Circulating tumor cells: Tools for monitoring and targets for therapy.

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Abstract: Background: Analysis of peripheral blood may help to early monitor the process of dissemination of metastatic cells into vital organs . The true number of circulating epithelial tumor cells (CETC) being still controversial, we, omitting all possibly selective enrichment procedures, detect a considerable number of such cells in breast cancer patients. CETC have been shown to respond to therapy in exactly the same way as the primary tumor and we have now probed CETC for monitoring effectiveness of adjuvant therapy. Methods: CETC were monitored in 97 patients before and after each cycle during adjuvant therapy using fluorchrome labeled antibody against epithelial antigen and laser scanning fluorimetry. Results: CETC could be detected in all patients after surgery. Four different forms of therapy response were observed: Patients with 1) CETC from ER+PR+ tumors responding only marginally with appreciable numbers remaining after therapy. These patients (about 40% of patients) have remained in CR; 2) rapidly decreasing CETC,sometimes to below the threshold of detection. These patients, too, remained in CR; 3) constantly or intermittently increasing resistant cells. All these patients have experienced early relapse 5-24 months after diagnosis); 4) Most interestingly, some cells initially respond very well to therapy but show a renewed increase during continuing therapy. These patients, too, have relapsed. Conclusion: Prognostic factors deduced from the primary tumor cannot predict outcome for the individual patient, whereas our approach monitoring CETC allows real-time survey of therapy response in individual

patients. We confirm the observation of low responsiveness of ER+ tumors also in disseminated cells, with dormant CETC in most cases, not eliminated by current therapies but also not leading to early relapse. In contrast, most patients with CETC increasing during therapy suffer early relapse. This indicates not only that these cells are an important indicator of imminent relapse but also distant metastases may be the result of growth or regrowth of these cells. In some patients treatment influences subpopulations differently with a resistant population emerging responsible for relapse.