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# Clusterin in human breast cancer

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## Keywords

Breast cancer, clusterin, immunohistochemistry, metastasis

# Introduction

Clusterin is an 80 KDa protein encoded by a gene located on chromosome 8 (8p21). It is highly conserved across species and shows wide tissue distribution. It is implicated in a variety of activities such as programmed cell death, regulation of complement mediated cell lysis, membrane recycling, cell-cell adhesion and src induced transformation. As a part of the MAC of complement, it acts as a complement inhibitor. Based on this role, it was postulated that tumors overexpressing clusterin may evade destruction by complement system and progress to more aggressive tumors.

# Aims

To evaluate expression of clusterin in benign, premalignant lesions, invasive and metastatic breast cancer. To study the relation of clusterin to other factors such as hormone receptors, proliferation and apoptosis and clinical outcome.

# Comments

This preliminary study evaluated the expression of clusterin, an inhibitor of membrane attack complex (MAC) of complement system, in breast cancer. As the authors hypothesized, its expression was significantly higher in more advanced lesions and was associated with several poor prognostic factors. However, it was not a predictor of clinical outcome. Lack of information regarding adjuvant therapy made it difficult to separate prognostic from predictive interactions in this study. The data showing lower apoptotic rate in clusterin overexpressing tumors are interesting and worth further exploration. Overall, clusterin is still a poorly understood protein, which appears to be involved in a multitude of functions and may be very useful in the study of tumor development and progression.

# Methods

Breast samples from 40 normal breasts, 42 benign lesions, 20 atypical hyperplasias, 35 *in situ* carcinomas, 114 invasive, and 40 metastatic breast cancers were studied using immunohistochemistry (IHC; monoclonal antibody E5) and *in situ* hybridization (ISH). In addition, hormone receptors, proliferation and apoptosis (TUNEL) were also evaluated. Greater than 10% staining was considered positive.

# Results

Clusterin signal was mainly seen in the cytoplasm of tumor samples. Normal breast epithelium did not express clusterin. Clusterin was found in 19% of benign, 47% of atypical hyperlasias, 49% *in situ*, 53% invasive and 80% metastatic tumors. In 67% of cases with clusterin negative primary cancer, metastatic tumors were positive. Of the clusterin positive primary cancers, 88% were also positive at the metastatic site. ISH and IHC results were concordant. Clusterin expression was significantly related to bad prognostic factors such as high histologic grade, larger tumor size, negative hormone receptor and lower apoptosis index. Clusterin was not related to clinical outcome in uni- or multivariate analysis.

# Discussion

Overexpression of clusterin is more common in the late stages of mammary tumor progression. Although inhibition of MAC of complement may be an explanation for these results, lower apoptosis in clusterin positive tumors could also be involved. However, the exact mechanism of clusterin function and its possible role in tumorigenesis remains unclear.

## References

1. Redondo M, Villar E, Torres-Munoz J, Tellez T, Morell M, Petito CK: Overexpression of clusterin in human breast cancer. Am J Pathol. 2000, 157: 393-399.