hierarchical clustering showed strong similarity among the basal-type cell lines. It is unlikely that the 15 basal-type cell lines all are of melanocytic origin because 4 of them carry a *BRCA1* mutation and 1 has the *CHEK2* 1100delC mutation. Also, 10 of the basal-type cell lines, including MDA-MB-435, are of the normal-like intrinsic subtype; a molecular subtype that had been defined on (uncultured) clinical breast tumors. Most interestingly, analysis of the genetic status of 27 well-known cancer genes in our collection of breast cancer cell lines identified two subtype-specific gene mutation profiles (3). The basal mutation profile involved mutations in the *BRCA1, RB1, RAS*, and *BRAF* genes and deletions of *p16* and *p14ARF*. Particularly, the combination of mutations in *p16, RB1*, and *RAS* pathway genes is characteristic for melanoma. These results thus suggest that basal-type breast cancers may have a genetic basis similar to melanomas, explaining their melanocytic phenotype and perhaps also their rather aggressive clinical course.

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Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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