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## Carbonic anhydrase expression in DCIS

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## Keywords

Carbonic anhydrase, CA IX, CA XII, DCIS, hypoxia, MIB1, necrosis

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## Context

Hypoxia has been associated with biologically aggressive tumors, possibly through upregulation of hypoxia-inducible genes. The authors recently identified two hypoxia identifiable genes, carbonic anhydrase (CA) *CA IX* and *CA XII*, in epithelial tumor cell lines. In this study, the researchers attempted to correlate expression of these genes with benign, preinvasive, and invasive carcinomas of the breast as well as with proliferative activity and mammographically detected calcification.

## Significant findings

CA XII protein was found in normal breast tissue and benign lesions. CA IX protein expression was focally present and specifically associated with areas of necrosis and high grade lesions. In contrast, CA XII protein expression was typically homogeneous and associated with lack of necrosis and low grade lesions. Neither marker was significantly associated with proliferative activity. The authors demonstrated a significant relationship between mammographically detected calcification and reduced CA XII protein levels. Although no such relationship existed when correlating CA IX protein levels with calcification, there was a trend toward increased CA IX protein in those cases where linear-type calcifications were present. Finally, the presence of both markers in 29-71% of invasive lesions associated with ductal carcinoma *in situ* (DCIS) suggests that these CAs may also play a role in the development of invasive carcinomas of the breast.

## Comments

Correlating CA expression with necrosis and nuclear grade suggests that CA IX (but not CA XII) expression is influenced by hypoxic state of the DCIS. As neither marker was associated with proliferation, there may not be a direct correlation between hypoxia or necrosis and proliferative activity. The mammographic findings suggest divergent roles for these markers in the development of mammographically detected calcification. While CA XII may be important in the initial formation of calcification, the presence of CA IX near the ductal lumen may influence the pattern of calcification. Additional studies are needed to verify this hypothesis. CA IX and CA XII proteins were detected in cases of invasive breast cancer, suggesting that these markers may have prognostic significance for certain forms and/or stages of breast cancer. This needs to be confirmed with additional studies of larger numbers of patients with significant clinical follow-up. Although speculative, *in vitro* studies of these markers in other forms of invasive cancer suggest that therapeutic manipulation of these CAs may have clinical benefits.

## Methods

Western blotting, immunohistochemistry

## Additional information

## References

1. Wykoff CC, Beasley N, Watson PH, Campo L, Chia SK, English R, Pastorek J, Sly WS, Ratcliffe P, Harris AL: Expression of the hypoxia-inducible and tumor-associated carbonic anhydrases in ductal carcinoma *in situ* of the breast. *Am J Pathol* . 2001, 158: 1011-1019.