

Titre : Rôle de la Protéine C, un anticoagulant naturel, dans l'association thrombose et cancer

Title: Role of Protein C, a natural anticoagulant, in thrombosis and cancer association

Name : Samaher BESBES

E-mail : samaher_besbes@yahoo.com
samaher.besbes@inserm.fr

Home Institute Address :

Faculté de Pharmacie. Rue Ibn Sina, 5000, Monastir, Tunisie.

Host Institute Address :

Université Paris Sud XI- Faculté de Médecine. 63 Rue Gabriel Péri,
94270 Le Kremlin-Bicêtre

Abstract

It is now recognized that the invasiveness of tumor cells is not only related to the genotype of these cells but also to their interaction with tumor microenvironment (TM). Within the TM, stromal matrix destabilization promotes tumor progression and metastatic dissemination. The extracellular matrix remodeling is often driven by proteolytic enzymes. However, few studies have investigated the effects of an impairment of the matrix formation. Given these facts and circumstances, we were interested in protein C (PC) and its endothelial receptor (EPCR), as well as in their role in tumorigenesis in leukemia and solid cancers.

EPCR is expressed by a wide range of cancer cell lines. It is also detected within the tumor compartment in patients with malignant diseases. EPCR gene is highly conserved but nevertheless contains polymorphisms. One of these SNPs (single nucleotide polymorphism) - 6936A/G – reflects – in the release of a soluble circulating form (EPCRs) resulting from the proteolysis of membrane-associated form. In leukemic patients a high incidence of 6936A/G SNP is observed and associated with thrombosis events.

Moreover, EPCR is detected in the majority of tumor biopsies and is abundantly secreted in ascitic fluid. The PC attachment to EPCR and its activation promotes cell survival and migratory potential of tumor cells. Also, APC is able to modulate, by a paracrine manner, interleukins and cytokines secretion. Thus, ovarian cancer cells stimulation by APC induces the synthesis of a functional ovarian thrombopoietin. As this cytokine has a regulatory effect on platelet production, APC may be once again at the interface between hemostasis disorders and coagulation.

The elucidation of the intricate role of APC and its endothelial receptor could permit not only to identify new therapeutic approaches but also to prevent cancer-associated thrombosis risk and to decrease morbidity in cancer patients.

Key words: Cancer, thrombosis, protein C, activated protein C, endothelial protein C receptor, thrombopoietin.