Role of Tumor suppressor gene (Ecadherin) in malignant cells

Progressive accumulation of somatic mutations in a number of different genes characterizes the process of tumorigenesis. Many genes involved in the process of tumorigenesis are components of one of a great many signal transduction pathways through which signals traffic via molecular networks. It is now apparent that epithelial malignancy can in certain aspects be explained by alterations in the adhesive properties of neoplastic cells. Epithelial-mesenchymal conversion is also observed in malignant tumors of epithelial origin. This process is similar to developmental events but with the important difference that it is uncontrolled. Malignant carcinoma cells are characterized in general by poor intercellular adhesion, loss of the differentiated epithelial morphology and increased cellular motility. Downregulation or a complete shutdown of E-cadherin expression, mutation of the E-cadherin gene, or other mechanisms that interfere with the integrity of the adherens junctions, are observed in carcinoma cells. In human tumors, the loss of E-cadherin-mediated cell adhesion correlates with the loss of the epithelial morphology and with the acquisition of metastatic potential by the carcinoma cells [12]. Thus, a tumor invasion/suppressor role has been assigned to this gene. Additional data also support this role. Loss of heterozygosity on 16q is detected frequently in metastasizing malignancies derived from the liver, prostate, and breast [31]. Mutations in CDH1 have been described in a number of human cancers including breast, stomach, endometrium, ovary and thyroid [32,33]. Transgenic mouse model with loss of Ecadherin expression developed invasive carcinoma from well-differentiated adenomas [34] and finally germ-line mutations have recently been reported in early onset, diffuse-type stomach cancers.
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