SA— 4

Cadherin Switching in Human Prostate Cancer Progression

University of Nijmegen Medical School
Jack A. Schalken

The progression of carcinomas is associated with loss of epithelial morphology and a concomitant acquisition of a more mesenchymal phenotype which in turn is thought to contribute to the invasive and/or metastatic behavior of the malignant process. Changes in the expression of cadherins, 'cadherin switching', plays a critical role during embryogenesis particularly in morphogenetic processes. Loss of E-cadherin is reported to be associated with a poor prognosis, however so far only in cell lines evidence for upregulation of other cadherins was found, i.e. we have found evidence for cadherin switching in prostate cancer cell lines (upregulation of N-cadherin and cadherin-11, two mesenchymal cadherins, in cell lines that lack a functional E-cadherin-catenin adhesion complex).

Here, we report on the immunohistochemical analysis of the expression of N-cadherin and cadherin-11 in human prostate cancer specimens. N-cadherin was not expressed in normal prostate tissue, however, in prostatic cancer N-cadherin was found to be expressed in the poorly differentiated areas, which mainly show aberrant or negative E-cadherin-staining. Cadherin-11 is expressed in the stroma of all prostatic tumors, in the area where stromal and epithelial cells are juxtaposed. In addition, cadherin-11 is also expressed in a dotted pattern or at the membrane of the epithelial cells of high-grade cancers. In a number of metastatic lesions N-cadherin and cadherin-11 are expressed homogeneously. We conclude that cadherin switching plays an important role in prostate cancer metastasis.