The goal of this study was to identify potential biomarkers in DCIS that might predict risk of disease progression, i.e., risk of invasiveness. They performed gene expression profiling of six cases each of pure DCIS, pure invasive ductal carcinoma (IDC), and IDC with an associated DCIS component; as well as three cases of non-neoplastic breast tissue. They found that pure DCIS had the most altered gene expression profile; and propose three genes as potential biomarkers of DCIS progression. This is an interesting study with analysis of a lot of data. However, the number of cases studies is small with sweeping conclusions. Furthermore, there is a bias towards more biologically aggressive tumors. Of the pure invasive carcinomas, only 1 of 6 is a luminal A and 3 of 6 are grade 3 tumors. All pure DCIS cases were grade 3. Of the IDC with a DCIS component, no luminal A tumors were included. 4 of the 6 IDC were grade 3 tumors and 4 of the 6 DCIS components were nuclear grade 3 (high grade). This paper might be more appropriate as a much shorter Preliminary Communication.

Specific Comments:

1. At the bottom of Table 1, it has "IDC-IDC with in situ component". Did the authors mean to have "IDC-DCIS"

2. Reference 12. Why use the 7th edition of the AJCC Cancer Staging Manual when the 8th edition has been out for 2 years?

3. Reference 13. Why use WHO Classification of Tumors published in 2003 rather than the more recent one published in 2010?
4. Materials and Methods. Study population. Why use clinical staging rather than pathologic staging?

5. Figure Captions. figure 2. "... most likely involved in the acquisition of pure DCIS invasive capacity" What does that mean? Do the authors mean "invasive capacity of pure DCIs"

6. Figure 5. What is "primary tumor"? What is "BC stages"?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

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