

## **CEACAM1, a cell adhesion molecule expressed in activated T-cells and many epithelial cells, directly associates with $\beta$ -catenin**

Jin L. and Shively JE. Division of Immunology, Graduate School of Biological Sciences, Beckman Research Institute of the City of Hope, Duarte, California 91010

The wnt/  $\beta$ -catenin pathway determines the fate of proliferating colonic epithelial cells where its disruption by either mutations in APC or E-cadherin lead to pre-malignant adenomas. Recent observations that gene silencing of CEACAM1 is more common and occurs earlier in colon cancer progression than disruptions in APC establish a potential link between two important opposing pathways, namely proliferation by wnt/  $\beta$ -catenin and apoptosis by the cell adhesion protein CEACAM1. The observation that the long cytoplasmic domain of CEACAM-1 is highly homologous to a portion of the amino acid sequence of TCF4 that is known to bind  $\beta$ -catenin suggests the attractive hypothesis that there are interactions between CEACAM-1 and  $\beta$ -catenin. Indeed, a yeast two hybrid analysis demonstrates that binding between CEACAM-1 and  $\beta$ -catenin is as strong as that of TCF4. In addition, scanning Ala mutagenesis identified residues H470 and K471 in CEACAM-1 as critical residues in its binding to  $\beta$ -catenin. Since both TCF4 and  $\beta$ -catenin are expressed in T-cells, and CEACAM1 is known to play an inhibitory role in their function, we examined their interactions in activated PBMCs and in CEACAM1 transfected Jurkat cells. CEACAM-1 and  $\beta$ -catenin were co-localized in membrane speckles in both types of cells when analyzed by confocal microscopy. In summary, our results demonstrate an interaction between CEACAM1 and  $\beta$ -catenin that may play an important role in the control of cell proliferation. A better understanding of this novel pathway could provide new insights into both the development of colon cancer and the control of T-cell proliferation.