

## PI-PLC beta2 expression in breast cancer evolution

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Despite the great advances that have been made over the last 20 years in its early detection and treatment, breast cancer remains one of the most frequently diagnosed malignancy and a leading cause of cancer-related deaths in women worldwide. Since the majority of breast cancer deaths occurs as a result of metastasis rather than from the effects of the primary lesion, markers useful to predict breast cancer evolution from carcinoma *in situ* to invasive tumor are crucial for the management of patients with breast diseases. Although several features have been recognized as having prognostic use in invasive tumors, at present, no marker has been clearly associated with the progression of breast lesions from *in situ* to invasive.

Among the intracellular signal transduction molecules, the phosphoinositide-dependent phospholipases C (PI-PLCs) are involved in malignant features of a wide variety of tissues, including breast. In particular, the expression of the beta2 isozyme in primary breast tumors positively correlates with the de-differentiation levels of malignant cells, with biological and clinical-pathological factors currently used to characterize invasive breast carcinomas and with a poor prognosis of breast tumor patients.

Based on the above reported considerations, we tried to elucidate whether PI-PLC beta2 expression could be involved in the switchover of breast tumors from *in situ* to invasive. With this intent, we have performed a retrospective analysis of PI-PLC beta2 expression in sample tissues from breast lesions, including *in situ* and invasive carcinomas, correlating the levels of PI-PLC beta2 with the most common histological and biological prognostic and predictive parameters for breast tumors.

The obtained data indicate that the expression of PI-PLC beta2 characterizes the transition of the mammary tissue from normal to tumoral but not the evolution of breast cancer from *in situ* to invasive. In addition, PI-PLC beta2 amount in invasive breast tumors positively correlates with their malignant properties. Finally, in ductal carcinoma *in situ*, the *in situ* breast cancer more frequently detected and that more often progresses to invasive, we have demonstrated the existence of sub-populations of cells expressing different PI-PLC beta2 amounts, possibly with a diverse functional meaning.

If it is true that most breast cancers evolve from precursors which gradually change over time, the identification of biological alterations associated with early lesions, before the development of invasion/metastasis-related features, may pave the way for designing strategies for the treatment of the majority of breast cancers and could provide important contributions in predicting the clinical course of individual patients.

Acknowledgments. This research was supported by grants from MIUR Cofin and local funds from University of Ferrara (Italy).

### Key words

PI-PLC beta2, breast cancer, tumor progression