Aberrant Wnt Signaling and E-Cadherin Expression in APC-Mutant DU4475 Human Breast Cancer Cells

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APC (adenomatous polyposis coli) mutation is known to be an initiating event in the development of colorectal cancer, and its mutation and silencing have been associated with other tumor types, including breast cancer. One major role of APC as a tumor suppressor is to facilitate the degradation of ß-catenin and prevent the activation of Wnt-target genes. Therefore, APC inactivation leads to the accumulation of ß-catenin and misregulated transcription of several genes implicated in tumorigenesis. Although the role of the Wnt pathway in mammary tumorigenesis in rodent models has been established, the contribution of aberrant activation of this pathway to human breast cancer has not been defined. Here, we describe the characterization of DU4475 human breast cancer cells that carry an APC mutation. Immunofluroscence demonstrated that unlike normal mammary epithelial cells, APC and ß-catenin were located diffusely throughout the cell. E-cadherin localization was also unusual; it was found in prominent aggregates in the cytosol toward the surface of the cell but not apparently associated with the membrane. TCF reporter gene assays demonstrated that these cells possess modest Wnt/TCF activity as compared to SW480 colorectal cancer cells that also carry an APC mutation. To investigate the consequence of APC re-introduction into DU4475 cells, they were transiently transfected with an APC-green fluorescent protein (GFP) expression vector. Unfortunately, DU4475 cells are completely resistant to re-introduction of APC using conventional means. Together, these data suggest that inappropriate activation of the Wnt pathway through APC mutation may be important in the development of breast tumors, and that DU4475 cells may serve as a useful model to dissect the mechanism by which APC may regulate mammary epithelial cell homeostasis.