lysis of normal human breast tissue and of human ER+ breast cancers indicates a typical apical staining in normal cells, opposed to a diffused overexpression of moesin in most invasive cancer cells.

Conclusions. – These results indicate that estrogen directs the interaction with the extracellular environment and the movement of ER+ breast cancer cells through the regulation of the assembly of the actin cytoskeleton, inducing the activation of moesin through a nongenomic activation of Ga13 at the cell membrane and the subsequent recruitment of RhoA and ROCK-2. These findings increase our understanding of breast cancer cell biology and may have direct clinical relevance for the development of new therapeutic strategies for the prevention or control of breast cancer in different clinical settings.

First line salvage hormone-immunotherapy in endocrine-dependent metastatic breast cancer

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We started an exploratory clinical trial based on the association of immunostimulating cytokines schedule (cyclic administration of beta-interferon and interleukin-2) with antiestrogens for first line salvage therapy of 32 hormone dependent breast cancer with distant metastases [1–2]. CRP, circulating immunocompetent cells and cytokines before and after interleukin-2 administration during clinical benefit and at the progression of metastatic disease was evaluated. Estimated and true 5–10 years overall survivals from first line antiestrogen and from distant metastases also were considered. The interleukin-2 administration was followed by a significant increase in total lymphocytes, CD4+, CD8+, CD16+56+ (NK) cells, IL-6, IL-12, CRP (from P < 0.04 to 0.000) and no change in IL-10 and TGFβ1 during clinical benefit, while no change of the former parameters concomitant with a significant increase in IL-10 (P = 0.020) and a significant decrease in TGFβ1 (P = 0.023) occurred during progressive disease. Estimated 5–10 years overall survivals were 68% ± 11%, 15% ± 10% and 80% ± 8%, 16% ± 10%, respectively. As to true 5-year overall survivals, up to date 13 (65%) of 20 and 16 (73%) of 22 patients with a potential follow-up > 60 months survived > 60 months from first line antiestrogen and from distant metastases, respectively. These findings confirm that cellular immunity is significantly stimulated by IL-2 only during clinical benefit. Furthermore they show that changes in the level of the proinflammatory cytokines, CRP and inhibiting factors are consistent with the concomitant clinical benefit and stimulated cellular immunity or the disease progression and the probable cellular immune inhibition.

References


Thyroid and endocrine tumors

1

The use of Laser Capture Microdissection in the identification of new putative oncosuppressor genes in thyroid cancer

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each thyroid lesion is composed of many different cell types, reflecting the marked heterogeneity of the normal thyroid tissue. To evaluate the mechanisms responsible for the development and progression of thyroid tumors, a detailed analysis of each single lesion, and of the specific cell population involved is needed. To identify new putative oncosuppressor gene involved in the early step of thyroid tumourigenesis, we recently analyzed the loss of heterozygozity (LOH) pattern at 7q21, a region specifically involved in malignant thyroid tumors, especially of the follicular type. This analysis was conducted in a large number of thyroid neoplastic and non-neoplastic lesions, directly at the single cell level recruited by LCM. This approach enabled us to study the LOH pattern directly on pure populations of follicular cells, subdivided according to their nuclear and cytoplasmic features. We find a strict correlation between cytological appearance and allelic loss at 7q21. In fact, allelic loss occurred exclusively in dark nucleus and eosinophilic cytoplasm (DN-EC) cells commonly observed in benign and malignant follicular thyroid lesions.