

Molecular characterization of male breast cancer by standardized quantitative RT-PCR analysis: First large genomic study of 347 male breast cancers compared to 82,434 female breast cancers.

Author(s): S. Shak, G. Palmer, F. L. Baehner, C. Millward, D. Watson, G. W. Sledge; Genomic Health, Redwood City, CA; Indiana University School of Medicine, Indianapolis, IN

Background: Because male breast cancer (BC) is rare, there is little known about the disease and treatment is extrapolated from female BC. Newer molecular technologies have not been used to profile male BC. We report here a study of quantitative gene expression by gender status in tumor specimens submitted for Recurrence Score testing.

Methods: All estrogen receptor positive tumor specimens successfully examined in the Genomic Health laboratory from June 2004 through December 2008 were included. Quantitative expression for each gene was measured by the 21 gene oncotype DX assay on a scale from 0 to 15 (relative to reference genes), where a one unit increment is associated with a 2-fold change in expression.

Results: There were 347 male and 82,434 female BCs. The males were older (mean age 63.8 vs 57.4 yrs). Standard histopathology was similar, although slightly more male BCs were ductal (83% vs 78%). Like female BC, there was a wide variation in gene expression in male BC. The distribution of RS in males and females was similar - RS mean (\pm SD) 18.1 (\pm 11.2) in males and 19.1 (\pm 10.2) in females ($p = \text{NS}$). The proportion of tumors with RS <18 , 18 - 30, and ≥ 31 was 53.6%, 35.2%, and 11.2% in males and 53.4%, 36.3%, and 10.3% in females. Although the patterns of expression of the Oncotype DX genes were more similar than different in males and females some differences were notable. Mean expression of ER, PR, and SCUBE2 were 0.5 units higher in males. Mean expression of the proliferation genes, Ki-67, MYBL2, Survivin, Cyclin B1, and STK15, were 0.5 units higher in males. Mean expression of STMY3 was 0.9 units higher in males. Of note, whereas the level of quantitative ER significantly increased with increasing patient age in females (0.4 units per decade), little increase was observed in males (<0.1 units per decade).

Conclusions: This large genomic study of male BC reveals a heterogeneous biology as measured by the standardized quantitative oncotype DX breast cancer assay, similar to that observed in female BC. Some differences, which may reflect the differences in hormone biology between males and females, were noted and deserve further study.