# THE MOLECULAR MECHANISMS OF CARCINOMA IN SITU EVOLUTION INTO INVASIVE DUCTAL BREAST CARCINOMA

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## INTRODUCTION

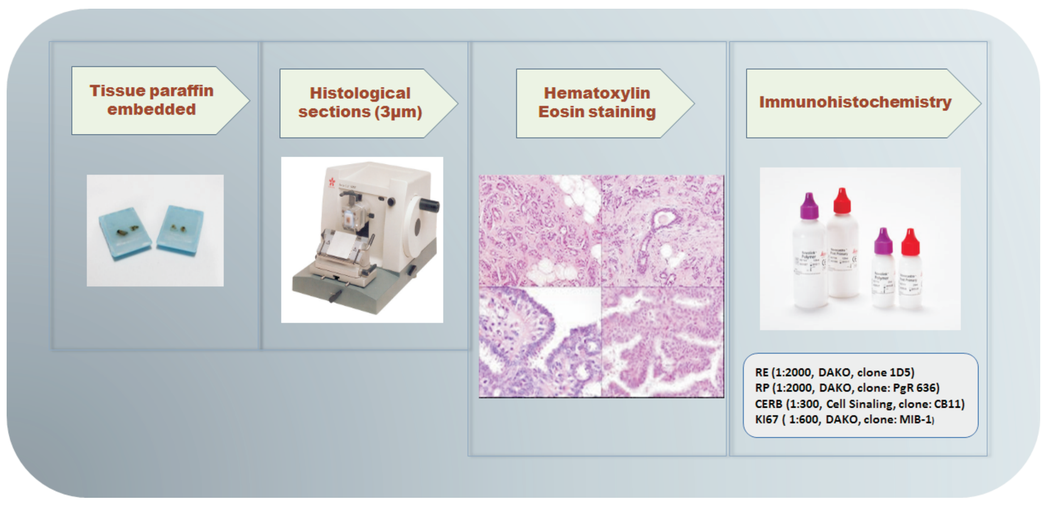
Breast cancer is the most frequent type of cancer in women and is responsible for high mortality rates in Brazil and worldwide. It is a heterogeneous tumor whose aberrant genes expression confer aggressiveness and a variety of clinical manifestations. Four intrinsic subtypes of Invasive Ductal Carcinoma (IDC), based on cellular receptors expression have been evidenced: Luminal; Luminal - HER2; HER2; triple Negative. This classification is important in the choice of therapy for each group of patients. Ductal Breast Carcinoma In Situ (DCIS) can be defined as an atypical epithelial proliferation with limited growth by the basal membrane of the ductal epithelium with no evidence of stromal invasion. The characteristics of the intrinsic subtypes of ICD have been used more recently to categorize DCIS based on cell proliferation (Ki67), Estrogen Receptor (ER) and HER2 epidermal growth receptor expression by immunohistochemistry. Unpublished data from the group have shown changes in the expression patterns of the c-jun, c-fos, and c-myc oncoproteins in the subtype of Luminal A breast neoplasm, all involved in cell proliferation and survival, suggesting these transcription factors may be potential regulators of an evolution that could be from DCIS to ICD.

## OBJECTIVE

In the sense that to analyze whether these transcription factors could be favoring the progression of DCIS to ICD the objective of the work is to evaluate gene and protein expression of these factors in different subtypes of BC tumors and also in normal ductal tissue.

## METHODOLOGY

The initial cohort included fifteen tissue specimens previously fixed and paraffin embedded from patients with DCIS. Biopsies were submitted to staining by hematoxylin eosin (HE) to corroborate diagnosis. Immunohistochemical labeling with antibodies that recognize ER, Progesterone (PR), HER2 and proliferation were analyzed.




## PRELIMINARY RESULTS

Hematoxilin Eosin staining showed presence of exacerbated glandular proliferation, nuclear pleomorphism, presence of microcalcification areas and necrosis in several cases. All patients presented ER positivity (90%). Only one patient did not present PR positivity (64%). 5 patient samples will be subjected to FISH labeling to confirm Her2 overexpression.

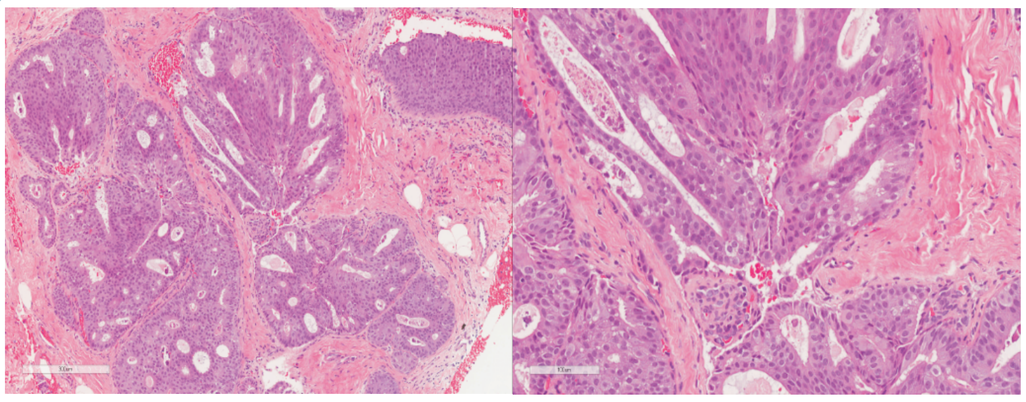


**Figure 1. Eosin Hematoxilin staining of patients diagnosed with ductal carcinoma in situ (DCIS) showed significant glandular proliferation, presence of microcalcification and mild pleomorphism.** (A)100X (B) 200X.

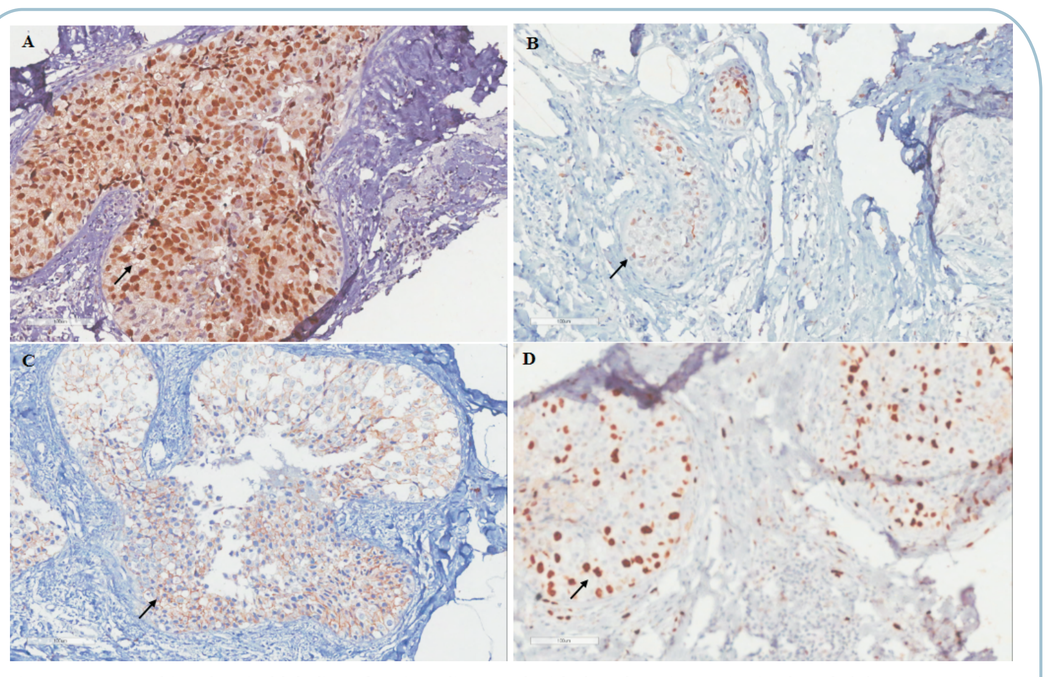



**Figure 3. Immunohistochemical labeling of patient diagnosed with ductal carcinoma in situ (DCIS).** (A) Positive nuclear staining for ER. Percentage of positivity: 100%. (B) Positive nuclear staining for PR. Percentage of positivity: 10%. (C) Positive membrane staining for HER2. Score: 2+. (D) Positive nuclear staining for Ki67. Percentage of positivity: 30%.

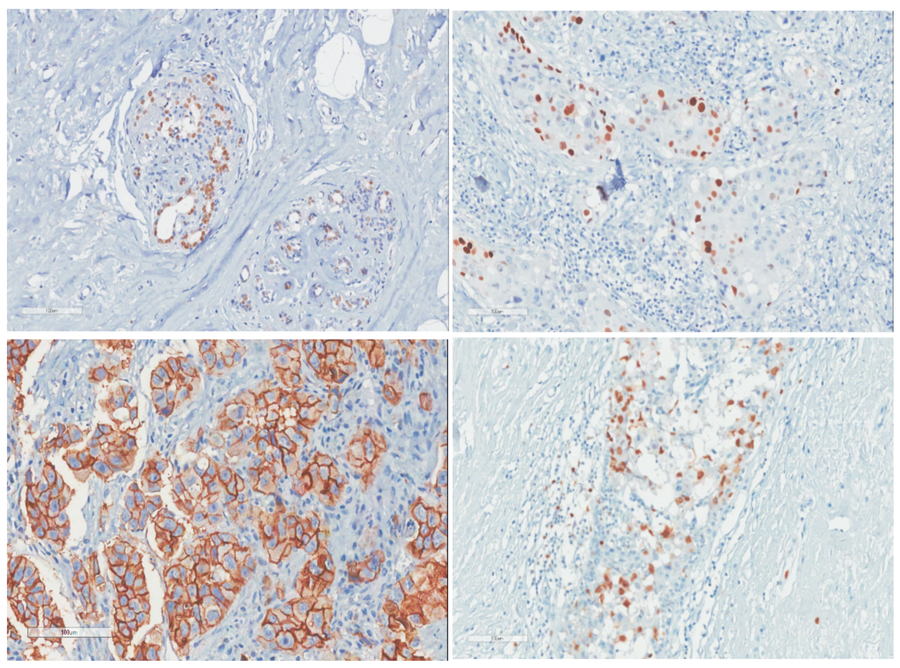


**Figure 2. Immuhistochemical's reaction control in invasive carcinoma.** (A) Positive nuclear staining for ER. Percentage of positivity: 67%. (B) Positive nuclear staining for PR. Percentage of positivity: 45%. (C) Positive membrane staining for HER2. Score: 3+. (D) Positive nuclear staining for Ki67. Percentage of positivity: 40%.

**Table 1 Data from patients with DCIS evaluated to date**

| Samples 2012-2018 | Age (Average 49) | Grade | ER | PR | CERB | Ki67 |
|---|---|---|---|---|---|---|
| 1 | 50 | 1 | 80 | 100 | 0 | 5 |
| 2 | 43 | 2 | 90 | 90 | 0 | 2 |
| 3 | 44 | 3 | 80 | 80 | 1 | 5 |
| 4 | 47 | 2 | 80 | 60 | 0 | 10 |
| 5 | 47 | 3 | 100 | 100 | 0 | 2 |
| 6 | 51 | 2 | 100 | 90 | 0 | 1 |
| 7 | 43 | 3 | 100 | 60 | 3 | 10 |
| 8 | 61 | 1 | 80 | 20 | 0 | 1 |
| 9 | 43 | 3 | 90 | 40 | 0 | 2 |
| 10 | 57 | 2 | 100 | 10 | 2 | 30 |
| 11 | 55 | 3 | 100 | 90 | 1 | 2 |
| 12 | 63 | 1 | 100 | 70 | 2 | 2 |
| 13 | 54 | 3 | 80 | 0 | 0 | 30 |
| 14 | 60 | 3 | 100 | 80 | 0 | 2 |
| 15 | 25 | 2 | 90 | 80 | 0 | 30 |

## CONCLUSION

Preliminary results suggest that DCIS already presents morphological characteristics similar to IDC and new microenvironmental assessments will precede to molecular analysis that may predict whether in situ carcinoma tends to invade.

Support: INCA/MS, FAPERJ and CNPq.
Key words: Breast Cancer, Carcinoma in situ, Hormonal Receptors, Proliferation

**Projeto Gráfico: Setor de Edição e Informação Técnico-Científica / INCA**

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