Introduction and Aim of Work

Introduction:

Cancer can be considered as a genetic disease. The unstable genome of cancer cells causes tumour progression through multiple alterations in suppressor and promoter genes, leading to loss of homeostatic and gain of oncogenic functions. Invasion is the critical step in the acquisition of malignancy. It implicates a continuous molecular conversation of the cancer cells with other cells and with the extracellular matrix in which adhesion molecules are crucial. One of these, is E-cadherin-catenin complex ***(Debruyne, et al., 1999)***.

Cadherin comprises a family of calcium-dependent glycoprotein that function in mediating cell-cell adhesion in virtually all solid tissue of multicellular organisms. The interacellular anchorage of cadherins is regulated by the dynamic associations with cytoplasmic protein, termed catenins ***(Aberle et al., 1996)***.

Cadherin cell adhesion molecules play an essential role in creating tight intercellular association and are considered to work as invasion suppressor system of cancer cells. They form a molecular complex with catenins, a group of cytoplasmic proteins including alpha, beta and gamma catenins ***(Oyama et al., 1994)***.

The catenins are polypeptides that bind to the conserved cytoplasmic tail of cadherin and are required for cadherin function. The catenins may be involved in the regulation of cadherin function during tissue morphogenesis and tumourogenesis ***(Gumbiner and McCrea, 1993)***.

E-cadherin and its associated cytoplasmic proteins alpha, beta and gamma-catenins, play a crucial role in epithelial cell-cell adhesions and

in maintenance of tissue architecture. Perturbation in expression or function of any of these molecules results in loss of intercellular adhesion, with possible consequent cell transformation and tumor progression ***(El-Bahrawy and Pignatelli, 1998)***.

Histologically carcinomas of the bladder are subdivided into transitional cell carcinomas (90%), squamous cell carcinomas (5%), mixed (5%) and adenocarcinomas (rare) ***(Robbins, 1979)***.

Transitional cell carcinomas range from in situ to invasive lesions, from flat to papillary macroscopically and from well-diffrentiated (Grade I) to highly anaplastic, aggressive cancers (Grade III) ***(Robbins, 1979)***.

Recent studies have shown that loss or reduction of either E-cadherin or catenin expression was strictly related to clinicopathological data in bladder tumors and E-cadherin might constitute prognostic factors in bladder carcinogenesis. Also alpha catenin is directly involved in tumour invasion and dedifferentiation ***(Mialhe et al., 1997)***.

There is compeling evidence from experiments in vitro as well as in vivo to accept that the E-cadherein/catenin complex acts as an invasion suppressor. The mechanism of this is not only through cell-cell adhesion but also through transduction of signals to the cell's motility system. Upregulation of the E-cadherin/catenin complex has been realized with a series of agents, some of which can be used therapeutically ***(Joo, et al., 2000)***.

Aim of work:

This work aims at detection of the importance of E-cadherin-catenin in cases of cancer bladder as regards the invasiveness of the tumor.