Gene predictive signature associated with ductal carcinoma in situ progression to invasive breast cancer

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A big challenge in oncology is to discriminate which breast cancer patients with non-invasive ductal carcinoma *in situ* (DCIS) would benefit from minimal clinical interventions versus those who require a more traditional treatment. Identification of molecular alterations that take place before (early stage) and after (late stage) the invasion process is crucial to better understand DCIS progression. Thus, to assess molecular alterations in the early and late stages of invasion, epithelial cells were captured by laser microdissection from the *in situ* component of pre-invasive lesions—pure DCIS and the *in situ* component that co-exists with invasive breast carcinoma lesions (DCIS-IBC)—and from *in situ* and invasive areas in the same specimen. We used cDNA microarray and RASH libraries for detecting robust and subtle differences in gene expression among the groups. For RT-qPCR validation, we included additional samples validating a gene signature composed of twenty-six genes, twenty differentially expressed in the early stage and six differentially expressed in the late stage of DCIS progression. The expression profile of the early stage was clearly marked by a preferential downregulation of invasion ability and was also capable of accurately segregating epithelial cells captured from the *in situ* component of DCIS-IBC from those captured from pure DCIS, implying that these genes are differently modulated in pre-invasive lesions with distinct malignant capacity. In contrast, the expression profile of the late stage was not able to discriminate epithelial cells from the morphologically different lesions (*in situ* and invasive components). Integrated analysis of the validated genes revealed networks enriched in gene categories related to cell death and survival, cell signaling, cellular function and maintenance. Altogether, this study showed that molecular changes occur before morphological manifestation of invasion and revealed a gene expression signature with potential for predicting DCIS progression, thereby providing options for tailoring the treatments of DCIS patients. Increasing evidence has been showing a critical role of the microenvironment in tumor progression, especially the interaction of myoepithelial-epithelial cells. Subsequently, our next concern will be to assess the transcriptional profile of myoepithelial cells in both pre-invasive lesions by RNAseq.