



# Tumor inactivation of E-cadherin: a new tool for breast cancer treatment?

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E-cadherin protein has a critical role for establishing and maintaining polarized and differentiated epithelia through intercellular adhesion complexes.

This molecule is considered an invasion suppressor, and its deregulation is often found in advanced cases of some epithelial carcinoma (1).

Deletion or deregulation of E-cadherin is correlated with the infiltrative and metastatic ability of the tumor, believed to be because of disruption of the cadherin-catenin complex with the consequent loss of cell adhesion and concomitant increase in cell motility (2,3).

In clinical practice, E-cadherin expression is evaluated to confirm lobular histopathology in breast cancer. Lobular breast tumors with low or absent E-cadherin expression are associated with high hormone receptors expression (estrogen and progesterone receptors) (4).

However, E-cadherin is not only a target to distinguish ductal carcinoma from lobular breast cancer. This obsolete concept should be abandoned.

In fact, a recent multicentric study on 5,933 female invasive breast cancers, demonstrated that E-cadherin low expression is significantly associated with poorly differentiated tumors, high tumor size volume (>T2), and HER2 negative expression (5).

The association with larger and low-grade tumors is due to the aggressiveness pattern of breast tumor in absence of E-cadherin function.

Instead the complex E-cadherin /HER2 is an important emerging molecular target for breast cancer care. Other study demonstrated that in lobular breast cancer E-cadherin

performs heterodimers with HER2 receptor (6). In particular, the presence of E-cadherin plus ERBB2 somatic mutations leads to a worse prognosis in lobular breast cancer (7). Instead the E-cadherin/HER2 negative association is not associated with breast cancer specific survival (5). This synergic effect of E-cadherin/ERBB2 complex is still not well clarified. It seems that inactivation of E-cadherin leads to an over-expression of HER2 with a worse impact on cancer prognosis. E-cadherin/HER2 heterodimer complex represents valid biomarkers for targeted therapies against breast cancer, never consider to date.

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## Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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